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UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

NOVO NORDISK INC. and NOVO NORDISK A/S, Plaintiffs, v. RIO BIOPHARMACEUTICALS, INC., Defendant.	C.A. No. _____ **(Filed Electronically)**

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs Novo Nordisk Inc. and Novo Nordisk A/S (collectively, "Novo Nordisk"), by their undersigned attorneys, bring this action against Defendant Rio Biopharmaceuticals, Inc. ("Rio"), and hereby allege as follows:

NATURE OF THE ACTION

1. This is an action for patent infringement under the patent laws of the United States, Title 35 of the United States Code, arising from Rio's submission of an Abbreviated New Drug Application ("ANDA") to the United States Food and Drug Administration ("FDA"), by which Rio seeks approval to market a generic version of Novo Nordisk's pharmaceutical product Saxenda® prior to the expiration of United States Patent Nos. 8,114,833 (the "'833 patent"), 8,684,969 (the "'969 patent"), 8,920,383 (the "'383 patent"), 9,108,002 (the "'002 patent"), 9,132,239 (the "'239 patent"), 9,457,154 (the "'154 patent"), 9,616,180 (the "'180 patent"), 9,687,611 (the "'611 patent"), 9,775,953 (the "'953 patent"), 9,861,757 (the "'757 patent"), 10,220,155 (the "'155 patent"), 10,357,616 (the "'616 patent"), 10,376,652 (the "'652 patent"), 11,097,063 (the "'063 patent"), 11,311,679 (the "'679 patent"), 11,446,443 (the "'443 patent"), and RE46,363 (the "'363 patent"), which cover, *inter alia*, Saxenda® and/or its use.

THE PARTIES

2. Plaintiff Novo Nordisk Inc. ("NNI") is a corporation organized and existing under the laws of the State of Delaware and has its principal place of business at 800 Scudders Mill Road, Plainsboro, New Jersey 08536.

3. Plaintiff Novo Nordisk A/S ("NNAS") is an entity organized and existing under the laws of the Kingdom of Denmark and has its principal place of business at Novo Allé, 2880 Bagsværd, Denmark. NNI is an indirect, wholly owned subsidiary of NNAS.

4. On information and belief, Rio is a corporation organized and existing under the laws of the State of Delaware, having its principal place of business at 116 Village Blvd, Suite 200, Princeton, NJ 08540. On information and belief, Rio is in the business of making and selling

generic pharmaceutical products, for distribution in the State of New Jersey and throughout the United States.

JURISDICTION AND VENUE

5. This action for patent infringement arises under 35 U.S.C. § 1 *et seq*. generally and 35 U.S.C. § 271 specifically.

6. This Court has subject matter jurisdiction over this dispute pursuant to 28 U.S.C. §§ 1331 and 1338(a).

7. Venue is proper in this Judicial District pursuant to 28 U.S.C. §§ 1391 and 1400(b).

8. This Court has personal jurisdiction over Rio because, upon information and belief, it has a physical presence in New Jersey; it conducts business in New Jersey; it derives revenue from conducting business in New Jersey; and it has engaged in systematic and continuous contacts with the State of New Jersey, either directly or through its affiliates and/or agents, including by marketing and/or selling pharmaceutical products in New Jersey, including in this Judicial District.

9. On information and belief, Rio intends to sell, offer to sell, use, and/or engage in the commercial manufacture of a generic version of liraglutide injection solution, 18 mg/3 ml (6 mg/ml) ("Rio's Product"), directly or indirectly, throughout the United States and in this Judicial District. Rio's filing of Rio's ANDA No. 218240 ("Rio's ANDA") confirms this intention and further subjects Rio to the specific personal jurisdiction of this Court.

THE PATENTS-IN-SUIT

10. On February 14, 2012, the United States Patent and Trademark Office issued the '833 patent, entitled "Propylene Glycol-Containing Peptide Formulations Which are Optimal for Production and for Use in Injection Devices," a copy of which is attached to this Complaint as Exhibit A. NNAS is the owner of all right, title, and interest in the '833 patent.

11. On April 1, 2014, the United States Patent and Trademark Office issued the '969 patent, entitled "Injection Device with Torsion Spring and Rotatable Display," a copy of which is attached to this Complaint as Exhibit B. NNAS is the owner of all right, title, and interest in the '969 patent.

12. On December 30, 2014, the United States Patent and Trademark Office issued the '383 patent, entitled "Dose Mechanism for an Injection Device for Limiting a Dose Setting Corresponding to the Amount of Medicament Left," a copy of which is attached to this Complaint as Exhibit C. NNAS is the owner of all right, title, and interest in the '383 patent.

13. On August 18, 2015, the United States Patent and Trademark Office issued the '002 patent, entitled "Automatic Injection Device with a Top Release Mechanism," a copy of which is attached to this Complaint as Exhibit D. NNAS is the owner of all right, title, and interest in the '002 patent.

14. On September 15, 2015, the United States Patent and Trademark Office issued the '239 patent, entitled "Dial-Down Mechanism for Wind-Up Pen," a copy of which is attached to this Complaint as Exhibit E. NNAS is the owner of all right, title, and interest in the '239 patent.

15. On October 4, 2016, the United States Patent and Trademark Office issued the '154 patent, entitled "Injection Device with an End of Dose Feedback Mechanism," a copy of which is attached to this Complaint as Exhibit F. NNAS is the owner of all right, title, and interest in the '154 patent.

16. On April 11, 2017, the United States Patent and Trademark Office issued the '180 patent, entitled "Automatic Injection Device with a Top Release Mechanism," a copy of which is attached to this Complaint as Exhibit G. NNAS is the owner of all right, title, and interest in the '180 patent.

17. On June 27, 2017, the United States Patent and Trademark Office issued the '611 patent, entitled "Injection Device with Torsion Spring and Rotatable Display," a copy of which is attached to this Complaint as Exhibit H. NNAS is the owner of all right, title, and interest in the '611 patent.

18. On October 3, 2017, the United States Patent and Trademark Office issued the '953 patent, entitled "Dose Mechanism for an Injection Device for Limiting a Dose Setting Corresponding to the Amount of Medicament Left," a copy of which is attached to this Complaint as Exhibit I. NNAS is the owner of all right, title, and interest in the '953 patent.

19. On January 9, 2018, the United States Patent and Trademark Office issued the '757 patent, entitled "Injection Device with an End of Dose Feedback Mechanism," a copy of which is attached to this Complaint as Exhibit J. NNAS is the owner of all right, title, and interest in the '757 patent.

20. On March 5, 2019, the United States Patent and Trademark Office issued the '155 patent, entitled "Syringe Device with a Dose Limiting Mechanism and an Additional Safety Mechanism," a copy of which is attached to this Complaint as Exhibit K. NNAS is the owner of all right, title, and interest in the '155 patent.

21. On July 23, 2019, the United States Patent and Trademark Office issued the '616 patent, entitled "Injection Device with an End of Dose Feedback Mechanism," a copy of which is attached to this Complaint as Exhibit L. NNAS is the owner of all right, title, and interest in the '616 patent.

22. On August 13, 2019, the United States Patent and Trademark Office issued the '652 patent, entitled "Automatic Injection Device with a Top Release Mechanism," a copy of which is

attached to this Complaint as Exhibit M. NNAS is owner of all right, title, and interest in the '652 patent.

23. On August 24, 2021, the United States Patent and Trademark Office issued the '063 patent, entitled "Syringe Device with a Dose Limiting Mechanism and an Additional Safety Mechanism," a copy of which is attached to this Complaint as Exhibit N. NNAS is the owner of all right, title, and interest in the '063 patent.

24. On April 26, 2022, the United States Patent and Trademark Office issued the '679 patent, entitled "Automatic Injection Device with a Top Release Mechanism," a copy of which is attached to this Complaint as Exhibit O. NNAS is the owner of all right, title, and interest in the '679 patent.

25. On September 20, 2022, the United States Patent and Trademark Office issued the '443 patent, entitled "Injection Device with Torsion Spring and Rotatable Display," a copy of which is attached to this First Amended Complaint as Exhibit P. NNAS is the owner of all right, title, and interest in the '443 patent.

26. On April 11, 2017, the United States Patent and Trademark Office issued the '363 patent, entitled "Dial-Down Mechanism for Wind-Up Pen," a copy of which is attached to this Complaint as Exhibit Q. NNAS is the owner of all right, title, and interest in the '363 patent.

SAXENDA®

27. NNI holds approved New Drug Application No. 206321 (the "Saxenda® NDA") for Saxenda® (liraglutide recombinant) Solution Injection, 18 mg/3 ml (6 mg/ml), which NNI sells under the trade name Saxenda®.

28. The claims of the '833 patent, the '969 patent, the '383 patent, the '002 patent, the '239 patent, the '154 patent, the '180 patent, the '611 patent, the '953 patent, the '757 patent, the

'155 patent, the '616 patent, the '652 patent, the '063 patent, the '679 patent, the '443 patent, and the '363 patent cover, *inter alia*, Saxenda® and/or its use.

29. Pursuant to 21 U.S.C. § 355(b)(1), and attendant FDA regulations, the '833 patent, '969 patent, '383 patent, '002 patent, '239 patent, '154 patent, '180 patent, '611 patent, '953 patent, '757 patent, '155 patent, '616 patent, '652 patent, '063 patent, '679 patent, '443 patent, and '363 patent are listed in the FDA publication, "Approved Drug Products with Therapeutic Equivalence Evaluations" (the "Orange Book"), with respect to Saxenda®.

RIO'S ANDA

30. On information and belief, Rio submitted Rio's ANDA to the FDA, pursuant to 21 U.S.C. § 355(j), seeking approval to market Rio's Product, which is a generic version of liraglutide injection solution, 18 mg/3 ml (6 mg/ml).

31. On information and belief, Rio's ANDA refers to and relies upon the Saxenda® NDA and contains data that, according to Rio, demonstrate the bioequivalence of Rio's Product and Saxenda®.

32. By letter to NNI and NNAS, dated December 22, 2023 (the "Notice Letter"), Rio stated that Rio's ANDA contained a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) that the '833 patent, '969 patent, '383 patent, '002 patent, '239 patent, '154 patent, '180 patent, '611 patent, '953 patent, '757 patent, '155 patent, '616 patent, '652 patent, '063 patent, '679 patent, '443 patent, and '363 patent are invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, or sale of Rio's Product (the "Paragraph IV Certification"). Rio attached a memorandum to the Notice Letter in which it purported to allege factual and legal bases for its Paragraph IV Certification. NNI and NNAS file this suit within 45 days of receipt of the Notice Letter.

COUNT I: INFRINGEMENT OF U.S. PATENT NO. 8,114,833

33. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–32 of this Complaint.

34. Rio has infringed the '833 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '833 patent.

35. Claims 1–15 of the '833 patent are directed to GLP-1 formulations. Claims 16–31 are directed to methods for preparing such formulations or methods of reducing deposits or reducing clogging by replacing the isotonicity agent in a formulation with propylene glycol. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '833 patent would infringe claims 1–31 of the '833 patent.

36. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '833 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '833 patent expires.

37. Novo Nordisk has no adequate remedy at law.

38. Rio was aware of the '833 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT II: INFRINGEMENT OF U.S. PATENT NO. 8,684,969

39. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–38 of this Complaint.

40. Rio has infringed the '969 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '969 patent.

41. Claims 1–26 of the '969 patent are directed to an injection device comprising a torsion spring operatively connected to a dose setting member and a rotatably mounted display member. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '969 patent would infringe claims 1–26 of the '969 patent.

42. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '969 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '969 patent expires.

43. Novo Nordisk has no adequate remedy at law.

44. Rio was aware of the '969 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT III: INFRINGEMENT OF U.S. PATENT NO. 8,920,383

45. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–44 of this Complaint.

46. Rio has infringed the '383 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '383 patent.

47. Claims 1–12 of the '383 patent are directed to a mechanism for preventing setting of a dose which exceeds the amount of a medicament left in a reservoir in an injection device.

Claim 13 of the ’383 patent is directed to a syringe device employing such a mechanism. Rio’s manufacture, use, offer for sale, or sale of Rio’s Product within the United States, or importation of Rio’s Product into the United States, during the term of the ’383 patent would infringe claims 1–13 of the ’383 patent.

48. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the ’383 patent and/or if the FDA is not enjoined from approving Rio’s ANDA before the ’383 patent expires.

49. Novo Nordisk has no adequate remedy at law.

50. Rio was aware of the ’383 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys’ fees under 35 U.S.C. § 285.

COUNT IV: INFRINGEMENT OF U.S. PATENT NO. 9,108,002

51. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–50 of this Complaint.

52. Rio has infringed the ’002 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio’s ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio’s Product prior to the expiration of the ’002 patent.

53. Claims 1–2 of the ’002 patent are directed to an injection device with a release member opposite the end of the device where a needle may be mounted. Rio’s manufacture, use, offer for sale, or sale of Rio’s Product within the United States, or importation of Rio’s Product into the United States, during the term of the ’002 patent would infringe claims 1–2 of the ’002 patent.

54. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '002 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '002 patent expires.

55. Novo Nordisk has no adequate remedy at law.

56. Rio was aware of the '002 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT V: INFRINGEMENT OF U.S. PATENT NO. 9,132,239

57. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–56 of this Complaint.

58. Rio has infringed the '239 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '239 patent.

59. Claims 1–3 of the '239 patent are directed to a dial-down mechanism for an injection device. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '239 patent would infringe claims 1–3 of the '239 patent.

60. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '239 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '239 patent expires.

61. Novo Nordisk has no adequate remedy at law.

62. Rio was aware of the '239 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT VI: INFRINGEMENT OF U.S. PATENT NO. 9,457,154

63. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–62 of this Complaint.

64. Rio has infringed the '154 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '154 patent.

65. Claims 1–17 of the '154 patent are directed to an injection device comprising a dose delivering mechanism which provides an audible feedback signal to a user at the end of injection of a set dose. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '154 patent would infringe claims 1–17 of the '154 patent.

66. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '154 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '154 patent expires.

67. Novo Nordisk has no adequate remedy at law.

68. Rio was aware of the '154 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT VII: INFRINGEMENT OF U.S. PATENT NO. 9,616,180

69. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–68 of this Complaint.

70. Rio has infringed the '180 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '180 patent.

71. Claims 1–14 of the '180 patent are directed to an injection device with a push button like release member opposite the end of the device where a needle may be mounted. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '180 patent would infringe claims 1–14 of the '180 patent.

72. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '180 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '180 patent expires.

73. Novo Nordisk has no adequate remedy at law.

74. Rio was aware of the '180 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT VIII: INFRINGEMENT OF U.S. PATENT NO. 9,687,611

75. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–74 of this Complaint.

76. Rio has infringed the '611 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '611 patent.

77. Claims 1–13 and 15 of the '611 patent are directed to an injection device with a torsion spring operatively connected to a dose setting member and a rotatably mounted display member. Claim 14 of the '611 patent is directed to an injection pen comprising a torsion spring and a dose indicator barrel having a helical scale. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '611 patent would infringe claims 1–15 of the '611 patent.

78. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '611 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '611 patent expires.

79. Novo Nordisk has no adequate remedy at law.

80. Rio was aware of the '611 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT IX: INFRINGEMENT OF U.S. PATENT NO. 9,775,953

81. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–80 of this Complaint.

82. Rio has infringed the '953 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '953 patent.

83. Claims 1–10 and 12–25 of the '953 patent are directed to a mechanism for preventing setting of a dose which exceeds the amount of a medicament left in a reservoir in an injection device. Claim 11 of the '953 patent is directed to a syringe device employing such a mechanism. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '953 patent would infringe claims 1–25 of the '953 patent.

84. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '953 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '953 patent expires.

85. Novo Nordisk has no adequate remedy at law.

86. Rio was aware of the '953 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT X: INFRINGEMENT OF U.S. PATENT NO. 9,861,757

87. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–86 of this Complaint.

88. Rio has infringed the '757 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '757 patent.

89. Claims 1–12 of the '757 patent are directed to an injection device comprising a mechanism which provides a tactile feedback signal to a user at the end of injection of a set dose. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or

importation of Rio's Product into the United States, during the term of the '757 patent would infringe claims 1–12 of the '757 patent.

90. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '757 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '757 patent expires.

91. Novo Nordisk has no adequate remedy at law.

92. Rio was aware of the '757 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT XI: INFRINGEMENT OF U.S. PATENT NO. 10,220,155

93. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–92 of this Complaint.

94. Rio has infringed the '155 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '155 patent.

95. Claims 1–8 of the '155 patent are directed to a syringe device with a dose limiting mechanism and a safety mechanism structure which prevents injection of a dose exceeding a set dose. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '155 patent would infringe claims 1–8 of the '155 patent.

96. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '155 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '155 patent expires.

97. Novo Nordisk has no adequate remedy at law.

98. Rio was aware of the '155 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT XII: INFRINGEMENT OF U.S. PATENT NO. 10,357,616

99. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–98 of this Complaint.

100. Rio has infringed the '616 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '616 patent.

101. Claims 1–9 of the '616 patent are directed to an injection device comprising a mechanism which provides an audible feedback signal to a user at the end of injection of a set dose. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '616 patent would infringe claims 1–9 of the '616 patent.

102. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '616 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '616 patent expires.

103. Novo Nordisk has no adequate remedy at law.

104. Rio was aware of the '616 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT XIII: INFRINGEMENT OF U.S. PATENT NO. 10,376,652

105. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–104 of this Complaint.

106. Rio has infringed the '652 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '652 patent.

107. Claims 1–15 of the '652 patent are directed to an injection device with a release member opposite the end of the device where a needle may be mounted and a display member. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '652 patent would infringe claims 1–15 of the '652 patent.

108. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '652 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '652 patent expires.

109. Novo Nordisk has no adequate remedy at law.

110. Rio was aware of the '652 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT XIV: INFRINGEMENT OF U.S. PATENT NO. 11,097,063

111. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–110 of this Complaint.

112. Rio has infringed the '063 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '063 patent.

113. Claims 1–7 of the '063 patent are directed to a syringe device with a dose limiting mechanism and a safety mechanism structure which prevent ejection of a dose exceeding a set dose. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '063 patent would infringe claims 1–7 of the '063 patent.

114. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '063 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '063 patent expires.

115. Novo Nordisk has no adequate remedy at law.

116. Rio was aware of the '063 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT XV: INFRINGEMENT OF U.S. PATENT NO. 11,311,679

117. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–116 of this Complaint.

118. Rio has infringed the '679 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '679 patent.

119. Claims 1–6 of the '679 patent are directed to an injection device with a release member on the end of the device opposite the injection needle. Rio's manufacture, use, offer for

sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '679 patent would infringe claims 1–6 of the '679 patent.

120. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '679 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '679 patent expires.

121. Novo Nordisk has no adequate remedy at law.

122. Rio was aware of the '679 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT XVI: FOR INFRINGEMENT OF U.S. PATENT NO. 11,446,443

123. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1-122 of this Complaint.

124. Rio has infringed the '443 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '443 patent.

125. Claims 1-19 of the '443 patent are directed to an injection device with a torsion spring operatively connected to a dose setting member and a rotatably mounted display member. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '443 patent would infringe claims 1-19 of the '443 patent.

126. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '443 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '443 patent expires.

127. Novo Nordisk has no adequate remedy at law.

128. Rio was aware of the '443 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT XVII: INFRINGEMENT OF U.S. PATENT NO. RE46,363

129. Novo Nordisk re-alleges and incorporates by reference the allegations of Paragraphs 1–128 of this Complaint.

130. Rio has infringed the '363 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting Rio's ANDA, by which Rio seeks approval from the FDA to manufacture, use, offer to sell, and sell Rio's Product prior to the expiration of the '363 patent.

131. Claims 1–8 of the '363 patent are directed to a dial-down mechanism for an injection device. Claims 9 and 10 of the '363 patent are directed to a medication delivery device comprising such a dial-down mechanism. Claim 11 of the '363 patent is directed to a method for using a wind up injection pen. Rio's manufacture, use, offer for sale, or sale of Rio's Product within the United States, or importation of Rio's Product into the United States, during the term of the '363 patent would infringe claims 1–11 of the '363 patent.

132. Novo Nordisk will be harmed substantially and irreparably if Rio is not enjoined from infringing the '363 patent and/or if the FDA is not enjoined from approving Rio's ANDA before the '363 patent expires.

133. Novo Nordisk has no adequate remedy at law.

134. Rio was aware of the '363 patent when it submitted its ANDA. Novo Nordisk is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Novo Nordisk prays for a judgment in its favor and against Rio and respectfully requests the following relief:

A. A Judgment that Rio has infringed the '833 patent;

B. A Judgment that Rio has infringed the '969 patent;

C. A Judgment that Rio has infringed the '383 patent;

D. A Judgment that Rio has infringed the '002 patent;

E. A Judgment that Rio has infringed the '239 patent;

F. A Judgment that Rio has infringed the '154 patent;

G. A Judgment that Rio has infringed the '180 patent;

H. A Judgment that Rio has infringed the '611 patent;

I. A Judgment that Rio has infringed the '953 patent;

J. A Judgment that Rio has infringed the '757 patent;

K. A Judgment that Rio has infringed the '155 patent;

L. A Judgment that Rio has infringed the '616 patent;

M. A Judgment that Rio has infringed the '652 patent;

N. A Judgment that Rio has infringed the '063 patent;

O. A Judgment that Rio has infringed the '679 patent;

P. A Judgment that Rio has infringed the '443 patent;

Q. A Judgment that Rio has infringed the '363 patent;

R. A Judgment ordering that, pursuant to 35 U.S.C. § 271(e)(4)(A), the effective date of any approval of Rio's ANDA, under § 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355(j)), shall not be earlier than the expiration of the '833 patent, '969 patent, '383 patent,

'002 patent, '239 patent, '154 patent, '180 patent, '611 patent, '953 patent, '757 patent, '155 patent, '616 patent, '652 patent, '063 patent, '679 patent, '443 patent, and '363 patent, including any extensions, adjustments, and exclusivities for those patents to which Novo Nordisk is or becomes entitled;

S. A Judgment, pursuant to 35 U.S.C. § 271(e)(4)(B), preliminarily and permanently enjoining Rio, its officers, agents, servants, and employees, and those persons in active concert or participation with any of them, from manufacturing, using, offering to sell, or selling Rio's Product within the United States, or importing Rio's Product into the United States, prior to the expiration of the '833 patent, '969 patent, '383 patent, '002 patent, '239 patent, '154 patent, '180 patent, '611 patent, '953 patent, '757 patent, '155 patent, '616 patent, '652 patent, '063 patent, '679 patent, '443 patent, and '363 patent, including any extensions, adjustments, and exclusivities for those patents to which Novo Nordisk is or becomes entitled;

T. If Rio commercially manufactures, uses, offers to sell, or sells Rio's Product within the United States, or imports Rio's Product into the United States, prior to the expiration of the '833 patent, '969 patent, '383 patent, '002 patent, '239 patent, '154 patent, '180 patent, '611 patent, '953 patent, '757 patent, '155 patent, '616 patent, '652 patent, '063 patent, '679 patent, '443 patent, and '363 patent, including any extensions, adjustments, and exclusivities, for those patents to which Novo Nordisk is or becomes entitled, a Judgment awarding Novo Nordisk monetary relief, including, but not limited to, lost profits, together with interest;

U. Attorneys' fees in this action as an exceptional case pursuant to 35 U.S.C. § 285;

V. Costs and expenses in this action; and

W. Such other relief as the Court deems just and proper.

Dated: February 5, 2024

By: s/ Charles M. Lizza

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CERTIFICATION PURSUANT TO LOCAL CIVIL RULES 11.2 & 40.1

I hereby certify that the matter *Novo Nordisk Inc., et al. v. Rio Biopharmaceuticals, Inc.*, Civil Action No. 24-330 (RMB)(SAK) (D.N.J.) is related to the matter in controversy because it involves the same plaintiffs, the same defendant, one of the same patents, and because Rio is seeking FDA approval to market a generic version of a similar pharmaceutical product. I further certify that *Novo Nordisk Inc., et al. v. Lupin Ltd.*, Civil Action No. 23-4027 (RMB)(SAK) (D.N.J.); *Novo Nordisk Inc., et al. v. Lupin Ltd.*, Civil Action No. 23-4031 (RMB)(SAK) (D.N.J.); *Novo Nordisk Inc., et al. v. ScinoPharm Taiwan Ltd.,* Civil Action No. 23-20935 (RMB)(SAK) (D.N.J.); and *Novo Nordisk Inc. et al. v. Dr. Reddy's Laboratories, Ltd. et al.*, C.A. No. 23-22112 (RMB)(SAK) (D.N.J.) are related to the matter in controversy because they involve the same plaintiffs, some of the same patents, and Rio is seeking FDA approval to market generic versions of the same or similar pharmaceutical products.

I hereby certify that the matter in controversy is also related to the following matters because they involve the same plaintiffs and some of the same patents: *Novo Nordisk Inc., et al. v. Biocon Pharma Ltd., et al.*, C.A. No. 22-937 (CFC) (D. Del.); *Novo Nordisk Inc., et al. v. Orbicular Pharm. Technologies Pvt. Ltd.*, C.A. Nos. 22-856 (CFC) and 23-179 (CFC) (D. Del.); *Novo Nordisk Inc., et al. v. Mylan Pharm., Inc.*, C.A. No. 22-1040 (CFC) (D. Del.); *Novo Nordisk Inc., et al. v. Sun Pharm. Indus. Ltd., et al.*, C.A. No. 22-296 (CFC) (D. Del.); and *Novo Nordisk Inc., et al. v. Dr. Reddy's Lab'ys, Ltd., et al.*, C.A. No. 22-298 (CFC) (D. Del.).

I hereby certify that, to the best of my knowledge, the matter in controversy is not the subject of any other action pending in any court or of any pending arbitration or administrative proceeding.

Dated: February 5, 2024

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EXHIBIT A

US008114833B2

(12) **United States Patent**
Pedersen et al.

(10) **Patent No.: US 8,114,833 B2**
(45) **Date of Patent: *Feb. 14, 2012**

(54) **PROPYLENE GLYCOL-CONTAINING PEPTIDE FORMULATIONS WHICH ARE OPTIMAL FOR PRODUCTION AND FOR USE IN INJECTION DEVICES**

(75) Inventors: **Tina Bjeldskov Pedersen**, Smørum (DK); **Claude Bonde**, Lyngby (DK); **Dorthe Kot Engelund**, Holte (DK)

(73) Assignee: **Novo Nordisk A/S**, Bagsvaerd (DK)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 663 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **11/435,977**

(22) Filed: **May 17, 2006**

(65) **Prior Publication Data**

US 2007/0010424 A1 Jan. 11, 2007

Related U.S. Application Data

(63) Continuation of application No. PCT/DK2004/000792, filed on Nov. 18, 2004.

(60) Provisional application No. 60/524,653, filed on Nov. 24, 2003.

(30) **Foreign Application Priority Data**

Nov. 20, 2003 (DK) 2003 01719

(51) **Int. Cl.**
A61K 38/26 (2006.01)

(52) **U.S. Cl.** **514/2**; 530/308

(58) **Field of Classification Search** ..... None
See application file for complete search history.

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(74) *Attorney, Agent, or Firm* — Michael J. Brignati

(57) **ABSTRACT**

The present invention relates to pharmaceutical formulations comprising a peptide and propylene glycol, to methods of preparing such formulations, and to uses of such formulations in the treatment of diseases and conditions for which use of the peptide contained in such formulations is indicated. The present invention further relates to methods for reducing the clogging of injection devices by a peptide formulation and for reducing deposits on production equipment during production of a peptide formulation.

31 Claims, 7 Drawing Sheets

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FIGURE 1

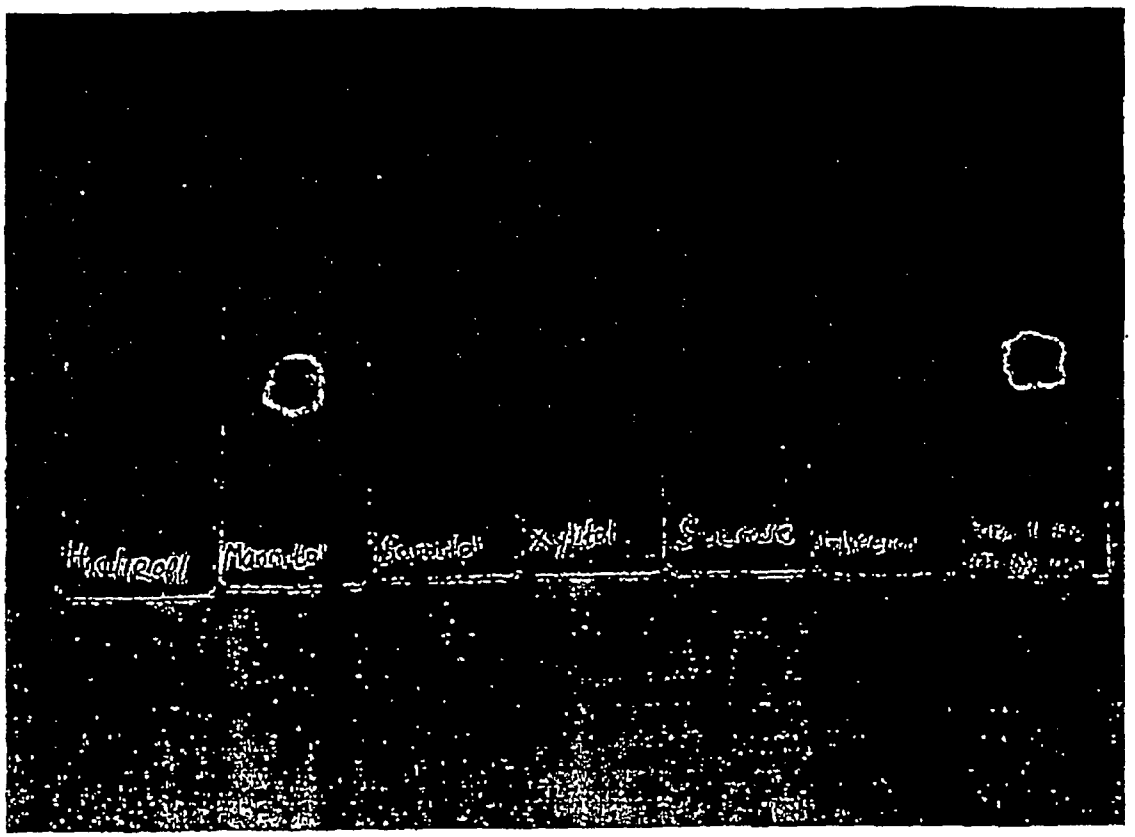
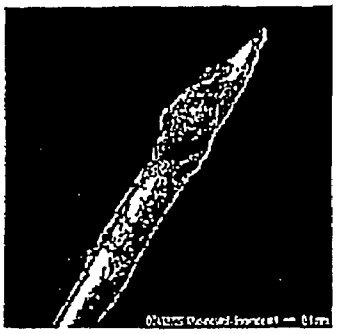


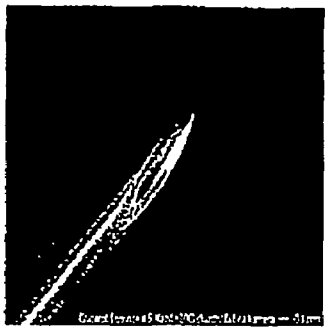
FIGURE 2

FIGURE 3



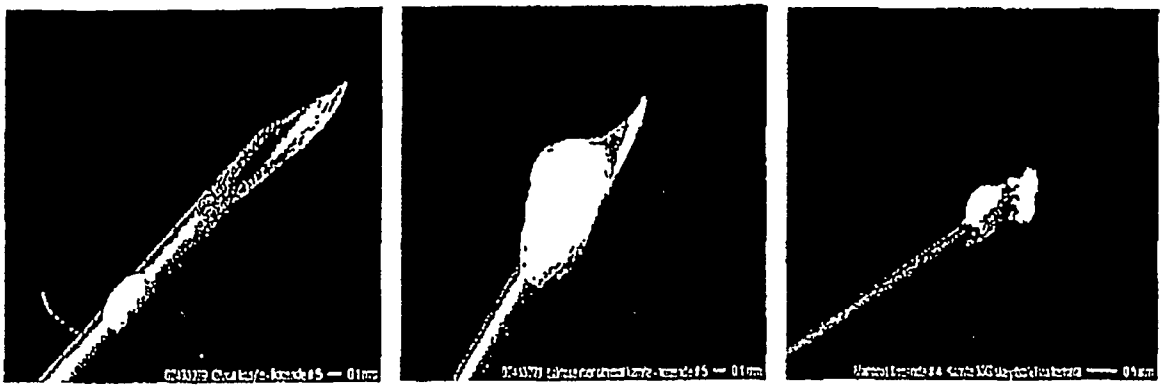
Myo-inositol

Maltose



Glycerol

FIGURE 4



Glycine Lactose Mannitol

FIGURE 5

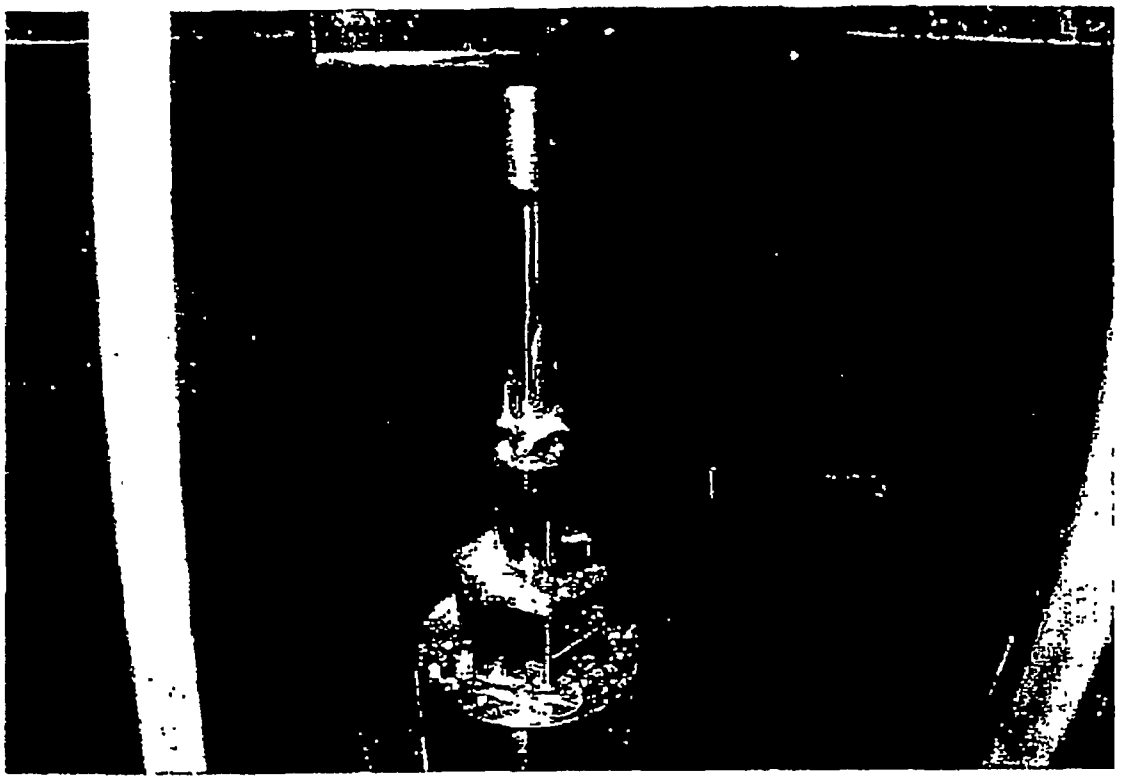


FIGURE 6

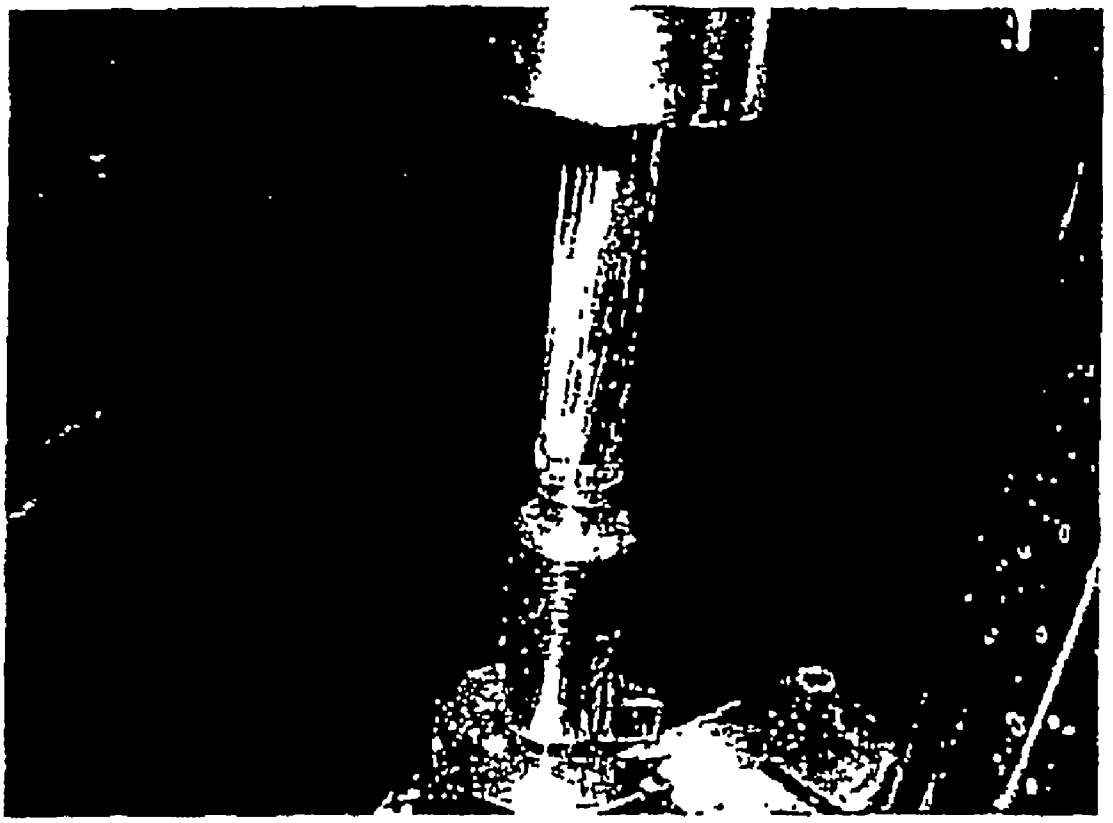
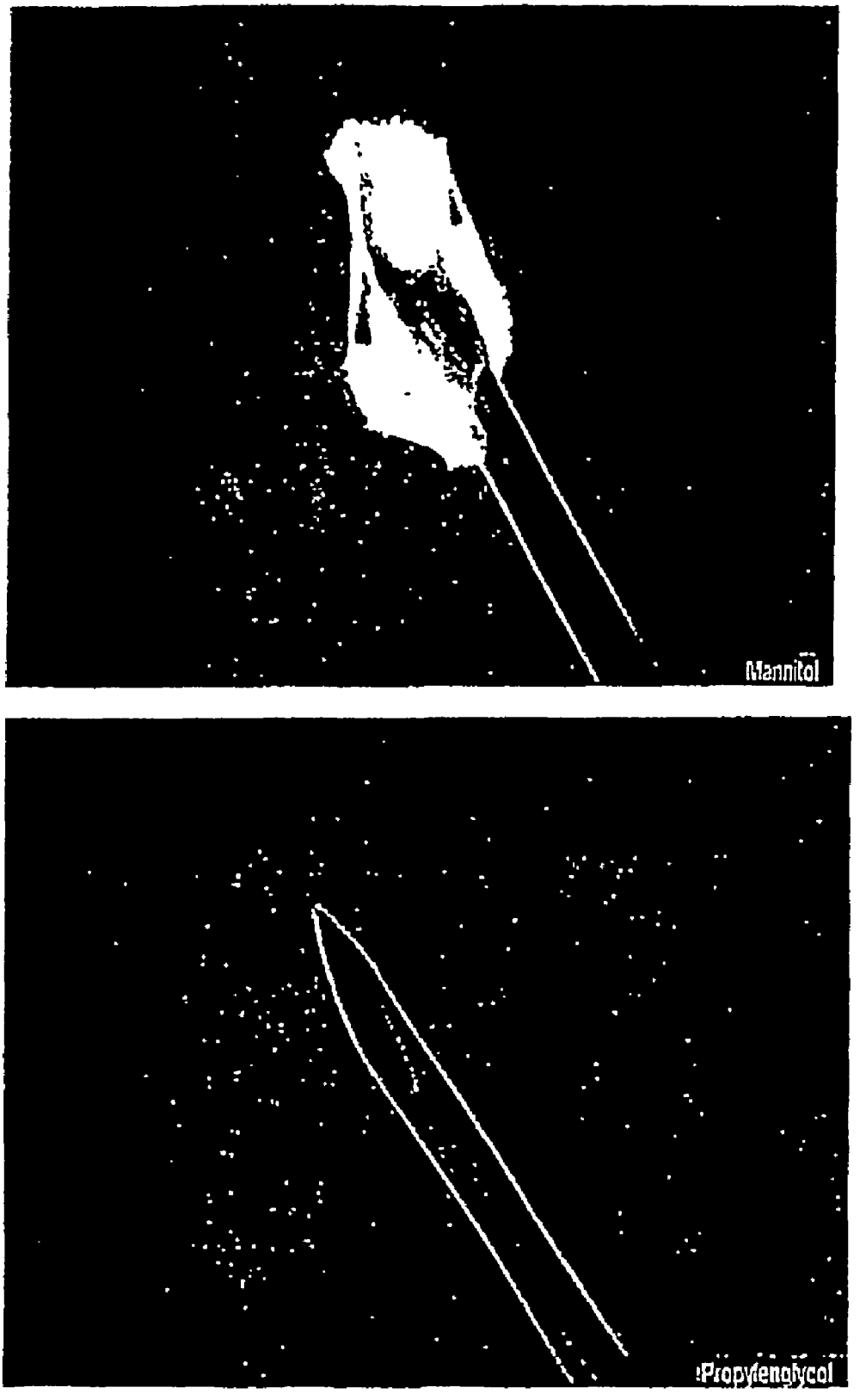


FIGURE 7



PROPYLENE GLYCOL-CONTAINING PEPTIDE FORMULATIONS WHICH ARE OPTIMAL FOR PRODUCTION AND FOR USE IN INJECTION DEVICES

CROSS REFERENCE TO RELATED APPLICATIONS

This Application is a continuation of International Application serial no. PCT/DK2004/000792 filed Nov. 18, 2004 and claims priority from U.S. application Ser. No. 60/524,653 filed Nov. 24, 2003 and from Danish Application serial no. PA 2003 01719 filed Nov. 20, 2003.

FIELD OF THE INVENTION

The present invention relates to pharmaceutical formulations comprising a peptide and propylene glycol, to methods of preparing such formulations, and to uses of such formulations in the treatment of diseases and conditions for which use of the peptide contained in such formulations is indicated. The present invention further relates to methods for reducing the clogging of injection devices by a peptide formulation and for reducing deposits on production equipment during production of a peptide formulation.

BACKGROUND OF THE INVENTION

The inclusion of isotonicity agents in peptide-containing pharmaceutical formulations is widely known and one of the more common isotonic agents used in such formulations is mannitol. However, the present inventors have observed that mannitol causes problems during the production of peptide formulations as it crystallizes resulting in deposits in the production equipment and in the final product. Such deposits increase the need to clean the filling equipment during production of the formulation and this results in reduced production capability. In addition, such deposits may also result in reduced yield of the final product since vials/cartridges containing the peptide formulation may need to be discarded if particles are present. Finally, the present inventors have observed that in peptide formulations to be administered by injection, the presence of mannitol results in clogging of injection devices.

Accordingly, it is desirable to identify an alternative isotonic agent to mannitol for inclusion in peptide-containing formulations and in particular, for inclusion in peptide formulations which are administered by injection.

SUMMARY OF THE INVENTION

The present inventors have discovered that peptide formulations containing propylene glycol at certain concentrations exhibit reduced deposits in production equipment and in the final product and also exhibit reduced clogging of injection devices. The present compositions may be formulated with any peptide and are also physically and chemically stable thus rendering them shelf-stable and suitable for invasive (e.g. injection, subcutaneous injection, intramuscular, intravenous or infusion) as well as non-invasive (e.g. nasal, oral, pulmonary, transdermal or transmucosal e.g. buccal) means of administration.

The present invention therefore relates to a pharmaceutical formulation comprising a peptide and propylene glycol, where the propylene glycol is present in a concentration of 1-100 mg/ml and the pH of the formulation is from 7-10. In a

preferred embodiment, the pharmaceutical formulations of the invention further contain a buffer and a preservative.

The present invention also relates to methods for producing the pharmaceutical formulations of the invention.

In one embodiment, the method for preparing a peptide formulation comprises:

a) preparing a first solution by dissolving preservative, propylene glycol and buffer in water;
b) preparing a second solution by dissolving the peptide in water;
c) mixing the first and second solutions; and
d) adjusting the pH of the mixture in c) to the desired pH.

In another embodiment, the method for preparing a peptide formulation comprises:

a) preparing a first solution by dissolving preservative and buffer in water;
b) adding propylene glycol to the first solution;
c) mixing the first solution with a second solution containing peptide dissolved in water; and
d) adjusting the pH of the mixture in c) to the desired pH.

In yet another embodiment, the method for preparing a peptide formulation comprises:

a) preparing a solution by dissolving preservative, buffer and propylene glycol in water;
b) adding the peptide to the solution of step a); and
c) adjusting the pH of the solution of step b) to the desired pH.

The present invention further relates to methods of treatment using the pharmaceutical formulations of the invention where the compositions are administered in an amount effective to combat the disease, condition, or disorder for which administration of the peptide contained in the formulation is indicated.

In addition the present invention also relates to a method for reducing deposits on production equipment during production of a peptide formulation, where the method comprises replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml.

In one embodiment, the reduction in deposits on the production equipment during production by the propylene glycol-containing formulation relative to that observed for the formulation containing the previously utilized isotonicity agent is measured by a simulated filling experiment.

The present invention also relates to a method for reducing deposits in the final product during production of a peptide formulation, where the method comprises replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml.

In one embodiment, the reduction in deposits in the final product is measured by a reduction in the number of vials and/or cartridges of the propylene glycol-containing formulation that must be discarded due to deposits relative to number of vials and/or cartridges of the formulation containing the previously utilized isotonicity agent that must be discarded due to deposits.

The present invention further relates to a method for reducing the clogging of injection devices by a peptide formulation, where the method comprises replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml.

In one embodiment, the reduction in clogging of the injection device by the propylene glycol-containing formulation relative to that observed for the formulation containing the previously utilized isotonicity agent is measured in a simulated in use study.

BRIEF DESCRIPTION OF THE FIGURES

FIG. **1** shows a photograph of dried droplets on microscope slides of from left to right, placebo (no peptide) formulations containing no isotonic agent (e only water, preservative and buffer), mannitol, sorbitol, xylitol, sucrose or glycerol as the isotonic agent with the far right slide containing mannitol with peptide Arg^{34}, $Lys^{26}(N^{\epsilon}$-(γ-Glu(N^{α}-hexadecanoyl)))-GLP-1(7-37).

FIG. **2** shows light microscopy pictures of from left to right, some of the dried droplets of placebo formulations containing mannitol, arginin, inositol or glycerol as the isotonic agent.

FIG. **3** shows light microscopy pictures of clogged needles dosed with placebo formulations containing myoinositol, maltose or glycerol as the isotonic agent.

FIG. **4** shows light microscopy pictures of deposits on needles dosed with placebo formulations containing glycine, lactose or mannitol as the isotonic agent.

FIG. **5** shows filling equipment after 24 hours simulated filling with Arg^{34}, $Lys^{26}(N^{\epsilon}$-(γ-Glu(N^{α}-hexadecanoyl)))-GLP-1(7-37) medium containing myo-inositol.

FIG. **6** shows deposits on filling equipment after 24 hours simulated filling with a mannitol-containing placebo formulation.

FIG. **7** shows deposits on needles dosed with mannitol (top panel) and propylene glycol (bottom panel)-containing Arg^{34}, $Lys^{26}(N^{\epsilon}$-(γ-Glu(N^{α}-hexadecanoyl)))-GLP-1(7-37) formulations.

DESCRIPTION OF THE INVENTION

The present invention relates to a pharmaceutical formulation comprising a peptide or a mixture of peptides and propylene glycol where the final concentration of propylene glycol in the formulation is 1-100 mg/ml and the pH of the formulation is in the range of from 7-10.

The pharmaceutical formulations of the invention are found to be optimal for production because they exhibit reduced deposits in production equipment relative to formulations containing other isotonicity agents as measured by the simulated filling studies described in the Examples. In addition, the pharmaceutical formulations of the invention are found to be optimal for use in injection devices because they exhibit reduced clogging of the injection devices relative to formulations containing other isotonicity agents as measured by the simulated in use studies described in the Examples.

The formulations of the present invention may be formulated with any peptide where examples of such peptides include, but are not limited to, glucagon, human growth hormone (hGH), insulin, aprotinin, FactorVII, tissue plasminogen activator (TPA), FactorVIIa, FFR-FactorVIIa, heparinase, ACTH, Heparin Binding Protein, corticotropin-releasing factor, angio-tensin, calcitonin, glucagon-like peptide-1, glucagon-like peptide-2, insulin-like growth factor-1, insulin-like growth factor-2, fibroblast growth factors, gastric inhibitory peptide, growth hormone-releasing factor, pituitary adenylate cyclase activating peptide, secretin, enterogastrin, somatostatin, somatomedin, parathyroid hormone, thrombopoietin, erythropoietin, hypothalamic releasing factors, prolactin, thyroid stimulating hormones, endorphins, enkephalins, vasopressin, oxytocin, opiods, DPP IV, interleukins, immunoglobulins, complement inhibitors, serine protease inhibitors, cytokines, cytokine receptors, PDGF, tumor necrosis factors, tumor necrosis factors receptors, growth factors and analogues as well as derivatives thereof where each of these peptides constitutes an alternative embodiment of the present invention.

In the present application, the designation "an analogue" is used to designate a peptide wherein one or more amino acid residues of the parent peptide have been substituted by another amino acid residue and/or wherein one or more amino acid residues of the parent peptide have been deleted and/or wherein one or more amino acid residues have been added to the parent peptide. Such addition can take place either at the N-terminal end or at the C-terminal end of the parent peptide or both. Typically "an analogue" is a peptide wherein 6 or less amino acids have been substituted and/or added and/or deleted from the parent peptide, more preferably a peptide wherein 3 or less amino acids have been substituted and/or added and/or deleted from the parent peptide, and most preferably, a peptide wherein one amino acid has been substituted and/or added and/or deleted from the parent peptide.

In the present application, "a derivative" is used to designate a peptide or analogue thereof which is chemically modified by introducing an organic substituent e.g. ester, alkyl or lipophilic functionalities, on one or more amino acid residues of the peptide or analogue thereof.

In one embodiment, the peptide to be included in the formulation of the invention is a GLP-1 agonist where "a GLP-1 agonist" is understood to refer to any peptide which fully or partially activates the human GLP-1 receptor. In a preferred embodiment, the "GLP-1 agonist" is any peptide that binds to a GLP-1 receptor, preferably with an affinity constant (K_D) or a potency (EC_{50}) of below 1 μM, e.g. below 100 nM as measured by methods known in the art (see e.g. WO 98/08871) and exhibits insulinotropic activity, where insulinotropic activity may be measured in vivo or in vitro assays known to those of ordinary skill in the art. For example, the GLP-1 agonist may be administered to an animal and the insulin concentration measured over time.

Methods for identifying GLP-1 agonists are described in WO 93/19175 (Novo Nordisk A/S) and examples of suitable GLP-1 analogues and derivatives which can be used according to the present invention includes those referred to in WO 99/43705 (Novo Nordisk A/S), WO 99/43706 (Novo Nordisk A/S), WO 99/43707 (Novo Nordisk A/S), WO 98/08871 (analogues with lipophilic substituent) and in WO 02/46227 (analogues fused to serum albumin or to Fc portion of an Ig).(Novo Nordisk A/S), WO 99/43708 (Novo Nordisk A/S), WO 99/43341 (Novo Nordisk A/S), WO 87/06941 (The General Hospital Corporation), WO 90/11296 (The General Hospital Corporation), WO 91/11457 (Buckley et al.), WO 98/43658 (Eli Lilly & Co.), EP 0708179-A2 (Eli Lilly & Co.), EP 0699686-A2 (Eli Lilly & Co.), WO 01/98331 (Eli Lilly & Co).

In one embodiment, the GLP-1 agonist is selected from the group consisting of GLP-1(7-36)-amide, GLP-1(7-37), a GLP-1(7-36)-amide analogue, a GLP-1(7-37) analogue, or a derivative of any of these.

In one embodiment, the GLP-1 agonist is a derivative of GLP-1(7-36)-amide, GLP-1(7-37), a GLP-1(7-36)-amide analogue or a GLP-1(7-37) analogue, which comprises a lipophilic substituent.

In this embodiment of the invention, the GLP-1 derivative preferably has three lipophilic substituents, more preferably two lipophilic substituents, and most preferably one lipophilic substituent attached to the parent peptide (ie GLP-1(7-36)-amide, GLP-1(7-37), a GLP-1(7-36)-amide analogue or a GLP-1(7-37) analogue), where each lipophilic substituent (s) preferably has 4-40 carbon atoms, more preferably 8-30

carbon atoms, even more preferably 8-25 carbon atoms, even more preferably 12-25 carbon atoms, and most preferably 14-18 carbon atoms.

In one embodiment, the lipophilic substituent comprises a partially or completely hydrogenated cyclopentanophenathrene skeleton.

In another embodiment, the lipophilic substituent is a straight-chain or branched alkyl group.

In yet another embodiment, the lipophilic substituent is an acyl group of a straight-chain or branched fatty acid. Preferably, the lipophilic substituent is an acyl group having the formula $CH_3(CH_2)_nCO$—, wherein n is an integer from 4 to 38, preferably an integer from 12 to 38, and most preferably is $CH_3(CH_2)_{12}CO$—, $CH_3(CH_2)_{14}CO$—,$CH_3(CH_2)_{16}CO$—, $CH_3(CH_2)_{18}CO$—, $CH_3(CH_2)_{20}CO$— and $CH_3(CH_2)_{22}CO$—. In a more preferred embodiment, the lipophilic substituent is tetradecanoyl. In a most preferred embodiment, the lipophilic substituent is hexadecanoyl.

In a further embodiment of the present invention, the lipophilic substituent has a group which is negatively charged such as a carboxylic acid group. For example, the lipophilic substituent may be an acyl group of a straight-chain or branched alkane α,ω-dicarboxylic acid of the formula $HOOC(CH_2)_mCO$—, wherein m is an integer from 4 to 38, preferably an integer from 12 to 38, and most preferably is $HOOC(CH_2)_{14}CO$—, $HOOC(CH_2)_{16}CO$—, $HOOC(CH_2)_{18}CO$—, $HOOC(CH_2)_{20}CO$— or $HOOC(CH_2)_{22}CO$—.

In the GLP-1 derivatives of the invention, the lipophilic substituent(s) contain a functional group which can be attached to one of the following functional groups of an amino acid of the parent GLP-1 peptide:

(a) the amino group attached to the alpha-carbon of the N-terminal amino acid,
(b) the carboxy group attached to the alpha-carbon of the C-terminal amino acid,
(c) the epsilon-amino group of any Lys residue,
(d) the carboxy group of the R group of any Asp and Glu residue,
(e) the hydroxy group of the R group of any Tyr, Ser and Thr residue,
(f) the amino group of the R group of any Trp, Asn, Gln, Arg, and His residue, or
(g) the thiol group of the R group of any Cys residue.

In one embodiment, a lipophilic substituent is attached to the carboxy group of the R group of any Asp and Glu residue.

In another embodiment, a lipophilic substituent is attached to the carboxy group attached to the alpha-carbon of the C-terminal amino acid.

In a most preferred embodiment, a lipophilic substituent is attached to the epsilon-amino group of any Lys residue.

In a preferred embodiment of the invention, the lipophilic substituent is attached to the parent GLP-1 peptide by means of a spacer. A spacer must contain at least two functional groups, one to attach to a functional group of the lipophilic substituent and the other to a functional group of the parent GLP-1 peptide.

In one embodiment, the spacer is an amino acid residue except Cys or Met, or a dipeptide such as Gly-Lys. For purposes of the present invention, the phrase "a dipeptide such as Gly-Lys" means any combination of two amino acids except Cys or Met, preferably a dipeptide wherein the C-terminal amino acid residue is Lys, His or Trp, preferably Lys, and the N-terminal amino acid residue is Ala, Arg, Asp, Asn, Gly, Glu, Gln, Ile, Leu, Val, Phe, Pro, Ser, Tyr, Thr, Lys, His and Trp. Preferably, an amino group of the parent peptide forms an amide bond with a carboxylic group of the amino acid residue or dipeptide spacer, and an amino group of the amino acid residue or dipeptide spacer forms an amide bond with a carboxyl group of the lipophilic substituent.

Preferred spacers are lysyl, glutamyl, asparagyl, glycyl, beta-alanyl and gamma-aminobutanoyl, each of which constitutes an individual embodiment. Most preferred spacers are glutamyl and beta-alanyl. When the spacer is Lys, Glu or Asp, the carboxyl group thereof may form an amide bond with an amino group of the amino acid residue, and the amino group thereof may form an amide bond with a carboxyl group of the lipophilic substituent. When Lys is used as the spacer, a further spacer may in some instances be inserted between the ε-amino group of Lys and the lipophilic substituent. In one embodiment, such a further spacer is succinic acid which forms an amide bond with the ε-amino group of Lys and with an amino group present in the lipophilic substituent. In another embodiment such a further spacer is Glu or Asp which forms an amide bond with the ε-amino group of Lys and another amide bond with a carboxyl group present in the lipophilic substituent, that is, the lipophilic substituent is a N^{ε}-acylated lysine residue.

In another embodiment, the spacer is an unbranched alkane α,ω-dicarboxylic acid group having from 1 to 7 methylene groups, which spacer forms a bridge between an amino group of the parent peptide and an amino group of the lipophilic substituent. Preferably, the spacer is succinic acid.

In a further embodiment, the lipophilic substituent with the attached spacer is a group of the formula $CH_3(CH_2)_pNH$—$CO(CH_2)_qCO$—, wherein p is an integer from 8 to 33, preferably from 12 to 28 and q is an integer from 1 to 6, preferably 2.

In a further embodiment, the lipophilic substituent with the attached spacer is a group of the formula $CH_3(CH_2)_rCO$—$NHCH(COOH)(CH_2)_2CO$—, wherein r is an integer from 4 to 24, preferably from 10 to 24.

In a further embodiment, the lipophilic substituent with the attached spacer is a group of the formula $CH_3(CH_2)_sCO$—$NHCH((CH_2)_2COOH)CO$—, wherein s is an integer from 4 to 24, preferably from 10 to 24.

In a further embodiment, the lipophilic substituent is a group of the formula $COOH(CH_2)_tCO$— wherein t is an integer from 6 to 24.

In a further embodiment, the lipophilic substituent with the attached spacer is a group of the formula —$NHCH(COOH)(CH_2)_4NH$—$CO(CH_2)_uCH_3$, wherein u is an integer from 8 to 18.

In a further embodiment, the lipophilic substituent with the attached spacer is a group of the formula $CH_3(CH_2)_vCO$—NH—$(CH_2)_z$—CO, wherein v is an integer from 4 to 24 and z is an integer from 1 to 6.

In a further embodiment, the lipophilic substituent with the attached spacer is a group of the formula —$NHCH(COOH)(CH_2)_4NH$—$COCH((CH_2)_2COOH)NH$—$CO(CH_2)_wCH_3$, wherein w is an integer from 10 to 16.

In a further embodiment, the lipophilic substituent with the attached spacer is a group of the formula —$NHCH(COOH)(CH_2)_4NH$—$CO(CH_2)_2CH(COOH)NHCO(CH_2)_xCH_3$, wherein x is zero or an integer from 1 to 22, preferably 10 to 16.

In yet another embodiment the GLP-1 agonist is Arg^{34}, $Lys^{26}(N^{\varepsilon}$-(γ-Glu(N^{α}-hexade-canoyl))))-GLP-1(7-37).

In yet another embodiment the GLP-1 agonist is selected from the group consisting of Gly^8-GLP-1(7-36)-amide, Gly^8-GLP-1(7-37), Val^8-GLP-1(7-36)-amide, Val^8-GLP-1(7-37), Val^8Asp^{22}-GLP-1(7-36)-amide, Val^8Asp^{22}-GLP-1(7-37), Val^8Glu^{22}-GLP-1(7-36)-amide, Val^8Glu^{22}-GLP-1(7-37), Val^8Lys^{22}-GLP-1(7-36)-amide, Val^8Lys^{22}-GLP-1(7-37), Val^8Arg^{22}-GLP-1(7-36)-amide, Val^8Arg^{22}-GLP-1(7-37),

$Val^{8}His^{22}$-GLP-1(7-36)-amide, $Val^{8}His^{22}$-GLP-1(7-37), analogues thereof and derivatives of any of these.

In yet another embodiment the GLP-1 agonist is selected from the group consisting of Arg^{26}-GLP-1(7-37); Arg^{34}-GLP-1(7-37); Lys^{36}-GLP-1(7-37); $Arg^{26,34}Lys^{36}$-GLP-1(7-37); $Arg^{26,34}$-GLP-1(7-37); $Arg^{26,34}Lys^{40}$-GLP-1(7-37); $Arg^{26}Lys^{36}$-GLP-1(7-37); $Arg^{34}Lys^{36}$-GLP-1(7-37); $Val^{8}Arg^{22}$-GLP-1(7-37); $Met^{8}Arg^{22}$-GLP-1(7-37); $Gly^{8}His^{22}$-GLP-1(7-37); $Val^{8}His^{22}$-GLP-1(7-37); $Met^{8}His^{22}$-GLP-1(7-37); His^{37}-GLP-1(7-37); Gly^{8}-GLP-1(7-37); Val^{8}-GLP-1(7-37); Met^{8}-GLP-1(7-37); $Gly^{8}Asp^{22}$-GLP-1(7-37); $Val^{8}Asp^{22}$-GLP-1(7-37); $Met^{8}Asp^{22}$-GLP-1(7-37); $Gly^{8}Glu^{22}$-GLP-1(7-37); $Val^{8}Glu^{22}$-GLP-1(7-37); $Met^{8}Glu^{22}$-GLP-1(7-37); $Gly^{8}Lys^{22}$-GLP-1(7-37); $Val^{8}Lys^{22}$-GLP-1(7-37); $Met^{8}Lys^{22}$-GLP-1(7-37); $Gly^{8}Arg^{22}$-GLP-1(7-37); $Val^{8}Lys^{22}His^{37}$-GLP-1(7-37); $Gly^{8}Glu^{22}His^{37}$-GLP-1(7-37); $Val^{8}Glu^{22}His^{37}$-GLP-1(7-37); $Met^{8}Glu^{22}His^{37}$-GLP-1(7-37); $Gly^{8}Lys^{22}$ His^{37}-GLP-1(7-37); $Met^{8}Lys^{22}His^{37}$-GLP-1(7-37); $Gly^{8}Arg^{22}His^{37}$-GLP-1(7-37); $Val^{8}Arg^{22}His^{37}$-GLP-1(7-37); $Met^{8}Arg^{22}His^{37}$-GLP-1(7-37); $Gly^{8}His^{22}His^{37}$-GLP-1(7-37); $Val^{8}His^{22}His^{37}$-GLP-1(7-37); $Met^{8}His^{22}His$ ^{37}-GLP-1(7-37); $Gly^{8}His^{37}$-GLP-1(7-37); $Val^{8}His^{37}$-GLP-1(7-37); $Met^{8}His^{37}$-GLP-1(7-37); $Gly^{8}Asp^{22}His^{37}$-GLP-1(7-37); $Val^{8}Asp^{22}His^{37}$-GLP-1(7-37); $Met^{8}Asp^{22}His^{37}$-GLP-1(7-37); Arg^{26}-GLP-1(7-36)-amide; Arg^{34}-GLP-1(7-36)-amide; Lys^{36}-GLP-1(7-36)-amide; $Arg^{26,34}Lys^{36}$-GLP-1(7-36)-amide; $Arg^{26,34}$-GLP-1(7-36)-amide; $Arg^{26,34}Lys^{40}$-GLP-1(7-36)-amide; $Arg^{26}Lys^{36}$-GLP-1(7-36)-amide; $Arg^{34}Lys^{36}$-GLP-1(7-36)-amide; Gly^{8}-GLP-1(7-36)-amide; Val^{8}-GLP-1(7-36)-amide; Met^{8}-GLP-1(7-36)-amide; $Gly^{8}Asp^{22}$-GLP-1(7-36)-amide; $Gly^{8}Glu^{22}His^{37}$-GLP-1(7-36)-amide; $Val^{8}Asp^{22}$-GLP-1(7-36)-amide; $Met^{8}Asp^{22}$-GLP-1(7-36)-amide; $Gly^{8}Glu^{22}$-GLP-1(7-36)-amide; $Val^{8}Glu^{22}$-GLP-1(7-36)-amide; $Met^{8}Glu^{22}$-GLP-1(7-36)-amide; $Gly^{8}Lys^{22}$-GLP-1(7-36)-amide; $Val^{8}Lys^{22}$-GLP-1(7-36)-amide; $Met^{8}Lys^{22}$-GLP-1(7-36)-amide; $Gly^{8}His^{22}His^{37}$-GLP-1(7-36)-amide; $Gly^{8}Arg^{22}$-GLP-1(7-36)-amide; $Val^{8}Arg^{22}$-GLP-1(7-36)-amide; $Met^{8}Arg^{22}$-GLP-1(7-36)-amide; $Gly^{8}His^{22}$-GLP-1(7-36)-amide; $Val^{8}His^{22}$-GLP-1(7-36)-amide; $Met^{8}His^{22}$-GLP-1(7-36)-amide; His^{37}-GLP-1(7-36)-amide; $Val^{8}Arg^{22}His^{37}$-GLP-1(7-36)-amide; $Met^{8}Arg^{37}$-GLP-1(7-36)-amide; $Gly^{8}His^{37}$-GLP-1(7-36)-amide; $Val^{8}His^{37}$-GLP-1(7-36)-amide; $Met^{8}His^{37}$-GLP-1(7-36)-amide; $Gly^{8}Asp^{22}$ His^{37}-GLP-1(7-36)-amide; $Val^{8}Asp^{22}His^{37}$-GLP-1(7-36)-amide; $Met^{8}Asp^{22}His^{37}$-GLP-1(7-36)-amide; $Val^{8}Glu^{22}His^{37}$-GLP-1(7-36)-amide; $Met^{8}Glu^{22}His^{37}$-GLP-1(7-36)-amide; $Gly^{8}Lys^{22}His^{37}$-GLP-1(7-36)-amide; $Val^{8}Lys^{22}His^{37}$-GLP-1(7-36)-amide; $Met^{8}Lys^{22}His^{37}$-GLP-1(7-36)-amide; $Gly^{8}Arg^{22}His^{37}$-GLP-1(7-36)-amide; $Val^{8}His^{22}His^{37}$-GLP-1(7-36)-amide; $Met^{8}His^{22}His^{37}$-GLP-1(7-36)-amide; and derivatives thereof.

In yet another embodiment the GLP-1 agonist is selected from the group consisting of $Val^{8}Trp^{19}Glu^{22}$-GLP-1(7-37), $Val^{8}Glu^{22}Val^{25}$-GLP-1(7-37), $Val^{8}Tyr^{16}Glu^{22}$-GLP-1(7-37), $Val^{8}Trp^{16}Glu^{22}$-GLP-1(7-37), $Val^{8}Leu^{16}Glu^{22}$-GLP-1(7-37), $Val^{8}Tyr^{18}Glu^{22}$-GLP-1(7-37), $Val^{8}Glu^{22}$ His^{37}-GLP-1(7-37), $Val^{8}Glu^{22}Ile^{33}$-GLP-1(7-37), $Val^{8}Trp^{16}Glu^{22}Val^{25}Ile^{33}$-GLP-1(7-37), $Val^{8}Trp^{16}Glu^{22}Ile^{33}$-GLP-1(7-37), $Val^{8}Glu^{22}Val^{25}Ile^{33}$-GLP-1(7-37), $Val^{8}Trp^{16}Glu^{22}Val^{25}$-GLP-1(7-37), analogues thereof and derivatives of any of these.

In yet another embodiment the GLP-1 agonist is exendin-4 or exendin-3, an exendin-4 or exendin-3 analogue or a derivative of any of these.

Examples of exendins as well as analogues, derivatives, and fragments thereof to be included within the present invention are those disclosed in WO 97/46584, U.S. Pat. No. 5,424,286 and WO 01/04156. U.S. Pat. No. 5,424,286 describes a method for stimulating insulin release with an exendin polypeptide. The exendin polypeptides disclosed include HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGX;
wherein X=P or Y, and HX1X2GTFITSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS;
wherein X1X2=SD (exendin-3) or GE (exendin-4)). WO 97/46584 describes truncated versions of exendin peptide(s). The disclosed peptides increase secretion and biosynthesis of insulin, but reduce those of glucagon. WO 01/04156 describes exendin-4 analogues and derivatives as well as the preparation of these molecules. Exendin-4 analogues stabilized by fusion to serum albumin or Fc portion of an Ig are disclosed in WO 02/46227.

In one embodiment, the exendin-4 analogue is HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSS-GAPPSKKKKKK-amide.

Where the peptide to be included in the formulation of the invention is a GLP-1 agonist, the GLP-1 agonist is present in a concentration from about 0.1 mg/ml to about 100 mg/ml, more preferably in a concentration from about 0.1 mg/ml to about 50 mg/ml, and most preferably in a concentration of from about 0.1 mg/ml to about 10 mg/ml.

In another embodiment, the peptide to be included in the formulation of the invention is insulin, where "insulin" is understood to mean human insulin, [where "human insulin" means insulin having the amino acid sequence shown in DSHW Nicol and L F Smith: *Nature,* (1960) 4736:483-485, which is hereby incorporated by reference], human insulin analogs, human insulin derivatives or mixtures thereof, where examples of insulin analogs and derivatives are those disclosed in EP 0 792 290 (Novo Nordisk A/S), EP 0 214 826 and EP 0 705 275 (Novo Nordisk A/S), U.S. Pat. No. 5,504,188 (Eli Lilly), EP 0 368 187 (Aventis), U.S. Pat. Nos. 5,750,497 and 6,011,007, EP 375437 and EP 383472 and where such insulins may include, but are not limited to, NPH insulin, Lys β29 (Nε-tetradecanoyl) des(B30) human insulin, Lys^{B29}-(N^{ϵ}-(γ-glutamyl-N^{α}-lithocholyl) des(B30) human insulin, N^{LB29}-octanoyl insulin, 30/70 mixtures of prompt insulin zinc (SEMILENTE®) with extended insulin zinc (ULTRALENTE®), sold commercially as LENTE®, insulin glargine (LANTUS®) or extended insulin zinc (ULTRALENTE®), Lys^{B28} Pro^{B29} human insulin (HUMALOG®), Asp^{B28} human insulin, insulin aspart (NOVOLOG®), or a 30/70 mixture of insulin aspart and insulin aspart protamine (NOVOMIX®).

In one embodiment, the insulin is a derivative of human insulin or a human insulin analogue where the derivative contains at least one lysine residue and a lipophilic substituent is attached to the epsilon amino group of the lysine residue.

In one embodiment, the lysine residue to which the lipophilic substituent is attached is present at position B28 of the insulin peptide.

In an alternative embodiment, the lysine residue to which the lipophilic substituent is attached is present at position B29 of the insulin peptide.

In yet another embodiment, lipophilic substituent is an acyl group corresponding to a carboxylic acid having at least 6 carbon atoms.

In another preferred embodiment, the lipophilic substituent is an acyl group, branched or unbranched, which corresponds to a carboxylic acid having a chain of carbon atoms 8 to 24 atoms long.

In another preferred embodiment, the lipophilic substituent is an acyl group corresponding to a fatty acid having at least 6 carbon atoms.

In another preferred embodiment, the lipophilic substituent is an acyl group corresponding to a linear, saturated carboxylic acid having from 6 to 24 carbon atoms.

In another preferred embodiment, the lipophilic substituent is an acyl group corresponding to a linear, saturated carboxylic acid having from 8 to 12 carbon atoms.

In another preferred embodiment, the lipophilic substituent is an acyl group corresponding to a linear, saturated carboxylic acid having from 10 to 16 carbon atoms.

In another preferred embodiment, the lipophilic substituent is an oligo oxyethylene group comprising up to 10, preferably up to 5, oxyethylene units.

In another preferred embodiment, the lipophilic substituent is an oligo oxypropylene group comprising up to 10, preferably up to 5, oxypropylene units.

In one preferred embodiment, the invention relates to a human insulin derivative in which the B30 amino acid residue is deleted or is any amino acid residue which can be coded for by the genetic code except Lys, Arg and Cys; the A21 and the B3 amino acid residues are, independently, any amino acid residues which can be coded for by the genetic code except Lys, Arg and Cys; Phe^{B1} may be deleted; the □-amino group of Lys^{B29} has a lipophilic substituent which comprises at least 6 carbon atoms; and 2-4 Zn^{2+} ions may be bound to each insulin hexamer with the proviso that when B30 is Thr or Ala and A21 and B3 are both Asn, and Phe^{B1} is not deleted, then 2-4 Zn^{2+} ions are bound to each hexamer of the insulin derivative.

In another preferred embodiment, the invention relates to a human insulin derivative in which the B30 amino acid residue is deleted or is any amino acid residue which can be coded for by the genetic code except Lys, Arg and Cys; the A21 and the B3 amino acid residues are, independently, any amino acid residues which can be coded for by the genetic code except Lys, Arg and Cys, with the proviso that if the B30 amino acid residue is Ala or Thr, then at least one of the residues A21 and B3 is different from Asn; Phe^{B1} may be deleted; and the □-amino group of Lys^{B29} has a lipophilic substituent which comprises at least 6 carbon atoms.

In another preferred embodiment, the invention relates to a human insulin derivative in which the B30 amino acid residue is deleted or is any amino acid residue which can be coded for by the genetic code except Lys, Arg and Cys; the A21 and the B3 amino acid residues are, independently, any amino acid residues which can be coded for by the genetic code except Lys, Arg and Cys; Phe^{B1} may be deleted; the □-amino group of Lys^{B29} has a lipophilic substituent which comprises at least 6 carbon atoms; and 2-4 Zn^{2+} ions are bound to each insulin hexamer.

Where the peptide to be included in the formulation of the invention is an insulin, the insulin is present in a concentration from about 0.5 mg/ml to about 20 mg/ml, more preferably in a concentration from about 1 mg/ml to about 15 mg/ml.

In another embodiment, the peptide to be included in the formulations of the invention is hGH or Met-hGH.

Where the peptide to be included in the formulation of the invention is hGH or Met-hGH, the hGH or Met-hGH is present in a concentration from about 0.5 mg/ml to about 50 mg/ml, more preferably in a concentration from about 1 mg/ml to about 10 mg/ml.

In yet another embodiment, the peptide to be included in the formulations of the invention is GLP-2 or an analogue or derivative thereof.

Where the peptide to be included in the formulation of the invention is GLP-2 or an analogue or derivative thereof, the GLP-2 or an analogue or derivative thereof is present in a concentration from about 1 mg/ml to about 100 mg/ml, more preferably in a concentration from about 1 mg/ml to about 10 mg/ml.

In yet a further embodiment, the peptide to be included in the formulations of the invention is Factor VII or Factor VIIa or an analogue or derivative thereof.

Where the peptide to be included in the formulation of the invention is Factor VII or Factor VIIa or an analogue or derivative thereof, the Factor VII or Factor VIIa or an analogue or derivative thereof is present in a concentration from about 0.1 mg/ml to about 10 mg/ml, more preferably in a concentration from about 0.5 mg/ml to about 5 mg/ml.

In one embodiment, the final concentration of propylene glycol in the formulations of the invention is from about 1 to about 50 mg/ml.

In another embodiment, the final concentration of propylene glycol in the formulations of the invention is from about 5 to about 25 mg/ml.

In yet another embodiment, the final concentration of propylene glycol in the formulations of the invention is from about 8 to about 16 mg/ml.

In yet a further embodiment, the final concentration of propylene glycol in the formulations of the invention is from about 13 to about 15 mg/ml.

In still another embodiment, the final concentration of propylene glycol in the formulations of the invention is from about 13.5 to about 14.5 mg/ml.

In another embodiment of the invention, the formulation has a pH in the range from about 7.0 to about 9.5 where the term "about" as used in connection with pH means + or −0.1 pH units from the stated number.

In a further embodiment of the invention, the formulation has a pH in the range from about 7.0 to about 8.0.

In yet a further embodiment of the invention, the formulation has a pH in the range from about 7.2 to about 8.0.

In a further embodiment of the invention, the formulation has a pH in the range from about 7.0 to about 8.3.

In yet a further embodiment of the invention, the formulation has a pH in the range from about 7.3 to about 8.3.

In a preferred embodiment of the invention, the formulations contain, in addition to a peptide and propylene glycol, a buffer and/or a preservative.

Where a buffer is to be included in the formulations of the invention, the buffer is selected from the group consisting of sodium acetate, sodium carbonate, citrate, glycylglycine, histidine, glycine, lysine, arginin, sodium dihydrogen phosphate, disodium hydrogen phosphate, sodium phosphate, and tris(hydroxymethyl)-aminomethan, or mixtures thereof. Each one of these specific buffers constitutes an alternative embodiment of the invention. In a preferred embodiment of the invention the buffer is glycylglycine, sodium dihydrogen phosphate, disodium hydrogen phosphate, sodium phosphate or mixtures thereof.

Where a pharmaceutically acceptable preservative is to be included in the formulations of the invention, the preservative is selected from the group consisting of phenol, m-cresol, methyl p-hydroxybenzoate, propyl p-hydroxybenzoate, 2-phenoxyethanol, butyl p-hydroxybenzoate, 2-phenylethanol, benzyl alcohol, chlorobutanol, and thiomerosal, or mixtures thereof. Each one of these specific preservatives constitutes an alternative embodiment of the invention. In a preferred embodiment of the invention the preservative is phenol or m-cresol.

In a further embodiment of the invention the preservative is present in a concentration from about 0.1 mg/ml to about 50 mg/ml, more preferably in a concentration from about 0.1 mg/ml to about 25 mg/ml, and most preferably in a concentration from about 0.1 mg/ml to about 10 mg/ml

The use of a preservative in pharmaceutical compositions is well-known to the skilled person. For convenience reference is made to Remington: *The Science and Practice of Pharmacy,* 19th edition, 1995.

In a further embodiment of the invention the formulation may further comprise a chelating agent where the chelating agent may be selected from salts of ethlenediaminetetraacetic acid (EDTA), citric acid, and aspartic acid, and mixtures thereof. Each one of these specific chelating agents constitutes an alternative embodiment of the invention.

In a further embodiment of the invention the chelating agent is present in a concentration from 0.1 mg/ml to 5 mg/ml. In a further embodiment of the invention the chelating agent is present in a concentration from 0.1 mg/ml to 2 mg/ml. In a further embodiment of the invention the chelating agent is present in a concentration from 2 mg/ml to 5 mg/ml.

The use of a chelating agent in pharmaceutical compositions is well-known to the skilled person. For convenience reference is made to Remington: *The Science and Practice of Pharmacy,* 19th edition, 1995.

In a further embodiment of the invention the formulation may further comprise a stabilizer selected from the group of high molecular weight polymers or low molecular compounds where such stabilizers include, but are not limited to, polyethylene glycol (e.g. PEG 3350), polyvinylalcohol (PVA), polyvinylpyrrolidone, carboxymethylcellulose, different salts (e.g. sodium chloride), L-glycine, L-histidine, imidazole, arginine, lysine, isoleucine, aspartic acid, tryptophan, threonine and mixtures thereof. Each one of these specific stabilizers constitutes an alternative embodiment of the invention. In a preferred embodiment of the invention the stabilizer is selected from the group consisting of L-histidine, imidazole and arginine.

In a further embodiment of the invention the high molecular weight polymer is present in a concentration from 0.1 mg/ml to 50 mg/ml. In a further embodiment of the invention the high molecular weight polymer is present in a concentration from 0.1 mg/ml to 5 mg/ml. In a further embodiment of the invention the high molecular weight polymer is present in a concentration from 5 mg/ml to 10 mg/ml. In a further embodiment of the invention the high molecular weight polymer is present in a concentration from 0 mg/ml to 20 mg/ml. In a further embodiment of the invention the high molecular weight polymer is present in a concentration from 20 mg/ml to 30 mg/ml. In a further embodiment of the invention the high molecular weight polymer is present in a concentration from 30 mg/ml to 50 mg/ml.

In a further embodiment of the invention the low molecular weight compound is present in a concentration from 0.1 mg/ml to 50 mg/ml. In a further embodiment of the invention the low molecular weight compound is present in a concentration from 0.1 mg/ml to 5 mg/ml. In a further embodiment of the invention the low molecular weight compound is present in a concentration from 5 mg/ml to 10 mg/ml. In a further embodiment of the invention the low molecular weight compound is present in a concentration from 10 mg/ml to 20 mg/ml. In a further embodiment of the invention the low molecular weight compound is present in a concentration from 20 mg/ml to 30 mg/ml. In a further embodiment of the invention the low molecular weight compound is present in a concentration from 30 mg/ml to 50 mg/ml.

The use of a stabilizer in pharmaceutical compositions is well-known to the skilled person. For convenience reference is made to Remington: *The Science and Practice of Pharmacy,* 19th edition, 1995.

In a further embodiment of the invention the formulation of the invention may further comprise a surfactant where a surfactant may be selected from a detergent, ethoxylated castor oil, polyglycolyzed glycerides, acetylated monoglycerides, sorbitan fatty acid esters, poloxamers, such as 188 and 407, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene derivatives such as alkylated and alkoxylated derivatives (tweens, e.g. Tween-20, or Tween-80), monoglycerides or ethoxylated derivatives thereof, diglycerides or polyoxyethylene derivatives thereof, glycerol, cholic acid or derivatives thereof, lecithins, alcohols and phospholipids, glycerophospholipids (lecithins, kephalins, phosphatidyl serine), glycerolglycolipids (galactopyransoide), sphingophospholipids (sphingomyelin), and sphingoglycolipids (ceramides, gangliosides), DSS (docusate sodium, docusate calcium, docusate potassium, SDS (sodium dodecyl sulfate or sodium lauryl sulfate), dipalmitoyl phosphatidic acid, sodium caprylate, bile acids and salts thereof and glycine or taurine conjugates, ursodeoxycholic acid, sodium cholate, sodium deoxycholate, sodium taurocholate, sodium glycocholate, N-Hexadecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate, anionic (alkyl-aryl-sulphonates) monovalent surfactants, palmitoyl lysophosphatidyl-L-serine, lysophospholipids (e.g. 1-acyl-sn-glycero-3-phosphate esters of ethanolamine, choline, serine or threonine), alkyl, alkoxyl (alkyl ester), alkoxy (alkyl ether)-derivatives of lysophosphatidyl and phosphatidylcholines, e.g. lauroyl and myristoyl derivatives of lysophosphatidylcholine, dipalmitoylphosphatidylcholine, and modifications of the polar head group, that is cholines, ethanolamines, phosphatidic acid, serines, threonines, glycerol, inositol, and the postively charged DODAC, DOTMA, DCP, BISHOP, lysophosphatidylserine and lysophosphatidylthreonine, zwitterionic surfactants (e.g. N-alkyl-N,N-dimethylammonio-1-propanesulfonates, 3-cholamido-1-propyldimethylammonio-1-propanesulfonate, dodecylphosphocholine, myristoyl lysophosphatidylcholine, hen egg lysolecithin), cationic surfactants (quarternary ammonium bases) (e.g. cetyl-trimethylammonium bromide, cetylpyridinium chloride), non-ionic surfactants, polyethyleneoxide/polypropyleneoxide block copolymers (Pluronics/Tetronics, Triton X-100, Dodecyl β-D-glucopyranoside) or polymeric surfactants (Tween-40, Tween-80, Brij-35), fusidic acid derivatives—(e.g. sodium tauro-dihydrofusidate etc.), long-chain fatty acids and salts thereof C6-C12 (e.g. oleic acid and caprylic acid), acylcarnitines and derivatives, N^{α}-acylated derivatives of lysine, arginine or histidine, or side-chain acylated derivatives of lysine or arginine, N^{α}-acylated derivatives of dipeptides comprising any combination of lysine, arginine or histidine and a neutral or acidic amino acid, N^{α}-acylated derivative of a tripeptide comprising any combination of a neutral amino acid and two charged amino acids, or the surfactant may be selected from the group of imidazoline derivatives, or mixtures thereof. Each one of these specific surfactants constitutes an alternative embodiment of the invention.

The use of a surfactant in pharmaceutical compositions is well-known to the skilled person. For convenience reference is made to Remington: *The Science and Practice of Pharmacy,* 19th edition, 1995.

The formulations of the invention may be prepared by conventional techniques, e.g. as described in Remington's *Pharmaceutical Sciences,* 1985 or in Remington: *The Science and Practice of Pharmacy,* 19th edition, 1995, where

such conventional techniques of the pharmaceutical industry involve dissolving and mixing the ingredients as appropriate to give the desired end product.

As mentioned above, in a preferred embodiment, the formulations of the invention-contain, in addition to a peptide and propylene glycol, a buffer and/or a preservative.

In one embodiment, the method for preparing such a peptide formulation comprises:

a) preparing a first solution by dissolving preservative, propylene glycol and buffer in water;
b) preparing a second solution by dissolving the peptide in water;
c) mixing the first and second solutions; and
d) adjusting the pH of the mixture in c) to the desired pH.

In another embodiment, the method for preparing such a peptide formulation comprises:

a) preparing a first solution by dissolving preservative and buffer in water;
b) adding propylene glycol to the first solution;
c) mixing the first solution with a second solution containing peptide dissolved in water; and
d) adjusting the pH of the mixture in c) to the desired pH.

In yet another embodiment, the method for preparing a peptide formulation comprises:

a) preparing a solution by dissolving preservative, buffer and propylene glycol in water;
b) adding the peptide to the solution of step a); and
c) adjusting the pH of the solution of step b) to the desired pH.

As the formulations of the invention are optimal for production and for use in injection devices since they exhibit reduced deposits of production equipment and reduced clogging of injection devices, the above methods of production can be used to produce peptide formulations suitable for use in production and/or for use in injection devices.

The formulations of the invention are suitable for administration to a mammal, preferably a human. The route of administration of the formulations of the invention may be any route which effectively transports the peptide contained in the formulation to the appropriate or desired site of action, such as oral, nasal, buccal, pulmonal, transdermal or parenteral.

Due to the ability of propylene glycol to reduce clogging of injection devices when compared to other isotonic agents and to mannitol in particular, in a preferred embodiment, the formulations of the invention are to be administered parenterally to a patient in need thereof. Parenteral administration may be performed by subcutaneous, intramuscular or intravenous injection by means of a syringe, optionally a pen-like syringe. Alternatively, parenteral administration can be performed by means of an infusion pump.

A further option is a composition which may be a powder or a liquid for the administration of the formulation in the form of a nasal or pulmonal spray. As a still further option, the formulation can also be administered transdermally, e.g. from a patch, optionally a iontophoretic patch, or transmucosally, e.g. bucally. The above-mentioned possible ways to administer the formulations of the invention are not to be considered as limiting the scope of the invention.

Of course, it is understood that depending on the peptide or peptides included in the formulations of the invention, the formulations may be used in methods of treatment of diseases or conditions for which use of the peptide is indicated. One skilled in the art would understand that when used in such methods of treatment, the formulations would have to be administered in amount effective to treat the condition or disease for which the peptide was being administered where an "effective amount" or an "amount . . . effective" is understood to mean a dosage which is sufficient in order for the treatment of the patient with the disease or condition to be treated to be effective compared to treatment without the administered dosage. It is to be understood that "an effective amount" is the effective dose to be determined by a qualified practitioner, who may titrate dosages to achieve the desired response. Factors for consideration of dose will include potency, bioavailability, desired pharmacokinetic/pharmacodynamic profiles, the condition or disease to be treated (e.g. diabetes, obesity, weight loss, gastric ulcers), patient-related factors (e.g. weight, health, age, etc.), presence of co-administered medications (e.g. insulin), time of administration, or other factors known to a medical practitioner.

The present invention also relates to a method for reducing deposits on production equipment during production of a peptide formulation, where the method comprises replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml.

In one embodiment, the reduction in deposits on the production equipment during production by the propylene glycol-containing formulation relative to that observed for the formulation containing the previously utilized isotonicity agent is measured by a simulated filling experiment as described in the Examples.

In another embodiment, the isotonicity agent to be replaced by propylene glycol is selected from the group consisting of sorbitol, sucrose, glycine, mannitol, lactose monohydrate, arginin, myo-inositol and dimethylsulfon.

In a further embodiment, the isotonicity agent previously utilized in said formulation is replaced with propylene glycol in a concentration of from about 1 to about 50 mg/ml.

In another embodiment, the isotonicity agent previously utilized in said formulation is replaced with propylene glycol in a concentration of from about 5 to about 25 mg/ml.

In yet another embodiment, the isotonicity agent previously utilized in said formulation is replaced with propylene glycol in a concentration of from about 8 to about 16 mg/ml.

In another embodiment of the invention, the propylene glycol-containing formulation has a pH in the range from about 7.0 to about 9.5.

In a further embodiment of the invention, the propylene glycol-containing formulation has a pH in the range from about 7.0 to about 8.0.

In yet a further embodiment of the invention, the propylene glycol-containing formulation has a pH in the range from 7.2 to about 8.0.

In a further embodiment of the invention, the propylene glycol-containing formulation has a pH in the range from about 7.0 to about 8.3.

In a further embodiment of the invention, the propylene glycol-containing formulation has a pH in the range from 7.3 to about 8.3.

The present invention also relates to a method for reducing deposits in the final product during production of a peptide formulation, where the method comprises replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml.

In one embodiment, the reduction in deposits in the final product is measured by a reduction in the number of vials and/or cartridges of the propylene glycol-containing formulation that must be discarded due to deposits relative to number of vials and/or cartridges of the formulation containing the previously utilized isotonicity agent that must be discarded due to deposits.

In another embodiment, the isotonicity agent to be replaced by propylene glycol is selected from the group consisting of sorbitol, sucrose, glycine, mannitol, lactose monohydrate, arginin, myo-inositol and dimethylsulfon.

In a further embodiment, the isotonicity agent previously utilized in said formulation is replaced with propylene glycol in a concentration of from about 1 to about 50 mg/ml.

In another embodiment, the isotonicity agent previously utilized in said formulation is replaced with propylene glycol in a concentration of from about 5 to about 25 mg/ml.

In yet another embodiment, the isotonicity agent previously utilized in said formulation is replaced with propylene glycol in a concentration of from about 8 to about 16 mg/ml.

In another embodiment of the invention, the propylene glycol-containing formulation has a pH in the range from about 7.0 to about 9.5.

In a further embodiment of the invention, the propylene glycol-containing formulation has a pH in the range from about 7.0 to about 8.0.

In yet a further embodiment of the invention, the propylene glycol-containing formulation has a pH in the range from 7.2 to about 8.0.

In a further embodiment of the invention, the propylene glycol-containing formulation has a pH in the range from about 7.0 to about 8.3.

In a further embodiment of the invention, the propylene glycol-containing formulation has a pH in the range from 7.3 to about 8.3.

The present invention further relates to a method for reducing the clogging of injection devices by a peptide formulation, where the method comprises replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml.

In one embodiment, the reduction in clogging of the injection device by the propylene glycol-containing formulation relative to that observed for the formulation containing the previously utilized isotonicity agent is measured in a simulated in use study as described in the Examples.

In another embodiment, the isotonicity agent to be replaced by propylene glycol is selected from the group consisting of inositol, maltose, glycine, lactose and mannitol.

In a further embodiment, the isotonicity agent previously utilized in said formulation is replaced with propylene glycol in a concentration of from about 1 to about 50 mg/ml.

In another embodiment, the isotonicity agent previously utilized in said formulation is replaced with propylene glycol in a concentration of from about 5 to about 25 mg/ml.

In yet another embodiment, the isotonicity agent previously utilized in said formulation is replaced with propylene glycol in a concentration of from about 8 to about 16 mg/ml.

In another embodiment of the invention, the propylene glycol-containing formulation has a pH in the range from about 7.0 to about 9.5.

In a further embodiment of the invention, the propylene glycol-containing formulation has a pH in the range from about 7.0 to about 8.0.

In yet a further embodiment of the invention, the propylene glycol-containing formulation has a pH in the range from 7.2 to about 8.0.

All scientific publications and patents cited herein are specifically incorporated by reference. The following examples illustrate various aspects of the invention but are in no way intended to limit the scope thereof.

EXAMPLES

Example 1

As laboratory experiments have shown that with regards to clogging of needles and deposits on needles, formulations without peptide ("placebo") give the same conclusions as formulations with peptide at 0.3-5.0 mg/ml, the screening studies in Example 1 have been done using placebo except where indicated otherwise.

Preparation of Formulations with Different Isotonic Agents

Preservative (5.5 mg/ml phenol) and buffer 1.24 mg/ml disodium hydrogen phosphate, dihydrate) were dissolved in water and the isotonic agent was added while stirring. pH was adjusted to pH 7.9 using Sodium Hydroxide and/or Hydrochloric acid. Finally, the formulation was filtered through a 0.22 μm filter. The isotonic agents tested in each formulation and their concentrations are shown in Table 1.

TABLE 1

Composition of the tested formulations

Formulation no.	Tonicity modifier
1	Glucose monohydrate (38.0 mg/ml)
2	Laktose monohydrate (65.0 mg/ml)
3	Maltose (67.2 mg/ml)
4	Glycine (15.1 mg/ml)
5	Polyethylenglycol 400 (77.5 mg/ml)
6	L-arginin (24.6 mg/ml)
7	Myo-Inositol (35.2 mg/ml)
8	Propylene glycol (13.7 mg/ml)
9	Dimethylsulfon (18 mg/ml)
10	Mannitol (35.9 mg/ml)
11	Sorbitol (39.5 mg/ml)
12	Xylitol (39.5 mg/ml)
13	Sucrose (79.1 mg/ml
14	Glycerol (16 mg/ml)

Osmolarity

The osmolarity of the different placebo formulations was determined and the results are shown in Table 2.

An isotonic solution has an osmolarity of around 0.286 osmol/L. As can be seen from Table 2 three of the formulations (PEG 400, sucrose and xylitol) are more than 20% from being isotonic (0.229-0.343 osmol/l), however for these kind of experiments the osmolarity is not expected to influence the results, though, the tonicity of the formulations should be adjusted in future experiments.

TABLE 2

The measured osmolarity of the formulations

Formulation no.	Isotonic agent	Osmolarity
1	Glucose monohydrate (38.0 mg/ml)	0.315
2	Laktose monohydrate (65.0 mg/ml)	0.283
3	Maltose (67.2 mg/ml)	0.306
4	Glycine (15.1 mg/ml)	0.286
5	Polyethylenglykol 400 (77.5 mg/ml)	0.370
6	L-arginin(24.6 mg/ml)	0.318
7	Myo-Inositol (35.2 mg/ml)	0.285
8	Propylene glycol (13.7 mg/ml)	0.268
9	Dimethylsulfon (18 mg/ml)	0.274
10	Mannitol (35.9 mg/ml)	0.284
11	Sorbitol (39.5 mg/ml)	0.310
12	Xylitol (39.5 mg/ml)	0.351
13	Sucrose (79.1 mg/ml	0.346
14	Glycerol (16 mg/ml)	0.262

Drop Test

A droplet of each formulation is placed on a microscope slide and let to dry. The deposit is visually examined by eye and light microscope.

A photograph of the dried droplets of some of the formulations is shown in FIG. **1**. In this figure it is clearly observed that mannitol cause deposits on the microscope slide when let

to dry. No deposits were observed for sorbitol, xylitol, sucrose and glycerol. The droplet on the far right (Form 1) contains mannitol and Arg^{34}, $Lys^{26}(N^{\epsilon}$-(γ-Glu(N^{α}-hexadecanoyl)))-GLP-1(7-37).

In FIG. **2** the candidates causing the most deposits on the microscope slide are shown. For comparison glycerol, which does not cause deposits, is shown (mannitol, arginine, inositol).

Clogging Test

In this test 10 NOVOPENS® 1.5 ml mounted with NOVOFINE 30® G (G 30 needle) were tested for each formulation, 5 of them placed in upright and 5 in horizontal position. The Pensystems were stored at room temperature in between testing. Each day the needle was examined for deposits and an air shot was performed prior to injection into a tissue. Degree of resistance and clogging, if any, was noted. Injections were made on a daily basis with the same needle, and this was done for 9 working days for all the formulations.

The results from the clogging test are shown in Table 3.

TABLE 3

Clogging test in NovoPen 1.5 using 30G NovoFine

Isotonic agent (no. of observations)	Some resistance	Resistance	Much resistance	Clogged	Drop at top of needle	Dried drop at needle top	Gel-like drop on needle	Deposits on needle
Mannitol (90)	10	0	0	0	0	2	0	43
Glycerol (90)	13	0	0	0	1	0	3	0
Sucrose (90)	23	0	0	0	0	0	21	0
Propylene glycol (90)	20	0	0	0	0	0	0	0
PEG 400 (90)	25	1	0	0	12 (5 at needle)	0	0	0
arginin (90)	26	2	0	0	3 (2 at needle)	1	0	0
Xylitol (90)	14	0	0	0	5	0	0	0
Dimethyls ulfon (90)	21	0	0	0	4	0	0	0
sorbitol (90)	12	0	0	0	9	1	0	1
Myo-inositol (90)	20	1	2	6	6	0	0	47
Glucose (90)	32	11	5	0	16 (7 at needle)	1	0	(1 at needle)
glycine (90)	41	9	2	0	1 (2 at needle)	0	0	31 (2 at needle)
maltose (90)	35	8	7	4	16 (6 at needle)	0	0	1 (5 at needle)
laktose (90)	44	10	8	0	5	0	0	31 (2 at needle)

In Table 3 and in FIG. **3** it was observed that inositol and maltose clogged the needle. For comparison glycerol which does not clog the needle is shown in FIG. **3**. In FIG. **4**, and in Table 3, it was observed that formulations containing glycine, lactose and mannitol gave rise to a lot of deposits on the needle. For glycine, the deposits were a droplet deposited down the needle, whereas for lactose and mannitol the deposits occurred at the top of the needle.

Simulated Filling

1 L of each formulation was subjected to a simulated filling experiment which lasted for 24 hours. After 24 hours the filling equipment was inspected for the presence of deposits.

Based on the results from the simulated filling studies (data not shown), the placebo formulations can be divided into three categories. 1. Those isotonic agents that do not cause deposits on the filling equipment: Xylitol, glycerol, glucose monohydrate, maltose, PEG 400 and propylene glycol. 2. Those isotonic agent that cause few deposits and have superior filling properties compared to mannitol: Sorbitol, sucrose and glycine. 3. Those isotonic agent that are comparable or worse than mannitol: Mannitol, lactose monohydrate, arginin, myo-inositol and dimethylsulfon.

Conclusion

In the simulated filling experiment xylitol, glycerol, glucose, maltose, PEG 400, propylene glycol, sorbitol, sucrose and glycine were found to be suitable replacements candidates for mannitol. However, as glucose is a reducing saccharide, and therefore is able to initiate unwanted degradation in the formulation, this tonicity modifier is ruled out. Furthermore, maltose is ruled out due to clogging of needles. This leads to the following candidates: glycerol, xylitol, sorbitol, sucrose, glycine, propylene glycol and PEG 400, which are found to have suitable properties as replacements candidates for mannitol in peptide formulations with regards to drop test, clogging of needles and simulated filling.

However, on the basis of the following considerations, propylene glycol was chosen as the isotonic agent over the other candidates to be further investigated in head to head comparison studies with mannitol:

a. propylene glycol was observed to have no influence on the physical and chemical stability of Arg^{34}, $Lys^{26}(N^{\epsilon}$-(γ-Glu(N^{α}-hexadecanoyl)))-GLP-1(7-37)-containing formulations;
b. propylene glycol was observed to have no influence on antimicrobial preservative testing; and
c. use of propylene glycol would no require that further toxicity studies be tested

Example 2

Comparison of Mannitol and Propylene Glycol-Containing Placebo Formulations in Simulated Filling Studies and Simulated Use Studies

Preparation of Formulations

Preservative and buffer were dissolved in water and the isotonic agent was added while stirring. pH was adjusted to the aimed pH using Sodium Hydroxide and/or Hydrochloric acid. Finally, the formulation was filtered through a 0.22 μm filter. The compositions of the formulations were as follows:

Disodium hydrogen phosphate, dihydrate: 1.42 mg/ml
Phenol: 5.5 mg/ml
Propylene glycol or mannitol: 13.7 or 35.9 mg/ml
Water for Injection: up to 1.0 ml.
pH: 7.90

Simulated Filling Study

A simulated filling study lasting 24 hours was performed as described in Example 1 and after 24 hours, the filling equipment was inspected for the presence of deposits. No deposits were observed on the filling equipment for the propylene glycol formulation. By comparison, after 24 hours, a lot of deposits were observed on the filling equipment for the mannitol formulation (see FIG. **6**).

Simulated in Use Study

For the simulated in use study, a clogging test was conducted as described in Example 1. The same needle was used during the study period of ten working days and each day, the needle was inspected for the presence of deposits. FIG. **7** shows photographs of needles dosed with the propylene glycol (top panel) or mannitol (bottom panel) containing formulations. Deposits on the needle were observed in 48% of the cases when mannitol was used as an isotonic agent whereas no deposits were observed when propylene glycol was used as the isotonic agent.

Example 3

Comparison of Propylene Glycol to Mannitol in Arg^{34}, Lys^{26}(N^{ϵ}-(γ-Glu(N^{α}-hexadecanoyl)))-GLP-1(7-37) Containing Formulations

Preparation of Formulations

Preservative, isotonic agent (mannitol or propylene glycol) and buffer were dissolved in water and pH was adjusted to the desired pH. Arg^{34}, Lys^{26}(N^{ϵ}-(γ-Glu(N^{α}-hexadecanoyl)))-GLP-1(7-37) was dissolved in water while stirring slowly. The two solutions were then mixed and pH adjusted to the desired pH using sodium hydroxide and/or hydrochloric acid. Finally, the formulation was filtered through a 0.22 μm filter. The compositions of the formulations were as follows:

Arg^{34}, Lys^{26}(N^{ϵ}-(γ-Glu(N^{α}-hexadecanoyl)))-GLP-1(7-37) (6.25 mg/ml),
Disodium hydrogen phosphate, dihydrate (1.42 mg/ml),
Phenol (5.5 mg/ml),
mannitol or propylene glycol (35.9 or 14.0 mg/ml),
Water for Injection (up to 1.0 ml),
pH: 8.15

Simulated in Use Study

For the simulated in use study, a clogging test was conducted as described in Example 1 except that a G31 needle was used. The same G31 needle was used during the study period of ten working days and each day, the needle was inspected for the presence of deposits. FIG. **7** shows photographs of needles with no deposits when dosed with the propylene glycol (bottom panel) or showing deposits when dosed with the mannitol (top panel) containing formulations.

For the mannitol containing formulation, clogging of the needle was observed in 1 out of 10 cases on day 4, 2 out of 10 cases on day 5, 3 out of 10 cases on day 8 and 4 out of 10 cases on day 9. By comparison, no clogging of needles was observed for the propylene glycol containing formulation.

It is believed that similar results to those obtained with the above-described propylene glycol-containing formulation would also be obtained if the pH was adjusted to 7.40, 7.70 or 7.90. In addition, additional formulations which could be tested include those having the following compositions:

Buffering agents: glycylglycine (1.32 mg/ml), L-Histidine (1.55 mg/ml), Hepes (2.38 mg/ml), or bicine (1.63 mg/ml)
Preservatives: phenol (5.0 or 5.5 mg/ml), benzylalcohol (18 mg/ml) or a mixture of m-cresol and phenol (2.5/2.0 mg/ml)
Propylene glycol: 14.0 or 14.3 mg.ml
Water for injection: up to 1.0 ml
pH: 7.40, 7.70, 7.90 or 8.15

Example 4

Influence of Peptide Concentration on Clogging of Needles

Arg^{34}, Lys^{26}(N^{ϵ}-(γ-Glu(N^{α}-hexadecanoyl)))-GLP-1(7-37) formulations were prepared as described in Example 3 using peptide concentrations ranging from 0-5 mg/ml of Arg^{34}, Lys^{26}(N^{ϵ}-(γ-Glu(N^{α}-hexadecanoyl)))-GLP-1(7-37). The compositions of the formulations were as follows:

Liraglutide: 0, 0.3, 3 and 5 mg/ml
Disodium hydrogen phosphate, dihydrate: 0.71 mg/ml
Sodium dihydrogenphosphate, dihydrate: 0.62 mg/ml
Mannitol: 36.9 mg/ml
Phenol: 5.0 mg/ml
Water for injection: up to 1.0 ml
pH 7.40

A simulated in use study was conducted as in Example 3 except that a G30 needle was used and the results (data not shown) indicated that the clogging effect of the mannitol-containing formulations relative to the absence of clogging with the propylene glycol formulations was observed independent of the peptide concentration.

Example 5

Clogging of Needles in Lys β29 (Nε-tetradecanoyl) des(B30) Human Insulin and NovoMix 30 Formulations Containing Mannitol

Preparation Of Formulations

The Lys β29 (Nε-tetradecanoyl) des(B30) human insulin-containing formulation was prepared as follows:

a) Prepared a first solution by dissolving buffer, sodium chloride, preservatives (phenol and m-cresol) and mannitol in water
b) Prepared a second solution of Lys β29 (Nε-tetradecanoyl) des(B30) human insulin and zinc acetate dissolved in water
c) added the peptide-containing solution of step b) to the solution of step a); and
d) adjusted the pH of the solution to the desired pH

The composition of Lys β29 (Nε-tetradecanoyl) des(B30) human insulin-containing formulation prepared in the above manner was as follows:

Lys β29 (Nε-tetradecanoyl) des(B30) human insulin (2400 nmol), Phenol (1.80 mg/ml), m-cresol (2.06 mg/ml), Mannitol (30.0 mg/ml), disodiumphosphate, dihydrate (0.890 mg/ml), Sodium chloride (1.17 mg/ml), Zinc acetate (65.4 ug/ml), water for injection (up to 1.0 ml), pH: 7.4

The NOVOMIX® 30-containing formulation was prepared as follows:

a) Prepared a solution by dissolving buffer, sodium chloride, phenol, mannitol and sodium hydroxide in water
b) Prepared a solution of sodium chloride, phenol and mannitol in water
c) Prepared a solution of protamine sulphate in water
d) Prepared a solution of insulin, hydrochloric acid and zinc in water
e) Solutions b), c) and d) were mixed
f) Solution e) was added to the solution of step a)
g) Adjusted the pH of the solution to the desired pH and crystallized at room temperature
h) Prepared a solution by dissolving m-cresol, phenol and mannitol in water
i) Solution h) is added to the crystalline fraction of step g); and
j) Adjusted the pH to the desired pH

The composition of the NOVOMIX® 30-containing formulation prepared in the above manner was as follows:

Insulin aspart (100 units/ml), protamine sulphate (approx. 0.33 mg/ml), phenol (1.50 mg/ml), m-cresol (1.72 mg/ml), mannitol (30.0 mg/ml), disodiumphosphate dihydrate (1.25 mg/ml), sodium chloride (0.58 mg/ml), zinc (19.6 ug/ml), water for injection (up to 1.0 ml), pH: 7.3.

Results

A simulated in use study was conducted as described in Example 3 using G31 needles where 20 needles were investigated for 10 days. The results were as follows: Clogging of needles was observed for Lys β29 (Nε-tetradecanoyl) des (B30) human insulin on day 2 (5%), day 3 (70%) and on day 4 (100%). Clogging of needles for NovoMix 30 was observed on day 3 (5%), day 4 (10%), day 5 (35%), day 6 (40%), day 8 (50%), day 9 (55%) and day 10 (80%). Thus, the effect of mannitol on the clogging of needles is independent of the type of peptide included in the formulations since a comparable clogging effect was observed with Arg^{34}, Lys^{26}(N^{ϵ}-(γ-Glu (N^{α}-hexadecanoyl)))-GLP-1(7-37), Lys β29 (Nε-tetradecanoyl) des(B30) human insulin and NovoMix 30.

Example 6

Testing of Lys β29 (Nε-tetradecanoyl) des(B30) human insulin and NOVOMIX® 30 formulations containing propylene glycol

The preparation and composition of the Lys β29 (Nε-tetradecanoyl) des(B30) human insulin and NOVOMIX® 30 formulations will be as described in Example 5 except that mannitol will be replaced with a concentration of propylene glycol that assures tonicity. A simulated in use test will then be conducted as described in Example 5.

Based on the fact that the clogging effect of Lys β29 (Nε-tetradecanoyl) des(B30) human insulin and NOVOMIX® 30 mannitol-containing formulations was similar to that observed with Arg^{34}, Lys^{26}(N^{ϵ}-(γ-Glu(N^{α}-hexadecanoyl)))-GLP-1(7-37) mannitol-containing formulations, it is believed that the effect of propylene glycol on the clogging effect of Lys β29 (Nε-tetradecanoyl) des(B30) human insulin and NovoMix 30-containing formulations will be similar to that observed with Arg^{34}, Lys^{26}(N^{ϵ}-(γ-Glu(N^{α}-hexadecanoyl)))-GLP-1(7-37)-containing formulations.

SEQUENCE LISTING

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            20                  25                  30

Ser Gly Ala Pro Pro Ser Lys Lys Lys Lys Lys Lys
        35                  40
```

The invention claimed is:

1. A pharmaceutical formulation comprising at least one GLP-1 agonist, a disodium phosphate dihydrate buffer and propylene glycol, wherein said propylene glycol is present in said formulation in a final concentration of from about 1 mg/ml to about 100 mg/ml and wherein said formulation has a pH of from about 7.0 to about 10.0.

2. The formulation according to claim **1**, wherein the concentration of propylene glycol is from about 1 mg/ml to about 50 mg/ml.

3. The formulation according to claim **1**, wherein the concentration of propylene glycol is from about 5 mg/ml to about 25 mg/ml.

4. The formulation according to claim **1**, wherein the concentration of propylene glycol is from about 8 mg/ml to about 16 mg/ml.

5. The formulation according to claim **1**, wherein the pH of said formulation is about 7.0 to about 9.5.

6. The formulation according to claim **1**, wherein the pH of said formulation is about 7.0 to about 8.3.

7. The formulation according to claim 1, wherein the pH of said formulation is about 7.3 to about 8.3.

8. The formulation according to claim 1, further comprising a preservative.

9. The formulation according to claim 8, wherein said preservative is present in a concentration from 0.1 mg/ml to 20 mg/ml.

10. The formulation according to claim 1, wherein said GLP-1 agonist is selected from the group consisting of GLP-1(7-36)-amide, GLP-1(7-37), a GLP-1(7-36)-amide analogue, a GLP-1(7-37) analogue, or a derivative of any of these.

11. The formulation according to claim 10, wherein said GLP-1 agonist is a derivative of GLP-1(7-36) or GLP-1(7-37) or a GLP-1(7-36)-amide analogue or a GLP-1(7-37) analogue, where said derivative has a lysine residue and a lipophilic substituent attached with or without a spacer to the epsilon amino group of said lysine.

12. The formulation according to claim 11, wherein said lipophilic substituent has from 8 to 40 carbon atoms.

13. The formulation according to claim 12, wherein said spacer is an amino acid.

14. The formulation according to claim 13, wherein said GLP-1 agonist is Arg^{34}, Lys^{26}(N-ε-(γ-Glu(N-α-hexadecanoyl)))-GLP-1(7-37).

15. The formulation according to claim 1, wherein said GLP-1 agonist is selected from the group consisting of Gly^{8}-GLP-1(7-36)-amide, Gly^{8}-GLP-1(7-37), Val^{8}-GLP-1(7-36) amide, Val^{8}-GLP-1(7-37), $Val^{8}Asp^{22}$-GLP-1(7-36)-amide, $Val^{8}Asp^{22}$-GLP-1(7-37), $Val^{8}Glu^{22}$-GLP-1(7-36) -amide, $Val^{8}Glu^{22}$-GLP-1(7-37), $Val^{8}Lys^{22}$-GLP-1(7-36)-amide, $Val^{8}Lys^{22}$-GLP-1(7-37), $Val^{8}Arg^{22}$-GLP-1(7-36)-amide, $Val^{8}Arg^{22}$-GLP-1(7-37), $Val^{8}His^{22}$-GLP-1(7-36)-amide, $Val^{8}His^{22}$-GLP-1(7-37), Arg^{34}GLP-1(7-37), $Arg^{26,34}Lys^{36}$GLP-1(7-36), Arg^{26}GLP-1(7-37), and Gly^{8}, $Arg^{26,34}Glu^{37}Lys^{38}$GLP-1(7-38) and derivatives of any of these.

16. A method of preparing a GLP-1 agonist formulation suitable for use in an injection device, said method comprising preparing a formulation containing a GLP-1 agonist, propylene glycol, a disodium phosphate dihydrate buffer, and a preservative, wherein said propylene glycol is present in a concentration from about 1 mg/ml to about 100 mg/ml, and wherein said formulation has a pH from about 7.0 to about 10.0, and wherein said GLP-1 agonist, said propylene glycol and said buffer and preservative are mixed together to produce said formulation as follows:

a) preparing a first solution by dissolving preservative, propylene glycol and buffer in water;

b) preparing a second solution by dissolving the GLP-1 agonist in water;

c) mixing the first and second solutions; and

adjusting the pH of the mixture in c) to a pH of from about 7.0 to about 10.0.

17. The method according to claim 16, wherein the concentration of propylene glycol is from about 1 mg/ml to about 50 mg/ml.

18. The method according to claim 16, wherein the concentration of propylene glycol is from about 5 mg/ml to about 25 mg/ml.

19. The method according to claim 16, wherein the concentration of propylene glycol is from about 8 mg/ml to about 16 mg/ml.

20. The method according to claim 16, wherein the pH of said formulation is about 7.0 to about 9.5.

21. The method according to claim 16, wherein the pH of said formulation is about 7.0 to about 8.0.

22. The method according to claim 16, wherein the pH of said formulation is about 7.2 to about 8.0.

23. A method for reducing deposits on production equipment during production of a GLP-1 agonist formulation, said method comprising replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml, and wherein said GLP-1 agonist formulation comprises a disodium phosphate dihydrate buffer.

24. The method according to claim 23, wherein the reduction in deposits on the production equipment during production by the propylene glycol-containing formulation relative to that observed for the formulation containing the previously utilized isotonicity agent is measured by a simulated filling experiment.

25. The method according to claim 23, wherein the isotonicity agent to be replaced by propylene glycol is selected from the group consisting of sorbitol, sucrose, glycine, mannitol, lactose monohydrate, arginin, myo-inositol and dimethylsulfon.

26. A method for reducing deposits in the final product during production of a GLP-1 agonist formulation, said method comprising replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml, and wherein said GLP-1 agonist formulation comprises a disodium phosphate dihydrate buffer.

27. The method according to claim 26, wherein the reduction in deposits in the final product is measured by a reduction in the number of vials and/or cartridges of the propylene glycol-containing formulation that must be discarded due to deposits relative to number of vials and/or cartridges of the formulation containing the previously utilized isotonicity agent that must be discarded due to deposits.

28. The method according to claim 26, wherein the isotonicity agent to be replaced by propylene glycol is selected from the group consisting of sorbitol, glycerol, sucrose, glycine, mannitol, lactose monohydrate, arginin, myo-inositol and dimethylsulfon.

29. A method for reducing the clogging of injection devices by a GLP-1 agonist formulation, said method comprising replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml, and wherein said GLP-1 agonist formulation comprises a disodium phosphate dihydrate buffer.

30. The method according to claim 29, wherein the reduction in clogging of the injection device by the propylene glycol-containing formulation relative to that observed for the formulation containing the previously utilized isotonicity agent is measured in a simulated in use study.

31. The method according to claim 29, wherein the isotonicity agent to be replaced by propylene glycol is selected from the group consisting of inositol, maltose, glycine, lactose and mannitol.

* * * * *

EXHIBIT B

US008684969B2

(12) **United States Patent**
Moller et al.

(10) **Patent No.: US 8,684,969 B2**
(45) **Date of Patent: *Apr. 1, 2014**

(54) **INJECTION DEVICE WITH TORSION SPRING AND ROTATABLE DISPLAY**

(71) Applicant: **Novo Nordisk A/S**, Bagsvaerd (DK)

(72) Inventors: **Claus Schmidt Moller**, Fredensborg (DK); **Tom Hede Markussen**, Bagsvaerd (DK); **Christian Peter Enggaard**, Vejby (DK)

(73) Assignee: **Novo Nordisk A/S**, Bagsvaerd (DK)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **13/626,541**

(22) Filed: **Sep. 25, 2012**

(65) **Prior Publication Data**

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Related U.S. Application Data

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(60) Provisional application No. 60/626,271, filed on Nov. 9, 2004.

(30) **Foreign Application Priority Data**

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(51) **Int. Cl.**
A61M 5/20 (2006.01)

(52) **U.S. Cl.**
USPC **604/135**; 604/207

(58) **Field of Classification Search**
USPC 604/131, 134, 135, 181, 207–211, 218, 604/224, 189
See application file for complete search history.

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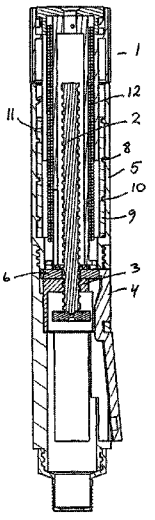
Primary Examiner — Laura Bouchelle
(74) *Attorney, Agent, or Firm* — Marc A. Began

(57) **ABSTRACT**

The present invention relates to an injection device comprising a torsion spring operatively connected to a dose setting member being adapted to set a dose to be ejected from the injection device. A rotatably mounted display member adapted to display the dose to be ejected in accordance with a setting of the dose setting member is also provided. The rotatably mounted display member is adapted to be rotated over an angle corresponding to at least one revolution of the display member. The display member may be implemented as a dose indicator barrel having numerals arranged along a helical path on an outer surface thereof, or alternatively, as a counting device having two or more display wheels having numerals arranged on an outer surface thereof.

26 Claims, 5 Drawing Sheets



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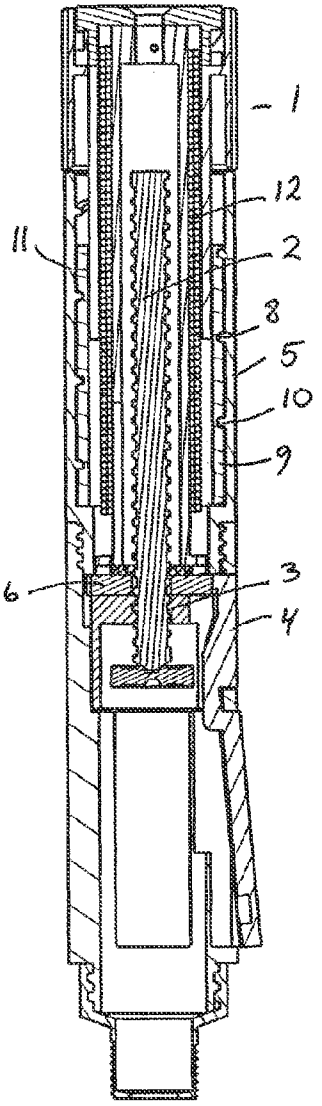

Fig. 1

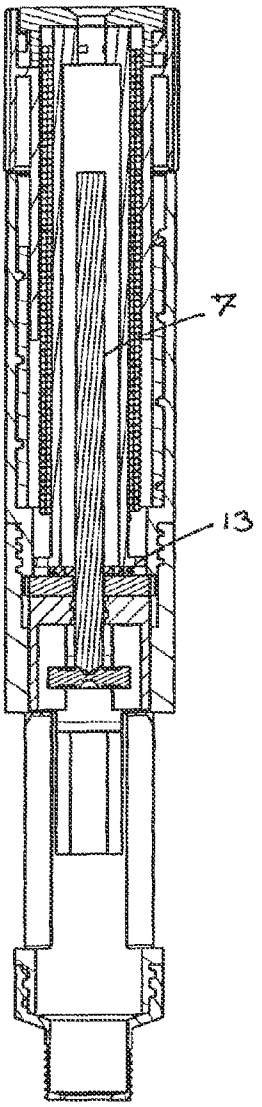

Fig. 2

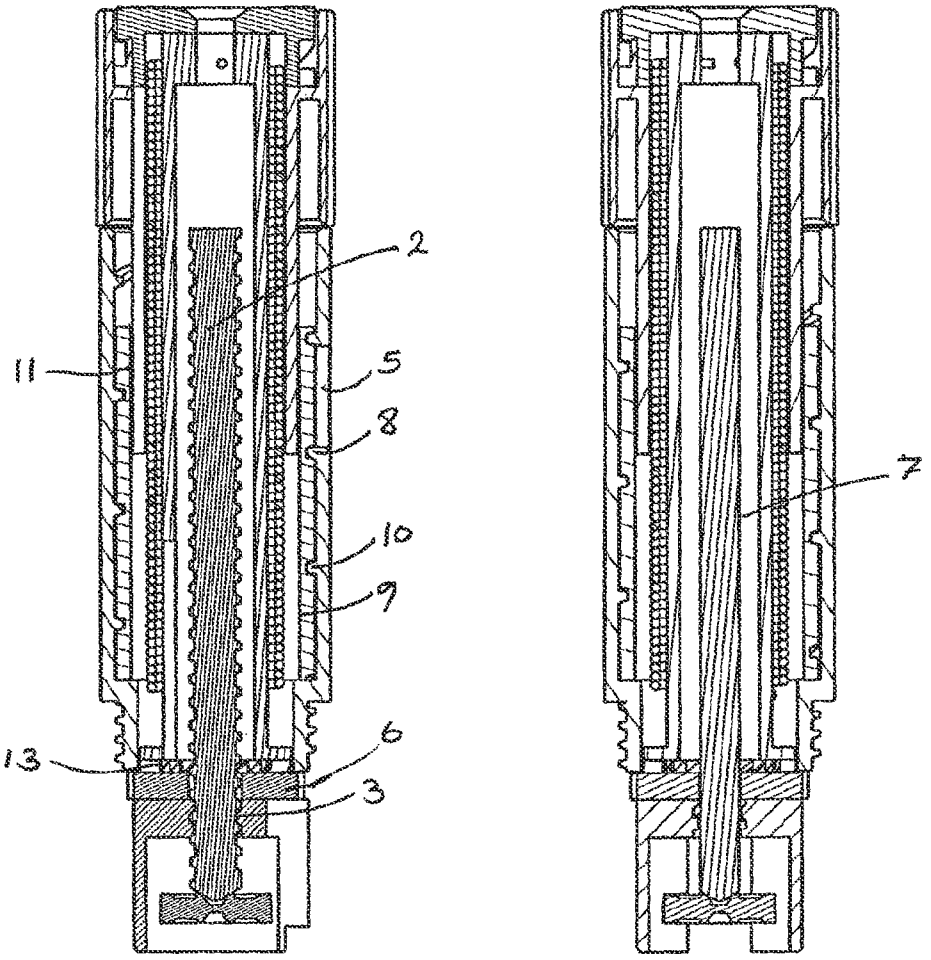

Fig. 3

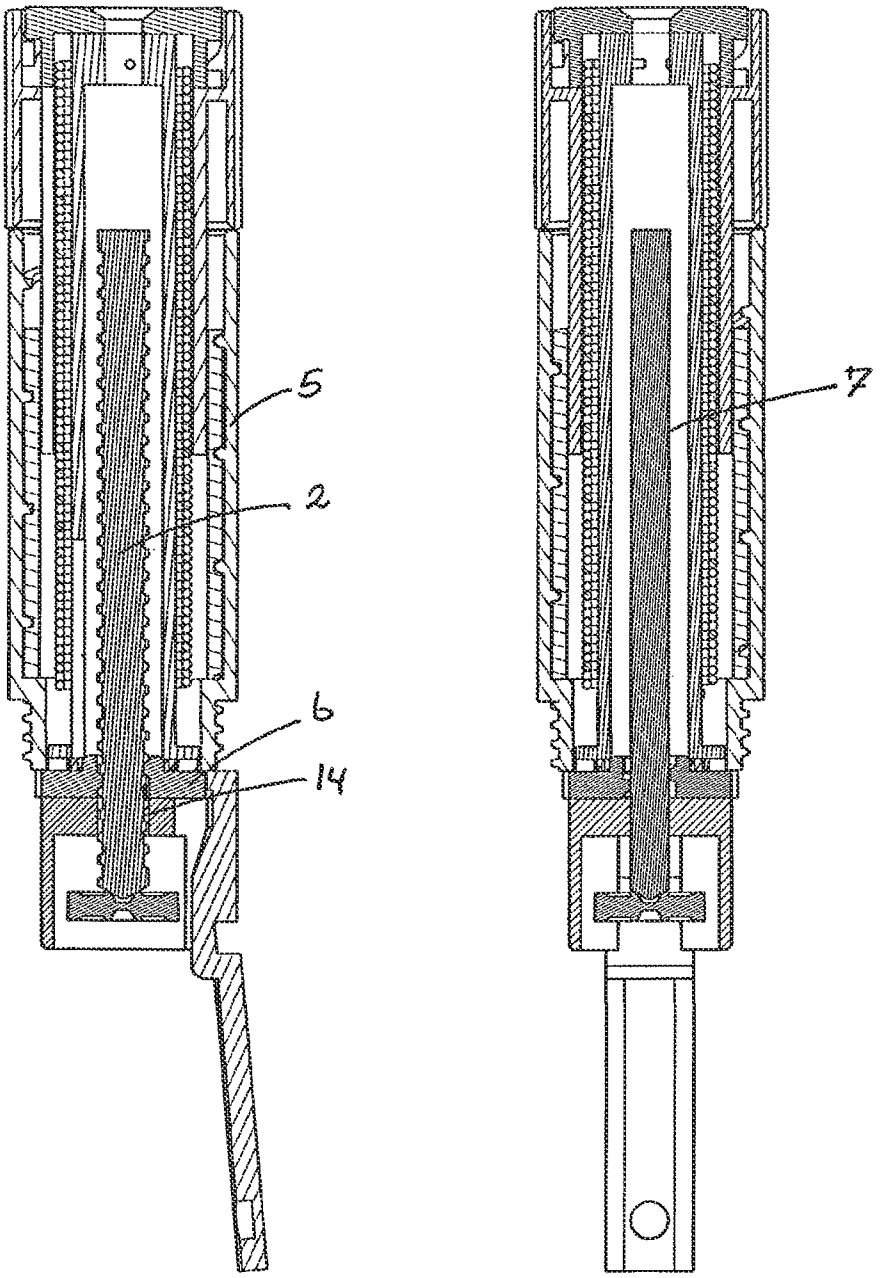

Fig. 4

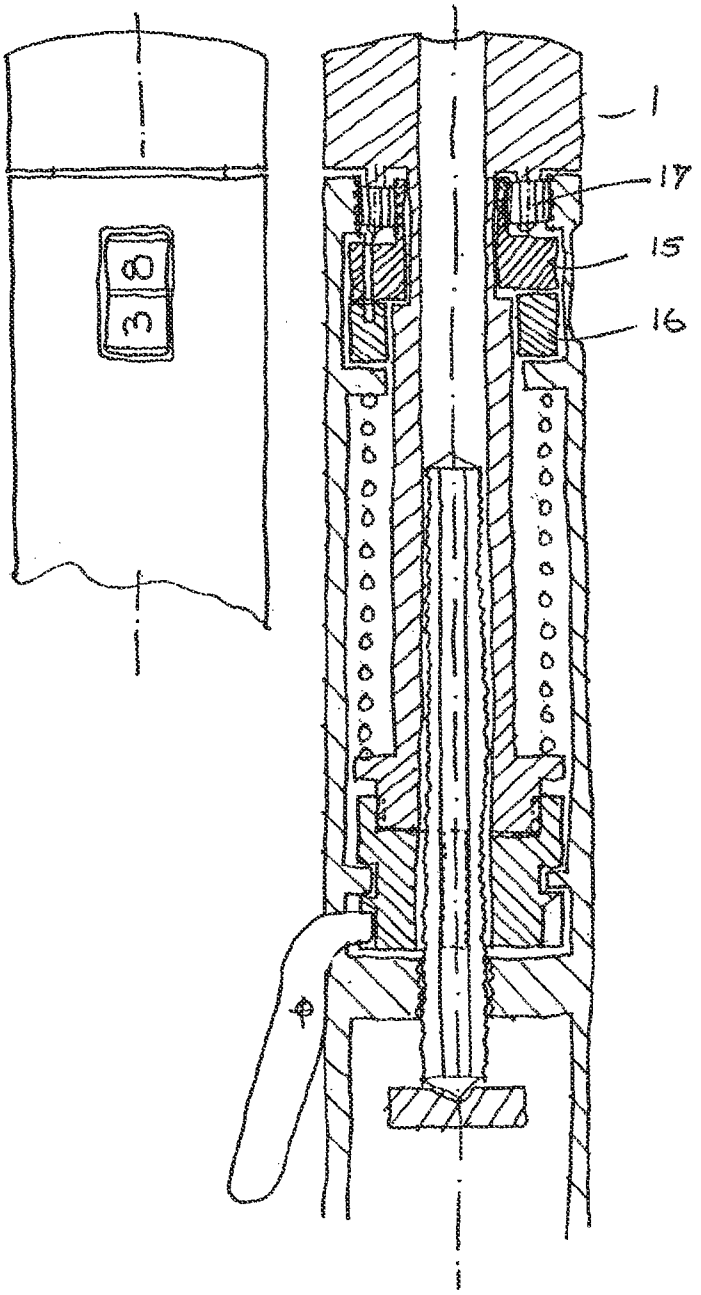

Fig. 5

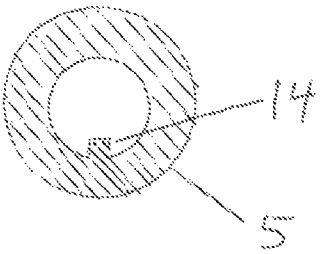

Fig. 6

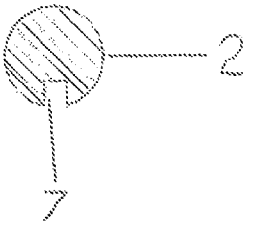

Fig. 7

INJECTION DEVICE WITH TORSION SPRING AND ROTATABLE DISPLAY

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. application Ser. No. 11/665,571, filed Dec. 5, 2007, which is a 35 U.S.C. §371 national stage application of International Patent Application PCT/EP2005/011287 (published as WO 2006/045528), filed Oct. 20, 2005, which claims priority of European Patent Application 04077899.5, filed Oct. 21, 2004; this application further claims priority under 35 U.S.C. §119 of U.S. Provisional Application 60/626,271, filed Nov. 9, 2004, all of which are hereby incorporated by reference.

FIELD OF THE INVENTION

The present invention relates to an injection device, such as a wind-up pen, wherein numerals indicating the dose to be ejected from the injection device are displayed over an angle of rotation exceeding one revolution. In particular, the numerals indicating the dose to be ejected are arranged along a helical path, or alternatively, numerals indicating the dose to be ejected are displayed on a counting device. The present invention ensures that an increased accuracy in dose setting may be obtained.

BACKGROUND OF THE INVENTION

Various types of automatic injection devices have been described in the literature. A majority of these automatic injection devices apply dose indicator barrels, dose indicator wheels or the like which, during dose setting, are only allowed to rotate less than one single revolution. The fact that the dose indicator barrel is only allowed to rotate less than one revolution during dose setting puts a limit to the obtainable angular resolution. This limited angular resolution also limits the accuracy of the dose setting procedure.

In prior art injection devices the dose setting scale arranged on the outer surface of the barrels or wheels contains only up to 42 scale units with an incremental of 2. Thus, the accuracy when setting a dose is limited by this rather rough incremental.

Examples of "one revolution" barrels or wheel may for example be found in U.S. Pat. No. 5,725,508, EP 0 338 806 or U.S. Pat. No. 5,104,380.

WO 02/053214 discloses an automatic injection device having a dose indicator barrel capable of rotating more than one revolution. However, the injection device according to WO 02/053214 applies a linear spring to move a piston rod in the distal direction of the injection device. Evidently, an injection device applying a linear spring has a built-in axial displacement due to compressions and extensions of the linear spring along the axial direction of the injection device. This linear movement may easily be utilized to provide axial movements of the dose indicator barrel. However, it is a disadvantage that linear springs are highly non-linear in terms of force vs. compression. In addition, a linear spring exhibits relative high mechanical looses. Thus, due to the problems relating to the non-linear properties and relatively high looses there is a need for injection devices having linear and more efficient injection assisting systems.

The above-mentioned problems may be solved by applying a torsion spring instead of the linear spring. An injection device applying a torsion spring is conceptually different from linear spring-based devices in that torsion-based systems do not have a built-in axial movement of the spring assisting the user in injecting a dose of medicament from the injection device. The advantages of torsion-based injection devices are many, the greatest of these probably being that torsion springs respond in a linear manner over a large working range.

Thus, there is a need for a torsion spring-based injection device providing an improved and more user friendly dose setting procedure. It is an object of the present invention to provide such torsion spring-based injection device having an expanded dose scale with a high resolution.

SUMMARY OF THE INVENTION

The above-mentioned object is complied with by providing, in a first aspect, an injection device comprising

- a torsion spring operatively connected to a dose setting member, the dose setting member being adapted to set a dose to be ejected from the injection device, and
- a rotatably mounted display member adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member, the rotatably mounted display member being rotatable over an angle corresponding to at least one revolution of the display member.

The display member may be adapted to be moved between two end positions. These two end positions may define or set an axial operation range of the display member. The axial operation range of the display member may be associated with a substantially linear working range of the torsion spring. The working range of the torsion spring utilized to move the display member between the two end positions may constitute only a fraction of the available working range provided by the torsion spring. Thus, by applying a torsion spring only a small and linear working range of the available working range is utilized.

The display member may comprise a dose indicator barrel having numerals arranged along a helical path on an outer surface thereof.

According to a first embodiment of the present invention, the injection device may further comprise

- a housing,
- a piston rod having a threaded outer surface with a drive track arranged in a longitudinal direction of the outer surface of the piston rod,

wherein the dose setting member is rotatably mounted and defines a passage for the piston rod, the dose setting member further having a guiding track arranged on an inner surface thereof,

- a rotatable drive member being adapted to at least partly engage with at least part of the drive track of the piston rod so as to drive the piston rod,

wherein the dose indicator barrel has a part engaging at least part of the guiding track of the dose setting member, the dose setting member and the dose indicator barrel being movable in relation to each other, the dose indicator barrel further having a threaded outer surface cooperating with a threaded inner portion of the housing whereby the dose indicator barrel undergoes a combined translational and rotational movement in relation to the housing upon rotation of the dose setting member, and

wherein the injection device has a threaded portion cooperating with the threaded outer surface of the piston rod so that rotation of the piston rod relative to the housing results in a longitudinal movement of the piston rod.

It is to be understood that the drive track dose not necessarily extend over the full length of the piston rod. For

example, the drive track may in some cases only extend over a part of the full length of the piston rod. Also, the drive track arranged in the piston rod may be an indentation or groove in the longitudinal direction of the piston rod. Alternatively, it may also be a planar surface or two opposing planar surfaces.

Similarly, it is to be understood that other arrangements in terms of the positioning of the threaded portion of for example the dose indicator barrel may be arranged differently.

According to a second embodiment of the present invention, the injection device further comprises

a housing,

a piston rod having a threaded outer surface with a track arranged in a longitudinal direction of the outer surface of the piston rod,

wherein the dose setting member is rotatably mounted and defines a passage for the piston rod, the dose setting member further having a guiding track arranged on an inner surface thereof,

a rotatable drive member having a threaded portion cooperating with at least part of the threaded outer surface of the piston rod,

wherein the dose indicator barrel has a part engaging at least part of the guiding track of the dose setting member, the dose setting member and the dose indicator barrel being movable in relation to each other, the dose indicator barrel further having a threaded outer surface cooperating with a threaded inner portion of the housing whereby the dose indicator barrel undergoes a combined translational and rotational movement in relation to the housing upon rotation of the dose setting member, and

wherein the injection device has a portion at least partly engaging the track of piston rod so that rotation of the drive member relative to the housing results in a longitudinal movement of the piston rod.

The drive member may be adapted to be connected to the dose setting member via a ratchet. This ratchet allows the dose setting member to be rotated in both directions so that a given dose may be either increased or reduced. Due to the force provided by the torsion spring onto the ratchet, the dose setting member will remain in any position—i.e. dose value—to which it has been brought.

The dose setting member may be adapted to be separated from the driving member. This separation may be achieved in several ways. In one way the separation may be obtained by a retraction of the dose setting member in the axial direction of the injection device. The retraction of the dose setting member must be over a distance sufficient to detach the dose setting member or the drive member from the teeth of the ratchet. Other separation mechanisms, such as pushing the dose setting member or twisting the dose setting member are also applicable.

The torsion spring may be arranged between the housing and the dose setting member in such a way that when the dose setting member is rotated around the piston rod, the torsion spring is strained. The torsion spring may be a helical spring which extends coaxially with the piston rod, and which interconnects the housing and the dose setting member in such a way that rotation of the dose setting member, in order to set the dose, strains the torsion spring.

The injection device may further comprise a locking member adapted to fixate the piston rod in such a way that no relative rotation of the piston rod and the housing is possible when the locking member is in its locking position. This fixation may be provided by a direct engagement of the locking member into the track of the piston rod, or via the drive member. The injection device may further comprise a release button adapted to release the locking member from its locking position. Preferably, the release button is positioned in the distal half of the length of the injection device.

The injection device may further comprise a first stopping member for defining an outer position of the dose indicator barrel. This outer position of the dose indicator barrel may correspond to a maximum obtainable dose. Another outer position of the dose indicator barrel, given by a second stopping member, may define a stop for providing further doses. The stopping members may form integral parts of the inner surface of the housing.

In a third embodiment, the display member may comprise a counting device having two or more display wheels having numerals arranged on an outer surface thereof. In this second embodiment the counting device may have a first and a second wheel. When the dose setting member is rotated, the first wheel is rotated via an optional gear mechanism, such as a planet gear. This first wheel may contain numerals with an incremental of one. The total scale on this wheel may be from 0 to 9. The second wheel next to the first wheel also contains numerals with an incremental of 1. However, this second wheel "counts" the number of revolutions of the first wheel, or alternatively, it "counts" the tens of the first wheel with an incremental of one.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will now be described in further details with reference to the accompanying figures, wherein

FIG. **1** shows a cross-sectional view of a first embodiment of the injection device according to the present invention,

FIG. **2** shows a cross-sectional view (rotated 90 degrees compared to FIG. **1**) of a first embodiment of the injection device according to the present invention,

FIG. **3** shows a detailed cross-sectional view of a first embodiment of the present invention,

FIG. **4** shows a detailed cross-sectional view of a second embodiment of the present invention, and

FIG. **5** shows a detailed cross-sectional view of a third embodiment of the present invention.

FIG. **6** shows a cross-section of a key in a housing component.

FIG. **7** shows a cross-section view of a piston rod with a track.

While the invention is susceptible to various modifications and alternative forms, specific embodiments have been shown by way of example in the drawings and will be described in detail herein. It should be understood, however, that the invention is not intended to be limited to the particular forms disclosed. Rather, the invention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the appended claims.

DETAILED DESCRIPTION OF THE INVENTION

In its most general aspect the present invention relates to an injection device comprising a torsion spring in combination with a rotatable dose indicator mechanism capable of being rotated at least one revolution—i.e. over an angle larger than 360 degrees. For example, the dose indicator mechanism may be implemented as a barrel (see FIGS. **1-4**) or as interconnected wheels (see FIG. **5**), the latter being operated as a counting device. In order to increase the angular resolution compared to known dose indicator mechanisms the dose indicator mechanism of the present invention is rotatable over an angle of rotation corresponding to at least one revolution. The fact that the dose to be ejected is displayed over at least one

revolution allows that the dose setting scale may contain at least 50, 60, 70, 80, 90, 100 units with an incremental of one.

FIGS. **1-3** show a cross-sectional view of the injection device according to a first embodiment of the present invention. The dose of medicament to be ejected from the injection device is set by rotating dose setting member **1**. The dose setting member **1** is attached to the housing **5** of the injection device via torsion spring **12**. When the dose setting member **1** is rotated in order to set a dose to be ejected from the injection device, energy is accumulated in torsion spring **12**. This energy may be released by releasing locking member **4** whereby the piston rod **2** will rotate and move in the distal direction of the injection device. The distal movement of the piston rod **2** is caused by a rotational movement of the piston rod **2** itself in that the piston rod **2** has a threaded outer surface. The threads of the piston rod **2** engage and co-operate with a threaded portion **3** of the injection device causing the piston rod **2** to perform the distal and axial movement.

The inner surface of housing **5** of the injection device is provided with threads **10**. These threads are adapted to engage and co-operate with outer threads **8** of a dose indicator barrel **9**. The dose indicator barrel **9** engages with sliding track **11** of the dose setting member **1** in such a way that the dose indicator barrel **9** is able to slide in said sliding track **11** in an axial direction of the injection device.

When the dose setting member **1** is rotated in order to set a dose, the dose indicator barrel **9** rotates with the dose setting member **1** causing the dose indicator barrel **9** to be axially displaced relative to the housing **5**. A window is provided in the housing **5** of the injection device. Through this window, the user of the injection device may view the actual dose setting level from numerals (not shown) provided on an exterior surface of the dose indicator barrel **9**. The numerals are arranged along a helical path.

An advantage of having the numerals arranged along a helical-like path is that a higher angular resolution is obtainable when a dose is to be set. Due to this higher angular resolution a dose can be set with a significantly higher accuracy. This greater accuracy is obtained since the helical-like path allows for more numerals to be arranged on the dose indicator barrel **9** compared to numerals arranged at the same height on the surface of the dose indicator barrel **9**.

When a dose has been ejected from the injection device, the dose indicator barrel **9** is adapted to be rotated back to its initial position and it is thereby ready to be set to a new dose. The same applies for an injection device applying a counting device as a dose meter.

As already mentioned, the piston rod **2** has a threaded outer surface. This threaded outer surface engages and co-operates with a threaded portion **3** of the injection device. The piston rod **2** is driven by the drive member **6** that engages a track in piston rod **2**. The axial movement of the piston rod **2** is provided by rotating piston rod **2** in the threaded portion **3** of the injection device.

Drive member **6** may be locked by the locking member **4**. In its locked position, drive member **6** is prevented from rotating. In order to release the drive member **6**, the user of the injection device may activate a spring-loaded push button **15** whereby drive member **6** causes the piston rod **2** to rotate in threaded part **3** of the housing whereby the piston rod **2** rotates and travels in the distal direction of the injection device. Thus, when the drive member **6** is released, the injection device ejects automatically. During ejection, the dose indicator barrel returns to zero dose.

The dose setting member **1** and the drive member **6** are mechanically connected via a self-tightening ratchet **13**. Preferably, the self-tightening ratchet **13** has saw-toothed teeth with approximately vertical oriented flanks as the self-tightening flanks.

In order to reset or reduce an already set dose, the dose setting member **1** is arranged to be axially retractable over a distance corresponding to the height of the teeth of the one-way ratchet **13**. Thus, by pulling the dose setting member **1** back, and thereby disengage the dose setting member **1** from the drive member **6**, an already set dose can be reduced or even reset. The amount of reduction obviously depends on the angle of rotation (in the opposite rotation direction as when a dose is set) of the dose setting member **1**.

The self-tightening ratchet may be formed as a separate component having first and second engaging parts. Alternatively, one of these parts may form an integral part of the dose setting member **1**, or alternatively, an integral part the drive member **6**.

FIG. **4** shows a second embodiment of the present invention. Compared to the first embodiment, the drive member **6** has a threaded portion cooperating with the threaded outer surface of the piston rod **2**. The main difference compared to the first embodiment is that the piston rod **2** is no longer rotatable relative to the housing **5**. This non-rotatable relationship is ensured in that the housing of the injection device has a key **14** which at least partly engages the track **7** of piston rod **2**. Thus, when the drive member **6** is free to rotate relative to the housing **5** the piston rod **2** will undergo a translational movement along the axial direction of the injection device.

FIG. **5** shows a third embodiment of the present invention. In this embodiment the dose indicator barrel of the first and second embodiment has been replaced by a counting device having two wheels **15**, **16**. In principle the number of wheels may be chosen arbitrary, but for simplicity, a counting device having only two wheels is illustrated in FIG. **5**. The counting device is operated as follows: When the dose setting member **1** is rotated, the wheel closest to the dose setting member **15** is rotated via an optional planet gear **17**. This wheel contains numerals with an incremental of one. The total scale on this wheel may contain 10 units distributed over a scale from 0 to 9, or alternatively, the total scale may contain for example 20 units distributed over two scales each having a scale from 0 to 9.

The second wheel **16** next to the first wheel **15** also contains numerals with an incremental of 1. However, this second wheel "counts" the number of revolutions of the first wheel, or alternatively, it "counts" the tens of the first wheel with an incremental of one. Alternatively, the second wheel "counts" the number of half resolutions of the first wheel in case the first wheel contains a scale having 20 units.

The invention claimed is:

1. An injection device comprising -p**1** a torsion spring (**12**) operatively connected to a dose setting member (**1**), the dose setting member (**1**) being adapted to set a dose to be ejected from the injection device, and

a rotatably mounted display member adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member (**1**), the rotatably mounted display member being rotatable over an angle corresponding to at least one revolution of the display member, wherein the rotatably mounted display comprises a dose indicator barrel;

wherein the display member is adapted to be moved between two end positions, said two end positions defining an operation range of the display member, said operation range being associated with a substantially linear working range of the torsion spring;

wherein the injection device further comprises:

a housing (**5**),

a piston rod (**2**) having a threaded outer surface with a drive track (**7**) arranged in a longitudinal direction of said outer surface,

wherein the dose setting member (**1**) is rotatably mounted and defines a passage for the piston rod (**2**), the dose setting member (**1**) further having a guiding track (**11**) arranged on an inner surface thereof,

a rotatable drive member (**6**) being adapted to at least partly engage with at least part of the drive track (**7**) of the piston rod (**2**) so as to drive the piston rod,

wherein the dose indicator barrel (**9**) has a part engaging at least part of the guiding track (**11**) of the dose setting member (**1**), the dose setting member (**1**) and the dose indicator barrel (**9**) being movable in relation to each other, the dose indicator barrel (**9**) further having a threaded outer surface (**8**) cooperating with a threaded inner portion (**10**) of the housing (**5**) whereby the dose indicator barrel (**9**) undergoes a combined translational and rotational movement in relation to the housing (**5**) upon rotation of the dose setting member (**1**), and

wherein the injection device has a threaded portion (**3**) cooperating with the threaded outer surface of the piston rod (**2**) so that rotation of the piston rod (**2**) relative to the housing (**5**) results in a longitudinal movement of the piston rod (**2**).

2. An injection device according to claim **1**, wherein the drive member (**6**) is adapted to be connected to the dose setting member (**1**) via a ratchet (**13**).

3. An injection device according to claim **1**, wherein the torsion spring (**12**) is arranged between the housing (**5**) and the dose setting member (**1**) in such a way that when the dose setting member (**1**) is rotated around the piston rod (**2**), the torsion spring (**12**) is strained.

4. An injection device according to claim **3**, wherein the torsion spring (**12**) is a helical spring which extends coaxially with the piston rod (**2**).

5. An injection device according to claim **1**, further comprising a locking member (**4**) adapted to fixate the piston rod (**2**) in such a way that no relative rotation between of the piston rod (**2**) and the housing (**5**) is possible when the locking member (**4**) is in its locking position.

6. An injection device according to claim **5**, further comprising a release button adapted to release the locking member (**4**) from its locking position.

7. An injection device according to claim **6**, wherein the release button is positioned in the distal half of the length of the injection device.

8. An injection device according to claim **1**, further comprising a stopping member for defining an outer position of the dose indicator barrel (**9**), the outer position of the dose indicator barrel (**9**) corresponding to a maximum obtainable dose.

9. An injection device according to claim **1**, wherein the dose the dose indicator barrel rotates to a zero position during ejection of a dose.

10. An injection device according to claim **1**, further comprising a release button located on the device that when pressed causes the spring to drive a dose from the injection device while simultaneously the dose indicator barrel rotates towards a zero position and wherein upon completion of the dose the indicator barrel is at the zero position and the device can then be reset to inject a new dose and where if the new dose can be reduced by dialing down the dose setting mechanism without expelling medication from the ejection device and wherein the new reduced dose can be ejected by pressing the release button.

11. An injection device comprising

a torsion spring (**12**) operatively connected to a dose setting member (**1**), the dose setting member (**1**) being adapted to set a dose to be ejected from the injection device, and

a rotatably mounted display member adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member (**1**), the rotatably mounted display member being rotatable over an angle corresponding to at least one revolution of the display member, wherein the rotatabley mounted display comprises a dose indicator barrel;

wherein the display member is adapted to be moved between two end positions, said two end positions defining an operation range of the display member, said operation range being associated with a substantially linear working range of the torsion spring;

wherein the injection device further comprises:

a housing (**5**),

a piston rod (**2**) having a threaded outer surface with a track (**7**) arranged in a longitudinal direction of said outer surface,

wherein the dose setting member (**1**) is rotatably mounted and defines a passage for the piston rod (**2**), the dose setting member (**1**) further having a guiding track (**11**) arranged on an inner surface thereof,

a rotatable drive member (**6**) having a threaded portion cooperating with at least part of the threaded outer surface of the piston rod (**2**),

wherein the dose indicator barrel (**9**) has a part engaging at least part of the guiding track (**11**) of the dose setting member (**1**), the dose setting member (**1**) and the dose indicator barrel (**9**) being movable in relation to each other, the dose indicator barrel (**9**) further having a threaded outer surface (**8**) cooperating with a threaded inner portion (**10**) of the housing (**5**) whereby the dose indicator barrel (**9**) undergoes a combined translational and rotational movement in relation to the housing (**5**) upon rotation of the dose setting member (**1**), and

wherein the injection device has a portion at least partly engaging the track (**7**) of piston rod (**2**) so that rotation of the drive member (**6**) relative to the housing (**5**) results in a longitudinal movement of the piston rod (**2**).

12. An injection device according to claim **11**, further comprising a release button that when pressed causes the spring to eject the drug and when pressed causes the dose indicator barrel to rotate toward a zero position.

13. An injection device according to claim **11**, further comprising a button that when pressed causes the spring to eject medication from the device.

14. An injection device according to claim **11**, wherein the dose indicator barrel rotates to the zero position when a button is depressed.

15. An injection device comprising:

a housing (**5**) with an inner surface provided with threads (**10**),

a dose setting member (**1**) adapted to set a dose to be ejected from the injection device,

a piston rod (**2**) having a threaded outer surface with a track (**7**) arranged in a longitudinal direction of its outer surface,

a rotatable drive member (**6**) that engages with the track (**7**) or with the threaded outer surface of the piston rod to drive the piston rod (**2**),

a torsion spring (**12**), operatively connected to the dose setting member and the housing, such that energy is accumulated in the torsion spring (**12**) upon rotation of the dose setting member (**1**) to set the dose and the accumulated energy is released to rotate the drive mem-

ber (6) whereby the piston rod moves in the distal direction of the injection device to eject the set dose automatically, wherein,

a rotatably mounted display member is threadedly engaged with the threads (10) of the housing (5) and operatively connected with the dose setting member (1) such that when the dose setting member (1) is rotated in order to set a dose[,] the display member rotates with the dose setting member (1) causing the display member to be axially displaced relative to the housing (5) and is adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose by the dose setting member (1), and

the rotatably mounted display member is rotatable over an angle corresponding to at least one revolution, and the display member further returns to return to zero during ejection.

16. An injection device according to claim 15, wherein the display member is adapted to be moved between two end positions, said two end positions defining an operation range of the display member, said operation range being associated with a substantially linear working range of the torsion spring.

17. An injection device according to claim 15, wherein the display member comprises a dose indicator barrel (9) having numerals arranged along a helical path on an outer surface thereof and wherein the angle is greater than one revolution and wherein the injection device further comprises a release button for releasing energy from the spring to drive the piston rod.

18. An injection device according to claim 17,

wherein the dose setting member (1) is rotatably mounted and defines a passage for the piston rod (2), the dose setting member (1) further having a guiding track (11) arranged on an inner surface thereof,

a rotatable drive member (6) being adapted to at least partly engage with at least part of the drive track (7) of the piston rod (2) so as to drive the piston rod,

wherein the dose indicator barrel (9) has a part engaging at least part of the guiding track (11) of the dose setting member (1), the dose setting member (1) and the dose indicator barrel (9) being movable in relation to each other, the dose indicator barrel (9) further having a threaded outer surface (8) cooperating with the threaded inner portion (10) of the housing (5) whereby the dose indicator barrel (9) undergoes a combined translational and rotational movement in relation to the housing (5) upon rotation of the dose setting member (1), and

wherein the injection device has a threaded portion (3) cooperating with the threaded outer surface of the piston rod (2) so that rotation of the piston rod (2) relative to the housing (5) results in a longitudinal movement of the piston rod (2).

19. An injection device according to claim 18, wherein the drive member (6) is adapted to be connected to the dose setting member (1) via a ratchet (13).

20. An injection device according to claim 18, wherein the torsion spring (12) is arranged between the housing (5) and the dose setting member (1) in such a way that when the dose setting member (1) is rotated around the piston rod (2), the torsion spring (12) is strained.

21. An injection device according to claim 20, wherein the torsion spring (12) is a helical spring which extends coaxially with the piston rod (2).

22. An injection device according to claim 18, further comprising a locking member (4) adapted to fixate the piston rod (2) in such a way that no relative rotation between of the piston rod (2) and the housing (5) is possible when the locking member (4) is in its locking position.

23. An injection device according to claim 22, further comprising a release button adapted to release the locking member (4) from its locking position.

24. An injection device according to claim 23, wherein the release button is positioned in the distal half of the length of the injection device.

25. An injection device according to claim 24, further comprising a stopping member for defining an outer position of the dose indicator barrel (9), the outer position of the dose indicator barrel (9) corresponding to a maximum obtainable dose.

26. An injection device according to claim 17,

wherein the dose setting member (1) is rotatably mounted and defines a passage for the piston rod (2), the dose setting member (1) further having a guiding track (11) arranged on an inner surface thereof,

a rotatable drive member (6) having a threaded portion cooperating with at least part of the threaded outer surface of the piston rod (2),

wherein the dose indicator barrel (9) has a part engaging at least part of the guiding track (11) of the dose setting member (1), the dose setting member (1) and the dose indicator barrel (9) being movable in relation to each other, the dose indicator barrel (9) further having a threaded outer surface (8) cooperating with the threaded inner portion (10) of the housing (5) whereby the dose indicator barrel (9) undergoes a combined translational and rotational movement in relation to the housing (5) upon rotation of the dose setting member (1), and

wherein the injection device has a portion at least partly engaging the track (7) of piston rod (2) so that rotation of the drive member (6) relative to the housing (5) results in a longitudinal movement of the piston rod (2).

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 8,684,969 B2
APPLICATION NO. : 13/626541
DATED : April 1, 2014
INVENTOR(S) : Claus S. Moller et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In The Claims

Please replace column 6, claim number 1, line number 52, with the following:

"An injection device comprising a torsion spring (12)..."

Please replace column 9, claim number 15, line number 8, with the following:

"...rotated in order to set a dose the display member..."

Signed and Sealed this
Eleventh Day of August, 2015

Michelle K. Lee

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EXHIBIT C

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Enggaard et al.

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(45) **Date of Patent: *Dec. 30, 2014**

(54) **DOSE MECHANISM FOR AN INJECTION DEVICE FOR LIMITING A DOSE SETTING CORRESPONDING TO THE AMOUNT OF MEDICAMENT LEFT**

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A61M 5/20 (2006.01)

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USPC **604/207**

(58) **Field of Classification Search**
USPC 604/181, 187, 207–211, 218–231
See application file for complete search history.

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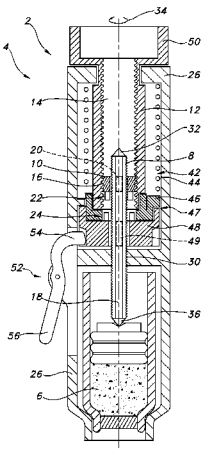
(57) **ABSTRACT**

A mechanism for preventing setting of a dose, which exceeds the amount of a medicament in a reservoir in an injection device. The device comprises a threaded piston rod, a limiter and a driver. The three elements are arranged such that during dose setting, the limiter is moved towards an end-of-contend position, wherein dose setting is limited. The invention comprises an accumulative and a non-accumulative embodiment. The invention further relates to a mechanism for prevention ejection of a dose exceeding the set dose.

13 Claims, 7 Drawing Sheets



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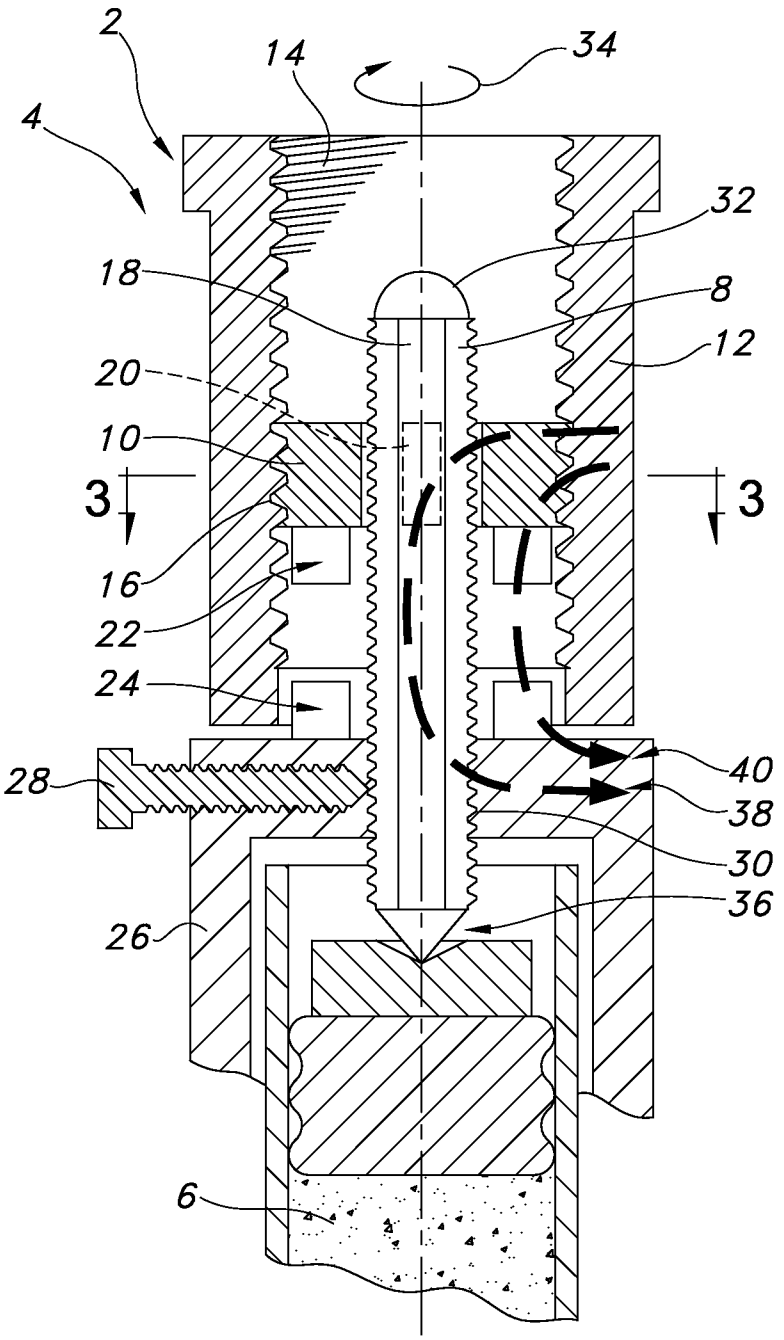

FIG. 1

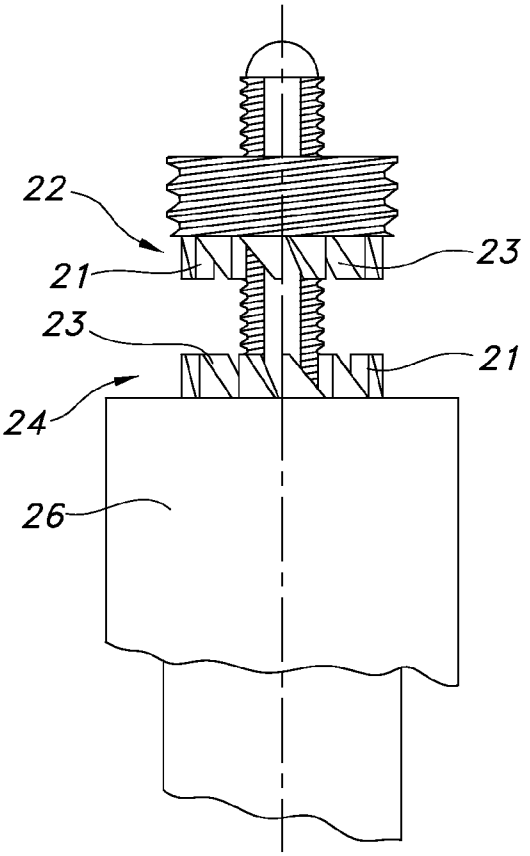

FIG. 2

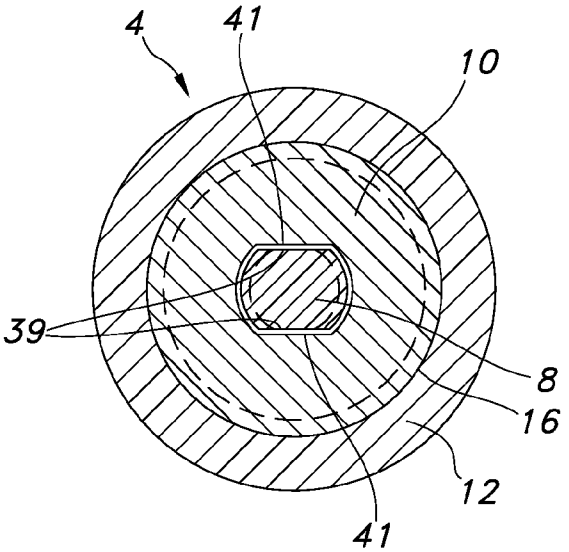

FIG. 3

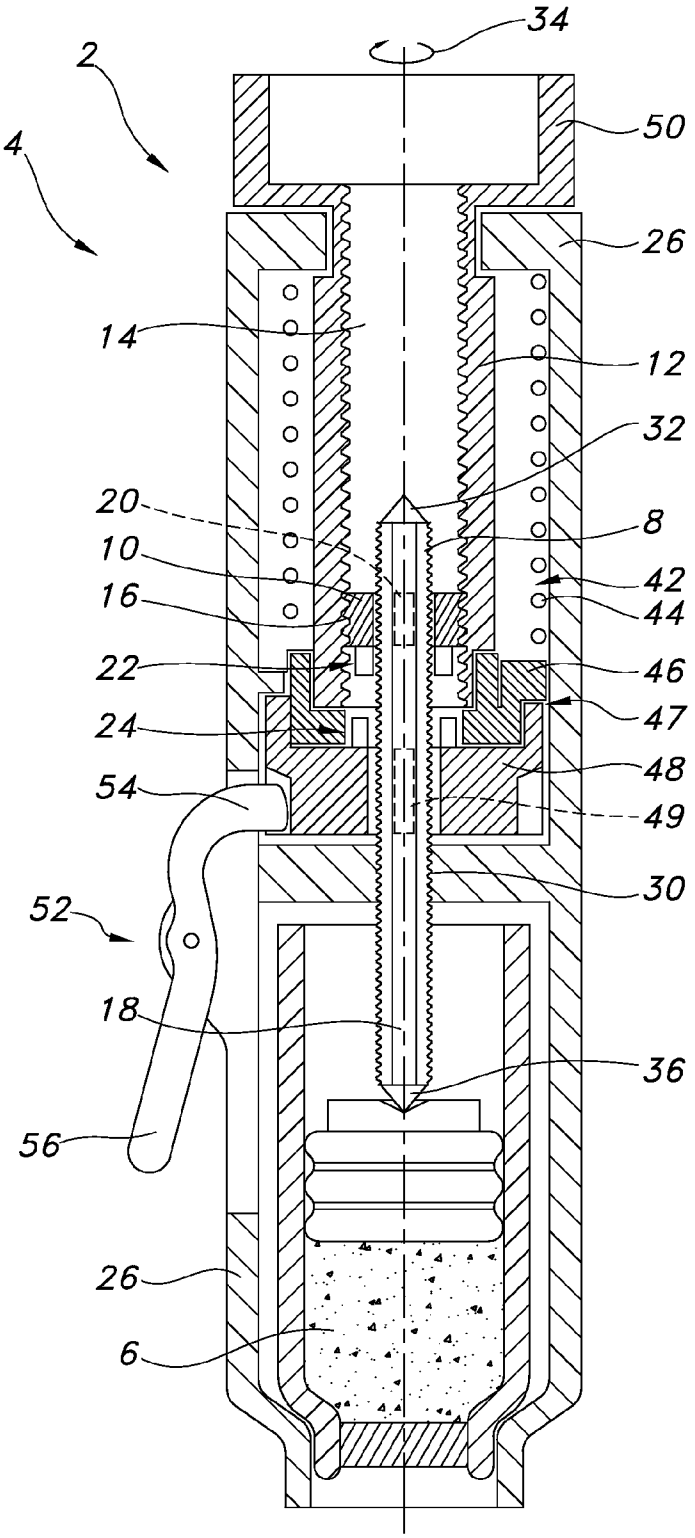
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FIG. 4

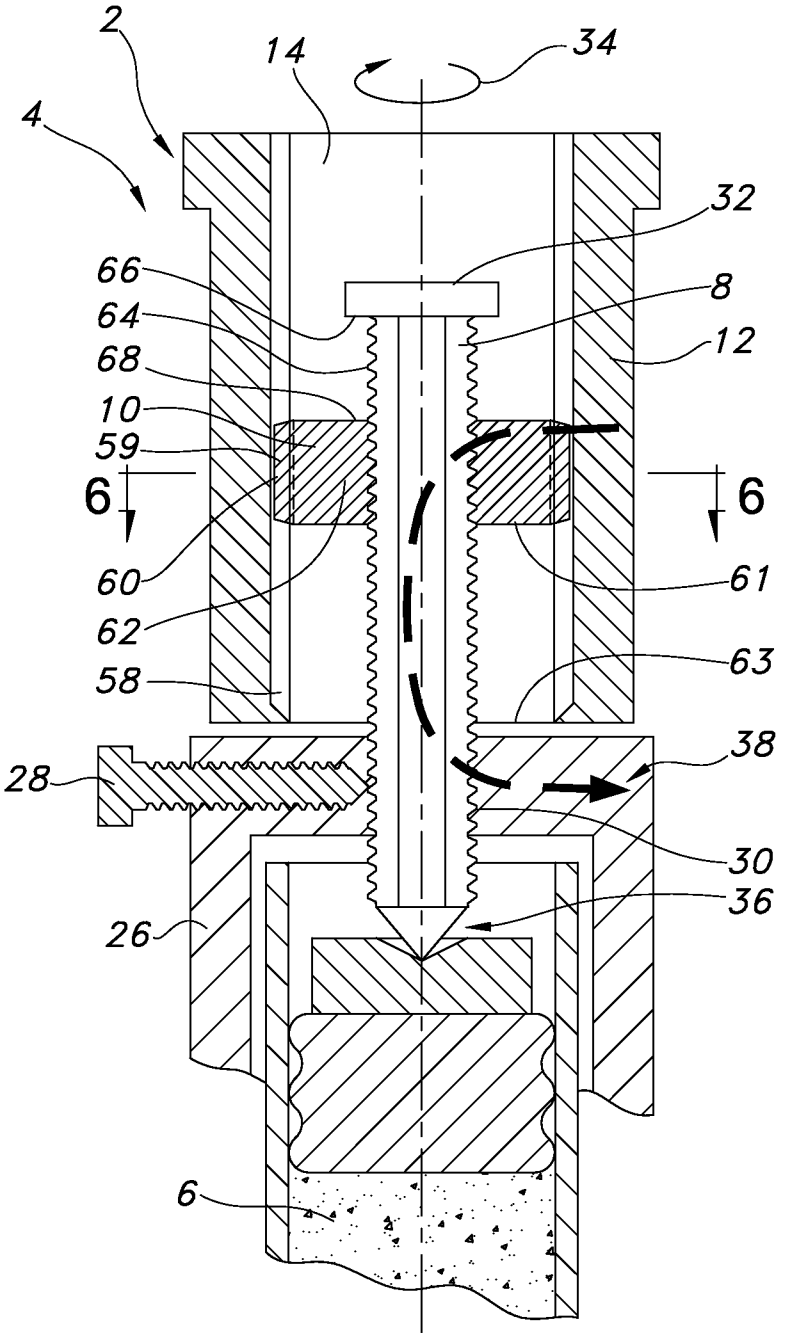

FIG. 5

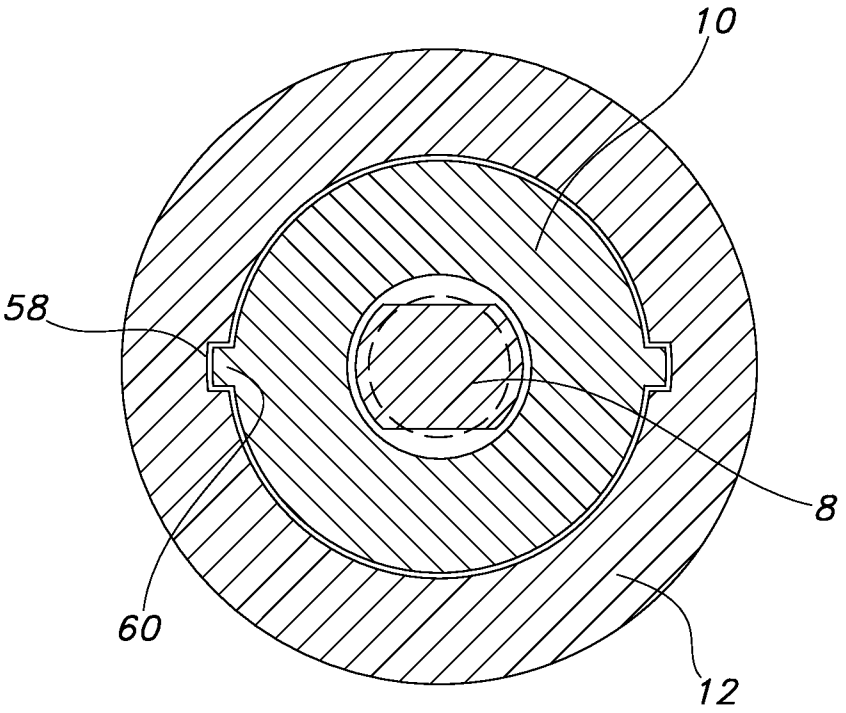

FIG. 6

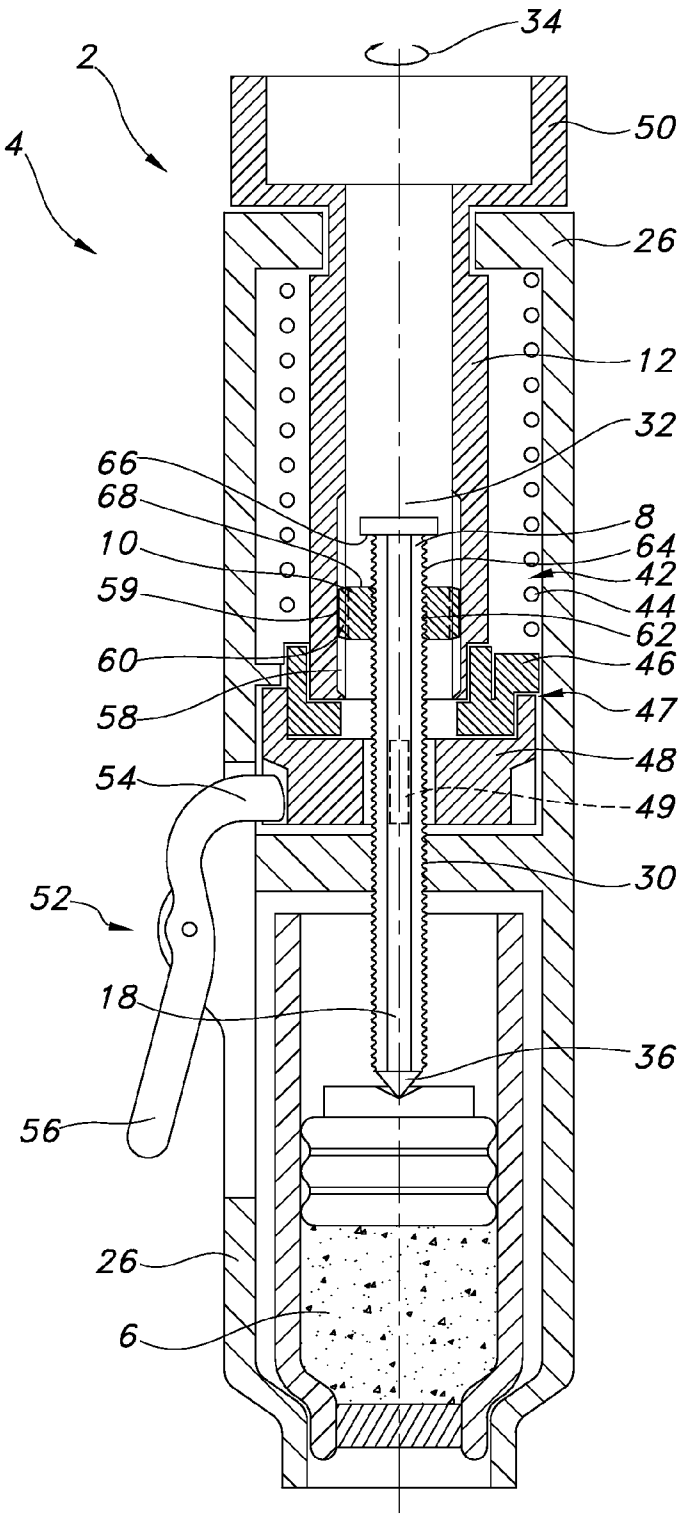
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FIG. 7

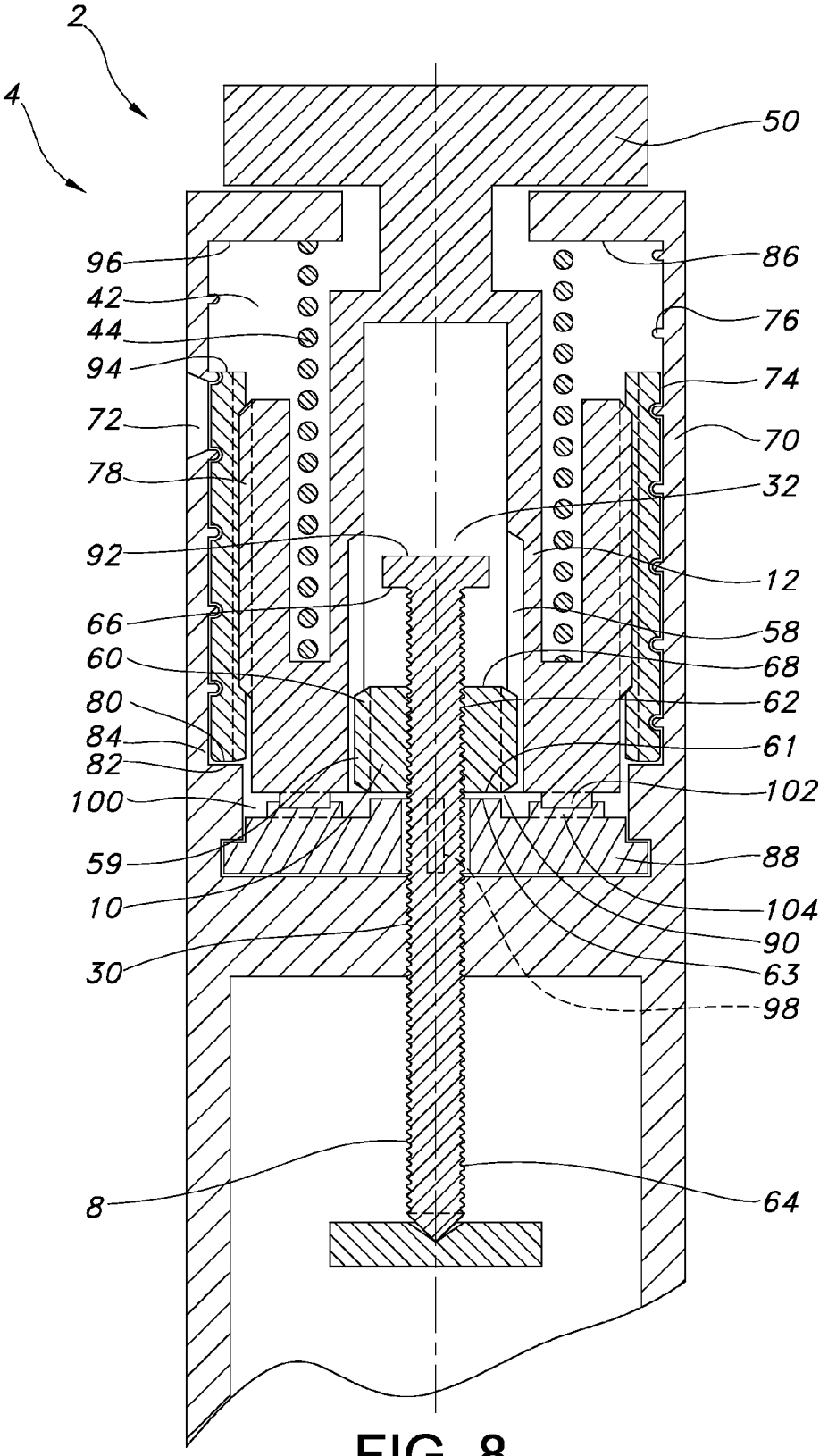
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FIG. 8

DOSE MECHANISM FOR AN INJECTION DEVICE FOR LIMITING A DOSE SETTING CORRESPONDING TO THE AMOUNT OF MEDICAMENT LEFT

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a 35 U.S.C. §371 national stage application of International Patent Application PCT/EP2006/007004 (published as WO 2007/017052), filed Jul. 17, 2006, which claimed priority of European Patent Application 05016291.6, filed Jul. 27, 2005; this application further claims priority under 35 U.S.C. §119 of U.S. Provisional Application 60/708,618, filed Aug. 16, 2005.

FIELD OF THE INVENTION

The present invention relates to a mechanism for preventing setting of a dose which exceeds the amount of a medicament in a reservoir in an injection device. In particular, the present invention relates to a mechanism wherein the piston rod forms part of said mechanism, whereby a compact structure may be provided.

BACKGROUND OF THE INVENTION

When drugs are to be injected into the human body, it is essential that the dose set by the user is the actual dose injected. If this is not the case, the medicating of the patient is not correct, which in some cases can have serious or even fatal consequences. In order to ensure that the dose selected by a dose setting member does not exceed the remaining amount of medication in a reservoir in a syringe device, an end-of-content mechanism may be provided.

End-of-content mechanisms are known in the art. One such example may be seen in WO 01/19434 A1 which discloses a limiting mechanism for an injection device. A dose is injected by rotating a dose setting member which during this rotation carries a driver with it to rotate this driver which moves a piston forward. The driver is provided with a track having a length which is engaged by a track follower coupled to the dose setting mechanism.

Another example may be seen in WO 2004/007003 A1.

It is an object of a preferred embodiment of the present invention to provide an alternative to the above solution. Especially, it is an object of the present invention to provide a solution which allows an outer surface of a driver to be directly coupled to the inner surface of a drum scale, and thus it is an object of the present invention to provide an end-of-content mechanism which may be positioned in the space defined by the inner walls of a driver.

SUMMARY OF THE INVENTION

The present invention provides an accumulative and a non-accumulative solution to the above problems.

In the accumulative solution which is described below under a first general embodiment of the invention a limiter is moved stepwise closer to a stopping position wherein the limiter acts together with other elements of the preventing mechanism to ensure that it is not possible to set a dose exceeding the amount of medicament left in a reservoir.

In the non-accumulative solution which is described under the second general embodiment of the invention the limiter is positioned in the same position prior to dose setting and after dose ejection.

The present invention relates to a mechanism for preventing setting of a dose which exceeds the amount of a medicament in a reservoir in an injection device, wherein a dose is set by rotating a dose setting member of a dose setting mechanism, the mechanism comprising:

- a piston rod having a threaded outer surface;
- a limiter defining a passage for the piston rod;
- a driver defining a passage for the limiter, the driver being coupled to the dose setting member such that rotation of the dose setting member during dose setting causes the driver to rotate; and

wherein the limiter is coupled to the driver and the piston rod such that relative rotation between the driver and the piston rod during dose setting causes the limiter to move towards a stopping position wherein the limiter prevents setting of a dose which exceeds the amount of a medicament in a reservoir in the injection device.

The mechanism may further comprise a housing defining a passage for the piston rod, the passage may have a threaded inner surface for engagement with the threaded outer surface of the piston rod, the housing may be arranged with respect to the piston rod such that rotation of the piston rod, in relation to the housing, causes the piston rod to be displaced relative to the housing in a longitudinal direction. The housing may form part of the housing of a syringe device into which the mechanism is integrated.

The mechanism may comprise a locking means for locking the piston rod against rotation in at least one direction, relative to the housing. Such a locking means may be a screw which may engage or disengage the piston rod. Advantageously, the screw may be arranged such that it engages a root part of the piston rod, whereby the walls of the thread and especially not the crest are not damaged. Alternatively, the locking means may be provided as a pivotable arm, which is operable from an outer surface of the device. The pivotable arm may be movable between an engaging and a non-engaging position, by means of an arm or button accessible from the outer surface of the syringe device.

The mechanism may comprise a ratchet mechanism interconnecting the driver and the housing. The ratchet mechanism may comprise a first and a second part. The first part may be coupled to the driver while the second part may be coupled to the housing e.g. via the locking means. The ratchet mechanism may be adapted to move in one or two rotational directions.

In order to assist patients with poor dexterity an ejection assisting system for providing an ejection force for assisting an operator during ejection may be provided. Such a system may comprise a spring which is strained when the dose setting member is rotated during dose setting. The spring may interconnect the housing and the first part of the ratchet e.g. in such a way that it co-extend the piston rod. Accordingly, when the driver is rotated by means of the dose setting member, whereby the first part of the ratchet is rotated, the spring is rotationally strained. The potential energy stored in the strained spring is released by disengaging the locking means whereby the ratchet mechanism is free to move, whereby the strained spring forces the ratchet mechanism to rotate. As the second part of the ratchet mechanism may be locked for rotation in relation to the piston rod, the rotating ratchet mechanism carries the piston rod with it.

In one embodiment the spring is pre-strained, such as one revolution, such as two revolutions, such as three revolutions, such as four revolutions, such as five revolutions.

In the context of the present invention the term "stopping thread" shall be understood as engaging threads of two elements, at least one of which threads prevents a first of the two

elements from being rotated beyond a predetermined position relative to a second of the two elements. Normally, said prevention of rotation is caused by engagement of surfaces of each of the two elements.

In the following a first general embodiment of the invention is described.

In a FIRST general embodiment the present invention relates to a mechanism for preventing setting of a dose which exceeds the amount of a medicament in a reservoir in an injection device, wherein a dose is set by rotating a dose setting member of a dose setting mechanism, the mechanism comprising:

- a piston rod having a threaded outer surface;
- a limiter defining a passage for the piston rod and being rotationally retained in relation to the piston rod, the limiter having a threaded outer surface;
- a driver defining a passage for the limiter, the passage having a threaded inner surface for engagement with the threaded outer surface of the limiter, the driver being coupled to the dose setting member such that rotation of the dose setting member during dose setting causes the driver to rotate; and

wherein relative rotation between the driver and the piston rod during dose setting causes the limiter to move towards a stopping position wherein the limiter prevents setting of a dose which exceeds the amount of a medicament in a reservoir in the injection device.

Rotation of the dose setting member during dose setting causes the driver to rotate. If the direction of rotation of the dose setting member and the driver is the same, the driver and the dose setting member may be made as one single unit. Alternatively, the two elements may be made be two separate elements attached or coupled to each other.

The direction of the thread of the piston rod and the driver may be opposite i.e. if the piston rod has a right-handed thread, the driver has a left-handed thread and vice versa. This ensures that the dose setting member is rotated back to the same position such that the user may set a dose starting from an initial dose of 0 IU.

The limiter may comprise a first engaging surface adapted to engage a corresponding second engaging surface of the driver. In one embodiment the limiter comprises a plurality of first engaging surfaces which are adapted to engage corresponding second engaging surfaces of the driver. In some embodiments, the number of first and second engaging surfaces is not identical. As an example there may be provided two first engaging surfaces while there is provided ten second engaging surfaces. Accordingly, the limiter may be locked in relation to each other in ten different positions, but at each position only two first and two second engaging surfaces engage each other.

The threaded outer surface of the piston rod may comprise the first surface and the threaded inner surface of the driver comprises the second surface. The piston rod and the driver may be arranged such that relative rotational movement may cause the first and the second surface to be brought into engagement, whereby further relative rotational movement is not possible.

Alternatively, the limiter may comprise a plurality of teeth adapted to engage corresponding teeth of the housing and/or the driver when the limiter is in the stopping position.

Accordingly, the teeth of the limiter comprise first engaging surfaces, while the teeth of the housing and/or driver may comprise the second stopping surfaces.

In one embodiment there is provided both teeth and a stopping thread. An advantage of this is that a larger torque may be transferred from the driver to the limiter, whereby it may be ensured that even when applying a large torque to the dose setting mechanism, a dose which exceeding the actual amount left in the reservoir cannot be set. Such a larger torque may be between 100 and 1000 Nmm, such as 250 Nmm, such as 500 Nmm, such as 750 Nmm.

In the following a second general embodiment of the invention is described.

In a SECOND general embodiment the present invention relates to a mechanism for preventing setting of a dose which exceeds the amount of a medicament in a reservoir in an injection device, wherein a dose is set by rotating a dose setting member of a dose setting mechanism, the mechanism comprising:

- a piston rod having a threaded outer surface;
- a limiter defining a passage for the piston rod, the passage having a threaded inner surface for engagement with the threaded outer surface of the piston rod;
- a driver defining a passage for the limiter, the driver being rotationally retained in relation to the limiter, the driver being coupled to the dose setting mechanism such that rotation of the dose setting member during dose setting causes the driver to rotate; and

wherein relative rotation between the driver and the piston rod during dose setting causes the limiter to move towards a stopping position wherein the limiter prevents setting of a dose which exceed the amount of a medicament in a reservoir in the injection device

As described above the invention according to the second general embodiment of the invention is a non-accumulative solution, wherein the limiter is positioned in the same position (the reference position) prior to dose setting and after dose ejection. The limiter may comprise a first engaging surface adapted to engage a corresponding second engaging surface of the piston rod. The engaging surface of the limiter may be an end surface extending in a radial direction of the limiter and facing a corresponding radial surface of a T-shaped piston rod. Accordingly, when the piston rod is rotated relative to the limiter, the two surfaces will abut each other such that the user is prevented from setting a higher dose. In the alternative the threaded outer surface of the piston rod comprises the first surface and the threaded inner surface of the driver comprises the second surface. The two latter surfaces may each define a plane parallel with the axis of the piston rod and the limiter.

DESCRIPTION OF THE DRAWINGS

The invention will now be described in further detail with reference to the drawings, in which:

FIG. **1** illustrates a mechanism according to the first general embodiment of the invention,

FIG. **2** illustrates teeth of the limiter and the housing according to the first general embodiment,

FIG. **3** illustrates a cross-section through of the piston rod, the limiter and the driver of FIG. **1**,

FIG. **4** illustrates a syringe device with injection assisting means and a mechanism according to the first general embodiment of the invention,

FIG. **5** illustrates a mechanism according to the second general embodiment of the invention,

FIG. **6** illustrates a cross-section through the piston rod, the limiter and the driver of FIG. **2**,

FIG. **7** illustrates a syringe device with injection assisting means and a mechanism according to the second general embodiment of the invention, and

FIG. **8** illustrates a syringe device according to the second general embodiment of the invention wherein the limiter is used both as an end-of-content and as a safety mechanism.

FIG. **1** discloses syringe device **2** comprising a mechanism **4** for preventing setting of a dose which exceeds the amount of a medicament in a reservoir **6**. The mechanism **4** comprises a piston rod **8**, a limiter **10** and a driver **12**. The driver is coupled to a dose setting member (not shown) such that rotation of the dose setting member during dose setting, causes the driver to rotate in the same direction—both when dialling up and down. The inner surface **14** of the driver **12** has a threaded surface which is adapted to engage a corresponding thread of the outer surface **16** of the limiter **10**. Moreover, the limiter **10** is locked for rotation in relation to the piston rod **8** by means of groove **18** in the piston rod **8** and a tongue **20** in the limiter **10** (in the figure the tongue is indicated by a dotted line). Due to the grove-tongue arrangement the limiter **10** and the piston rod **8** may move translationally (i.e. up and down in the figure) in relation to each other.

The limiter comprises a first set of teeth **22** adapted to engage a second set of teeth **24** of the housing **26**. The function of the teeth is to ensure that the dose set does not exceed the amount of a medicament left in the reservoir **6**. Furthermore, the threads of the inner surface **14** and the outer surface **16** comprises a stopping thread which are also used to ensure that that the user cannot set a dose which exceed the amount of a medicament in the reservoir. The two systems are redundant and designed to stop dose setting simultaneously.

The syringe device further comprises a locking means **28** in the form of a screw, which is used to lock the piston rod **8** for rotation in relation to the housing **26**. Due the threaded engagement **30** between the housing **26** and the piston rod **8**, rotational locking of said two elements, results in a translational lock. When the locking means is in the form of a screw, it is desirable that the tip of the screw engages the piston rod in a root of the thread, such that the crest of the thread is not damaged.

In the initial state i.e. when the pen is delivered to the user, the limiter **10** is located in proximal end **32** of the piston rod (i.e. the end opposite the needle of the syringe device).

In order to set a dose the user locks the piston rod for rotation by means of the locking means **28**. The dose is then set by rotating the driver as indicated by the arrow **34**. Due to the relative rotational movement between the piston rod **8** and the driver **12** the limiter **10** moves towards in a distal end **36** of the piston rod.

When the desired dose has been set, the driver, the limiter and the piston rod are locked rotationally in relation to each other such that when a dose is ejected, they all rotate together. Due to the threaded engagement **30** between the housing and the piston rod **8**, the rotation of the piston rod causes the piston rod to move in the distal direction. However, due to the grove-tongue between the piston rod and the limiter, the translational movement of the piston rod is not transmitted to the limiter and the driver. Accordingly, the limiter (and the driver) remains in the same longitudinal position.

It will be appreciated, that during each dose setting the limiter moves closer to the stopping position in which the first and second set of teeth engage and wherein the stopping thread engage. In this position the driver cannot be rotated further, and any torque applied to the dose setting member by the user is transferred from the dose setting member to the driver and via two torque paths. When the torque is transferred through the first torque path **38**, it is transferred from the driver to the limiter, further through the grove-tongue connection to the piston rod and finally from the piston rod to the housing, due to the rotational locking means **28**. When the torque is transferred through the second torque path **40** it is transferred from the driver to the limiter, further from the first set of teeth **22** to the second set of teeth **24** of the housing. By providing a first torque path and a second torque path it is possible to apply a larger torque without breaking the parts of the device e.g. the teeth, and, thus, the risk of user causing damage to the device is reduced.

FIG. **2** shows the housing **26** comprising the second set of teeth **24** which are adapted to engage the first set of teeth **22** of the housing. Each tooth may have a one surface **21** which is substantially parallel with the axial direction of the limiter and another surface **23** which is transverse to said axial direction.

FIG. **3** discloses an alternative to the grove-tongue described in connection with FIG. **1**. In the alternative the piston rod **8** has two flat surfaces **39** and due to corresponding flat surfaces **41** of the limiter **10**, the limiter and the piston rod are locked for relative rotational movement.

FIG. **4** discloses a syringe device **2** comprising the mechanism **4** described in relation to FIG. **1**. However, the syringe device of FIG. **4** further comprises an injection assisting mechanism **42** comprising a spring **44** interconnecting the housing **26** and a first part **46** of a ratchet mechanism **47**, which further comprises a second part **48**. When the dose setting member **50** is rotated, the rotation is transferred to the driver **12** and the first part **46** of the ratchet mechanism. During the rotation of the dose setting member, the spring **44** is strained whereby potential energy is stored. The stored energy may be released by disengaging the pawl **52** which during dose setting engages the second part **48** of the ratchet mechanism. The pawl **52** is pivotally connected to the housing and comprises an engaging part **54** and a button part **56**. When the pawl is disengaged the strained spring **44** causes the first part **46** to rotate. Due to the engagement between the first part **46** and the second part **48**, and due to the grove-tongue connection **49** between the second part **48** and the piston rod **8**, the rotation of the first part **46** causes the piston rod to rotate. As described under FIG. **1** the rotation of the piston rod causes the piston rod to move forward.

FIG. **5** discloses the mechanism according to the second general embodiment of the invention. Identical reference numbers refer to identical elements. In FIG. **5** the driver **12** is coupled to a dose setting member (not shown) such that rotation of the dose setting member during dose setting, causes the driver to rotate in the same direction—both when dialling up and down. The inner surface of the driver **12** comprises a groove **58** which is adapted to engage a corresponding radially extending spline **60** of the limiter **10**. Accordingly, the driver **12** and the limiter **10** are locked for relative rotational movement, while relative translational movement is possible. Furthermore, the limiter **10** has a threaded inner surface **62** which engages a corresponding threaded outer surface **64** of the piston rod **8**. Accordingly, relative rotation between the piston rod and the driver results in relative translational movement between the limiter and each of the piston rod and the driver.

Unlike FIG. **1** the device of FIG. **5** does not comprise first and second sets of teeth. However, it will be appreciated that such sets of teeth could have been provided in the same manner as in FIG. **1**. The only difference is that such sets of teeth should have been provided on the surface **66** and on the other, upper side of the limiter as the limiter moves in the direction of the proximal end **32** when a dose is set, as will be described in the following.

In the initial state i.e. when the pen is delivered to the user, the limiter is located in a reference position wherein a surface **61** of the limiter engages a surface **63** of the housing **26**. In

some embodiments the surfaces **61**,**63** are spaced apart when the limiter is positioned in the reference position.

In order to set a dose the user locks the piston rod for rotation by means of the locking means **28**. The dose is then set by rotating the driver as indicated by arrow **34**. Due to the relative rotational movement between the piston rod **8** and the driver **12** the limiter moves towards a proximal end **32** of the piston rod.

When the desired dose has been set, the driver, the limiter and the piston rod are locked rotationally in relation to each other such that, when a dose is ejected, they all rotate together. Due to the threaded engagement **30** between the housing and the piston rod **8**, the rotation of the piston rod causes the piston rod to move in the distal direction. Due to the grove-spline connection **59** between the driver and the limiter, the translational movement of the piston rod is not transmitted to the driver. However, due to the threaded connection between the piston rod and the limiter, the limiter will move with the piston rod and arrive at the reference position, i.e. the position it had prior to setting the dose. Accordingly, as described in the aforementioned, the invention according to the second general embodiment does not have the accumulative effect which is seen in connection with the invention according to first general embodiment (FIG. **1**-**4**). On the contrary the limiter returns to the reference position during ejecting of the set dose. This may be used to provide a safety mechanism adapted to prevent ejection of a dose exceeding the set dose, this is described in further detail in connection with FIG. **8**.

At a point the piston rod arrives in the stopping position wherein a first stopping thread **66** of the thread **64** of the piston rod engages a second stopping thread **68** of the limiter. The result is that a set dose may not be increased and any torque applied to the driver is transferred to the limiter due to the grove-spline-connection and further to the piston rod due to the stopping thread and finally from the piston rod to the housing—this is indicated by arrow **38**. As the piston rod is locked in relation to the housing by means of the locking means **28**, further rotation of the driver is not possible.

FIG. **6** discloses a cross-section through the piston rod **8**, the limiter **10** and the driver **12**. The limiter **10** is locked for rotational movement relative to the driver **12** due to engagement between the groove **58** and the radially extending spline **60** of the limiter **10**.

FIG. **7** discloses a syringe device **2** comprising the mechanism **4** described in relation to FIG. **5**. However, the syringe device of FIG. **6** further comprises an injection assisting mechanism **42** comprising a spring **44** interconnecting the housing **26** and a first part **46** of a ratchet mechanism **47**, which further comprises a second part **48**. When the dose setting member **50** is rotated, the rotation is transferred to the driver **12** and the first part **46** of the ratchet mechanism. During the rotation of the dose setting member **50**, the pre-strained spring **44** is strained even more whereby further potential energy is stored. The stored energy may be released by disengaging the pawl **52** which during dose setting engages the second part **48** of the ratchet mechanism. The pawl **52** is pivotally connected to the housing and comprises an engaging part **54** and a button part **56**. When the pawl is disengaged the strained spring **44** causes the first part **46** to rotate. Due to the engagement between the first part **46** and the second part **48**, and due to the grove-tongue connection **49** between the first part **46** and the piston rod **8**, the rotation of the first part **46** causes the piston rod to rotate. As described under FIG. **1** the rotation of the piston rod causes the piston rod to move forward.

In the embodiment disclosed in FIG. **8** the syringe device comprises means for preventing ejection of a dose exceeding the set dose. Said means comprises a dose limiting mechanism and a safety mechanism as will be described in detail below. An advantage of the two redundant mechanisms is that if one fails the other may still prevent ejection of a dose exceeding the set dose. The embodiment of FIG. **8** further comprises an end-of-content mechanism.

FIG. **8** discloses a syringe device **2** comprising a housing **4** and a piston rod **8**. The syringe device **2** further comprises a dose setting member **50** and a driver **12**, which in the figure are combined into one single unit. The syringe device further comprises a scale drum **70** for indicating a set dose through a window **72**. The scale drum **70** has a threaded outer surface **74** adapted to engage a corresponding threaded inner surface **76** of the housing. The scale drum **70** is rotationally retained relative to the driver **12** through a grove-tongue engagement **78**. The drum scale **70** comprises a first stopping surface **80** adapted to engage a second stopping surface **82** of the housing. The first stopping surface **80** and the second stopping surface **82** constitutes the dose limiting mechanism **84**. The first stopping surface **80** is moved away from the second stopping surface **82** during dose setting and towards each other during dose ejecting. When the two surfaces abut each other, the device is prevented from ejecting the medicament. Thus, a dose larger than the set dose cannot be expelled as the first and second stopping surfaces abut when the set dose has been expelled

The syringe device comprises an ejection assisting system **42** in the form of a pre-strained torsional spring **44** extending between a proximal part **86** of the housing and the driver **12**. Accordingly, when the dose setting member **50** is rotated to set a dose, the spring **44** is strained even further.

The piston rod **8** comprises a threaded outer surface **64** adapted to engage a corresponding threaded inner surface **30** of the housing and accordingly rotation of the piston rod relative to the housing causes the piston rod to move translationally in relation to the housing. The threaded outer surface **64** of the piston rod also engages a threaded inner surface **62** of a limiter **10**, which in FIG. **8** is positioned in a stopping position wherein a bottom surface **61** of the limiter engages an upper surface **63** of a piston rod guide **88**. The bottom surface **61** and the upper surface **63** constitute the safety mechanism **90**. An air gap may be provided between the bottom surface **61** and the upper surface **63** when the limiter is in said stopping position, which allows the limiter and the piston rod to rotate and angel corresponding to a non-lethal dose e.g. 3 IU of insulin, if the dose limiting mechanism **84** fails.

Moreover, an upper end-of-contend surface **68** of the limiter **10** is adapted to engage a lower end-of-contend surface **66** of a T-shaped end part **92** of the piston rod. The end-of-contend surfaces are adapted to engage when the set dose correspond to the amount of a medicament remaining in a reservoir (not shown) of the device. Accordingly, the engagement of the end-of-contend surfaces prevents setting of a dose exceeding the amount of a medicament remaining in the reservoir. It will be appreciated that the distance between the end-of-contend surfaces thus corresponds to the amount of the medicament remaining in the reservoir.

Moreover, an upper surface **94** of the drum **70** may be adapted to engage a lower surface **96** of the housing, when the maximum dose is set. The maximum dose is the largest dose which may be set for each ejection (provided that the syringe device comprises the required amount of medicament). The maximum dose does not correspond to the end-of-content dose which relates the remaining amount of a medicament in the device. Accordingly, as long as the remaining amount of medicament in the device is larger than the maximum dose, the end-of-content surfaces will not abut each other during

dose setting, whereas when the remaining amount of medicament in the device is lower than the maximum dose, the maximum dose surfaces may abut each other during dose setting, as the end-of-content surfaces prevents further rotation.

The limiter **10** and the driver **12** are locked for relative rotation by means of grove-tongue engagement **59**. Thus, when the piston rod is locked for rotation relative to the housing, a relative rotation between the driver **12** and the piston rod **8** causes the limiter to move away from the stopping position and towards the t-shaped end part **92** (i.e. upwards in the figure). The piston rod is locked for rotation relative to the housing when the piston rod guide **88** is locked for rotation relative to the housing (not shown), as the piston rod guide **88** and the piston rod are locked for relative rotation due to the grove-tongue engagement **98**.

The driver **12** and the piston rod guide **88** are interconnected by a two-way ratchet mechanism **100** comprising at least one first retaining member **102** defined by the driver **12** and at least one second retaining member **104** defined by the piston rod guide **88**. The two-way ratchet mechanism is adapted to allow relative rotational movement between the driver **12** and the piston rod guide **88** during dose setting and to ensure that rotational movement of the driver during dose ejection is transferred to the piston rod guide **88**.

The use of the device is as follows. Initially the piston rod guide is locked for rotation relative to the housing. Then the dose setting member is rotated which causes the driver and the drum scale to rotate and the pre-strained spring to be strained even further. At the same time, the limiter moves towards the T-shaped end part. If the user tries to set a dose exceeding the amount of medicament in the device, the limiter abuts the T-shaped end part whereby an even larger dose cannot be set. The dose is ejected by removing the rotational lock between the piston rod guide and the housing, whereby the strained spring forces the driver to rotate. The rotating driver forces the piston rod guide to rotate which again forces the piston rod to rotate. Due to the grove-tongue engagement **44** and the threaded interconnection between the piston rod and the housing, the rotating piston rod is forced to move forward and thus the medicament is expelled from the device.

The invention claimed is:

1. A mechanism for preventing setting of a dose which exceeds the amount of a medicament in a reservoir in an injection device, wherein a dose is set by rotating a dose setting member of a dose setting mechanism, the mechanism comprising:

a piston rod having a threaded outer surface, wherein the piston rod rotates and translates axially forward during expelling of medication from the reservoir;

a limiter that prevents the setting of a dose which exceeds the amount of medication in a reservoir in the device, the limiter defining a passage for the piston rod;

a driver defining a passage for the limiter, the driver being coupled to the dose setting member such that rotation of the dose setting member during dose setting causes the driver to rotate; and

wherein the limiter is coupled to the driver and the piston rod such that relative rotation between the driver and the piston rod during dose setting causes the limiter to move towards a stopping position.

2. A mechanism according to claim **1**, further comprising a housing defining a passage for the piston rod, the passage having a threaded inner surface for engagement with the threaded outer surface of the piston rod, the housing being arranged with respect to the piston rod such that rotation of the piston rod in relation to the housing causes the piston rod to be displaced relative to the housing in a longitudinal direction.

3. A mechanism according to claim **1**, further comprising a locking means for locking the piston rod against rotation in at least one direction relative to the housing.

4. A mechanism according to claim **1**, wherein:

the limiter has a threaded outer surface and is rotationally retained in relation to the piston rod; and

the passage of the driver has a threaded inner surface for engagement with the threaded outer surface of the limiter.

5. A mechanism according to claim **1**, wherein the limiter comprises a first engaging surface adapted to engage a corresponding second engaging surface of the driver.

6. A mechanism according to claim **1**, wherein the limiter comprises a plurality of teeth adapted to engage corresponding teeth of the housing and/or the driver when the limiter is in the stopping position.

7. A mechanism according to claim **1**, wherein:

the passage of the limiter has a threaded inner surface for engagement with the threaded outer surface of the piston rod; and

the driver is rotationally retained in relation to the limiter.

8. A mechanism according to claim **1**, wherein the limiter comprises a first engaging surface adapted to engage a corresponding second engaging surface of the piston rod.

9. A mechanism according to claim **5**, wherein the threaded outer surface of the piston rod comprises the first engaging surface and the threaded inner surface of the driver comprises the second engaging surface.

10. A mechanism according to claim **1**, further comprising a ratchet mechanism interconnecting the driver and the housing.

11. A mechanism according to claim **10**, wherein the ratchet mechanism comprises a first and a second part, the first part being coupled to the driver and the second part being adapted to be locked for rotation relative to the housing by means of the locking means.

12. A mechanism according to claim **10**, further comprising an ejection assisting system for providing an ejection force for assisting an operator during ejection.

13. A syringe device according to claim **12**, wherein the ejection assisting system comprises a spring which is strained when the dose setting member is rotated during dose setting.

* * * * *

EXHIBIT D

US009108002B2

(12) **United States Patent**
Markussen

(10) **Patent No.: US 9,108,002 B2**
(45) **Date of Patent: Aug. 18, 2015**

(54) **AUTOMATIC INJECTION DEVICE WITH A TOP RELEASE MECHANISM**

(75) Inventor: **Tom Hede Markussen**, Bagsværd (DK)

(73) Assignee: **Novo Nordisk A/S**, Bagsvaerd (DK)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **13/326,738**

(22) Filed: **Dec. 15, 2011**

(65) **Prior Publication Data**

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Related U.S. Application Data

(63) Continuation of application No. 11/813,435, filed as application No. PCT/DK2006/000032 on Jan. 20, 2006, now Pat. No. 8,096,978.

(60) Provisional application No. 60/647,320, filed on Jan. 26, 2005.

(30) **Foreign Application Priority Data**

Jan. 21, 2005 (DK) 2005 00113

(51) **Int. Cl.**

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A61M 5/315	(2006.01)
A61M 5/20	(2006.01)
A61M 5/24	(2006.01)

(52) **U.S. Cl.**

CPC ***A61M 5/31525*** (2013.01); ***A61M 5/20*** (2013.01); ***A61M 5/31553*** (2013.01); *A61M 5/24* (2013.01); *A61M 5/3156* (2013.01); *A61M 5/31583* (2013.01); *A61M 5/31593* (2013.01); *A61M 2005/202* (2013.01)

(58) **Field of Classification Search**

CPC A61M 5/20; A61M 2005/2026; A61M 2005/2073

USPC 604/134–139, 151–153, 187, 207–211

See application file for complete search history.

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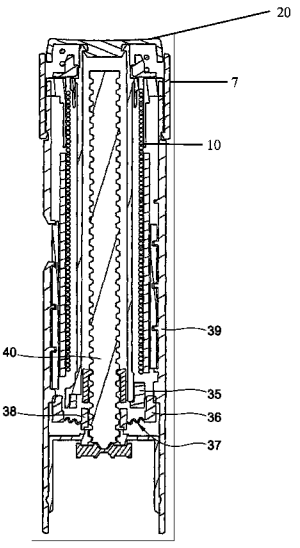
Primary Examiner — Laura Bouchelle

(74) *Attorney, Agent, or Firm* — Wesley Nicolas

(57) **ABSTRACT**

The present invention relates to a handheld mechanical injection device by which set doses of a liquid medicament can be injected from a medical reservoir. The medicament is expelled through an injection needle by release of a power reservoir in the device, the power reservoir being fully or partially released by actuation of a user operable release member being positioned at or near an upper end of the injection device, the upper end being that end of the injection device which is opposite the injection needle.

2 Claims, 13 Drawing Sheets



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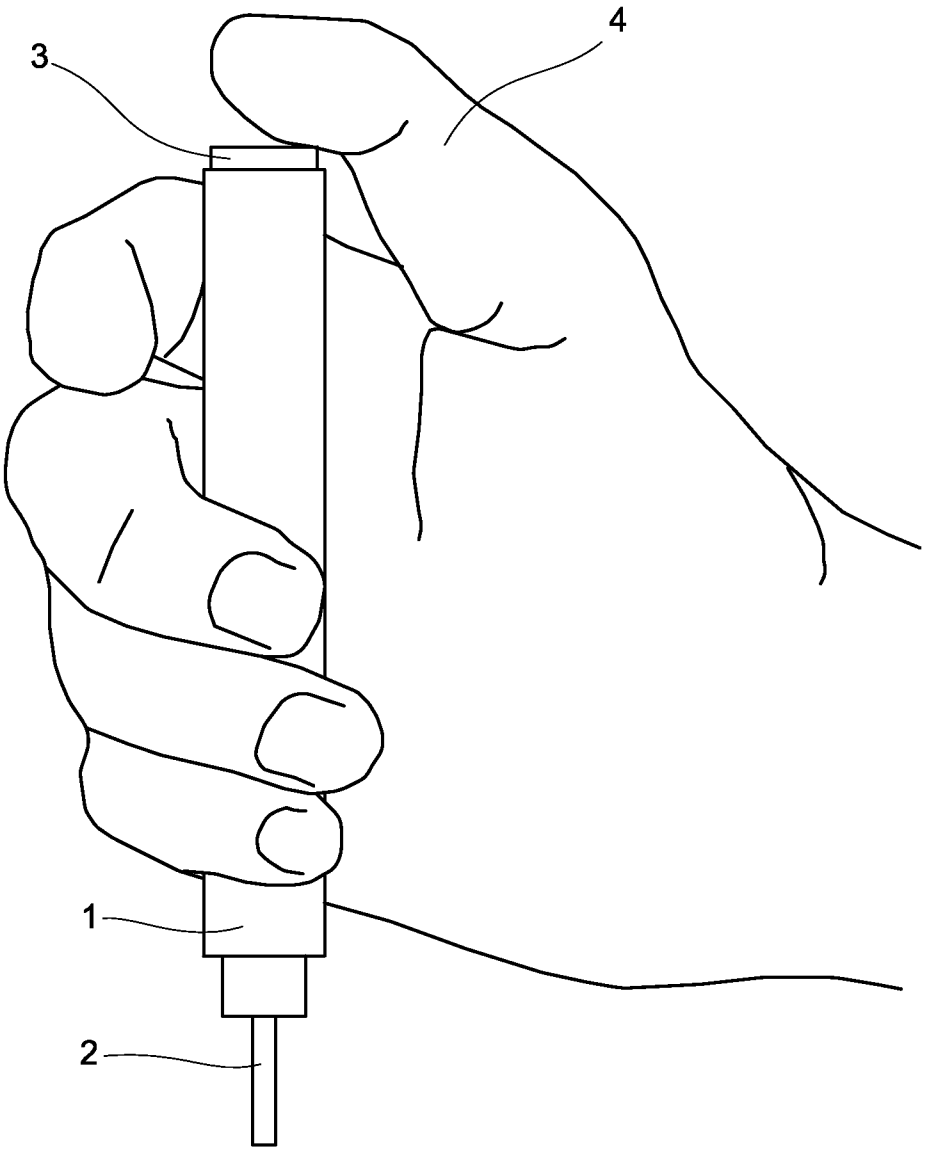

FIG. 1

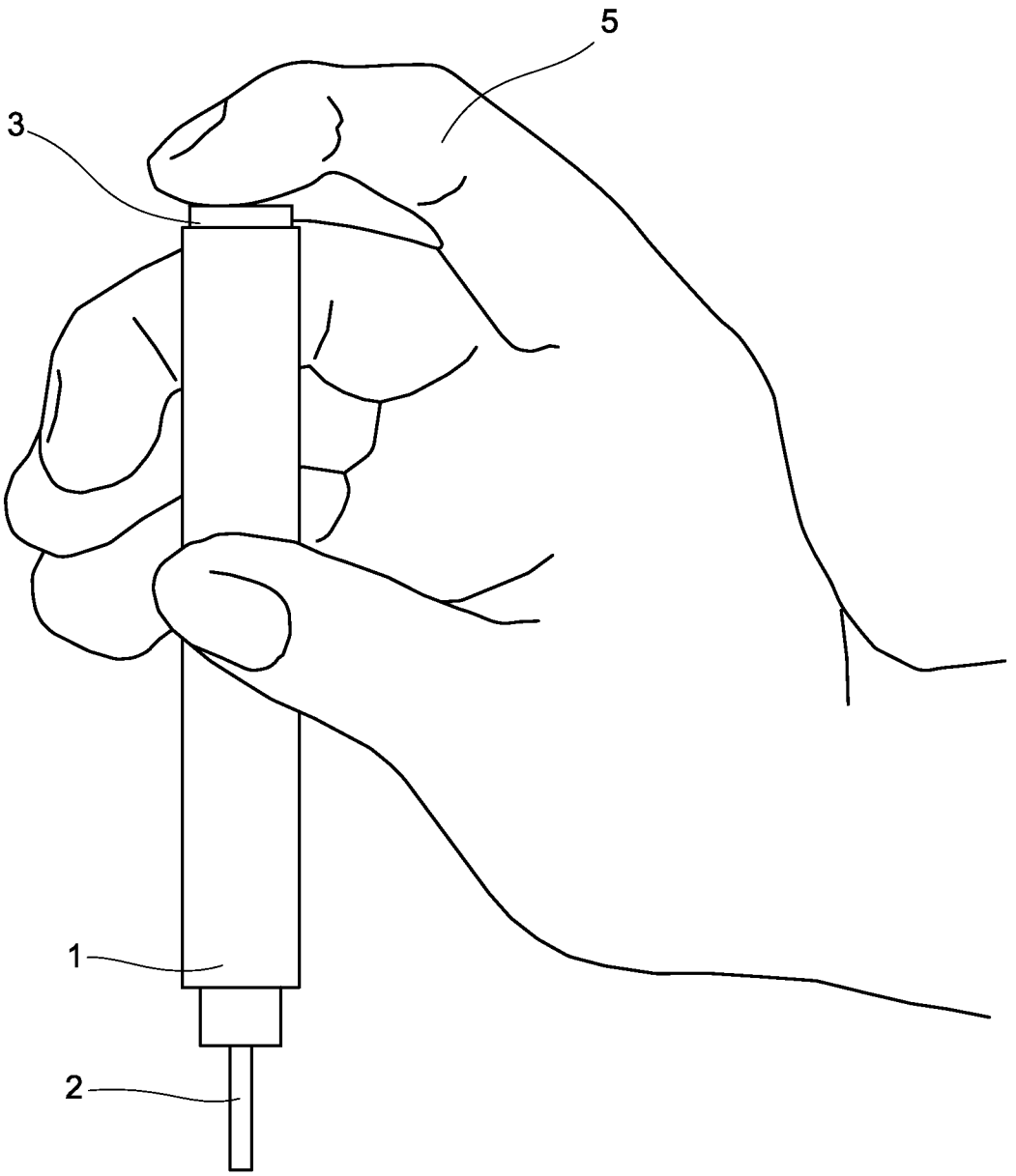

FIG. 2

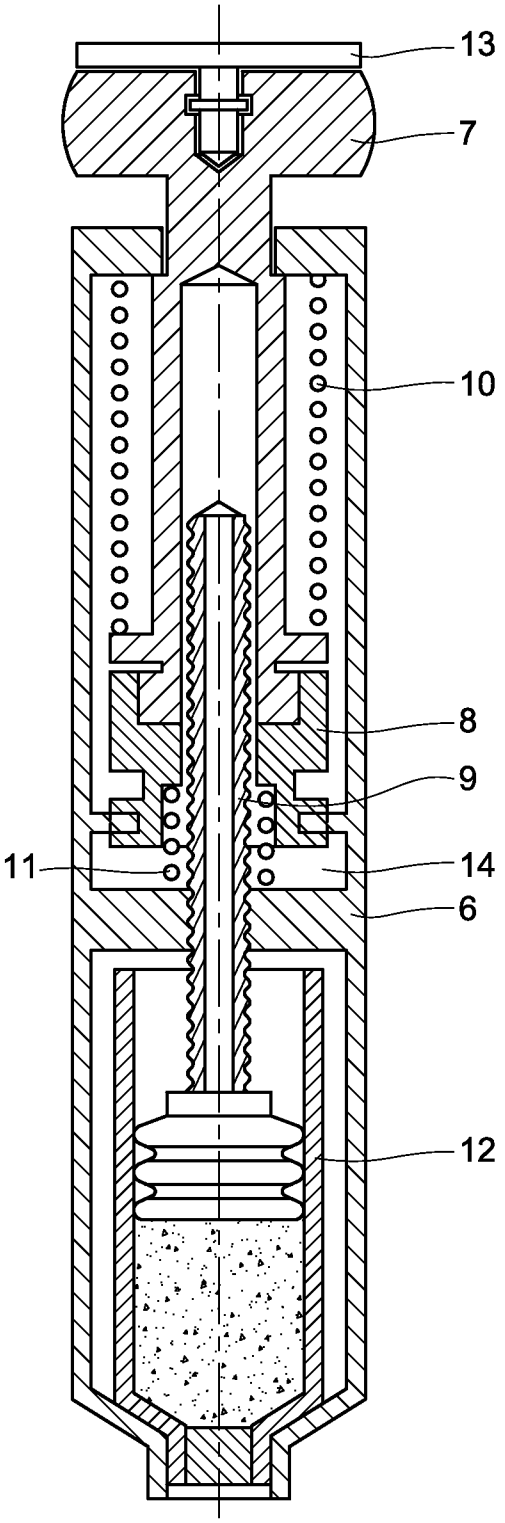

FIG. 3

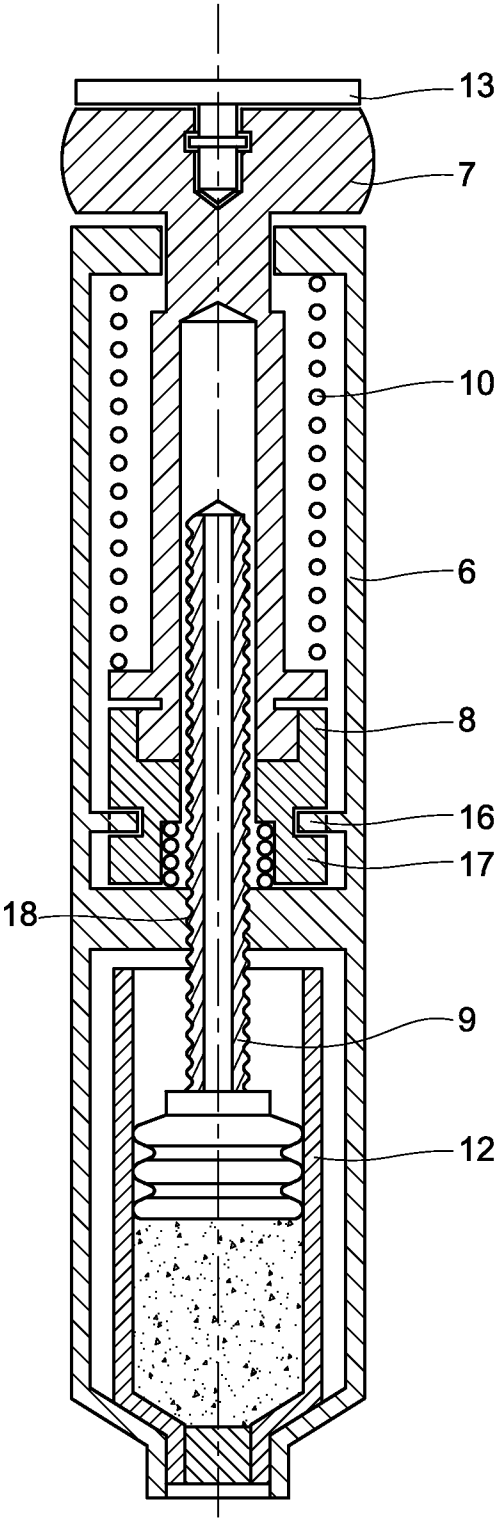

FIG. 4

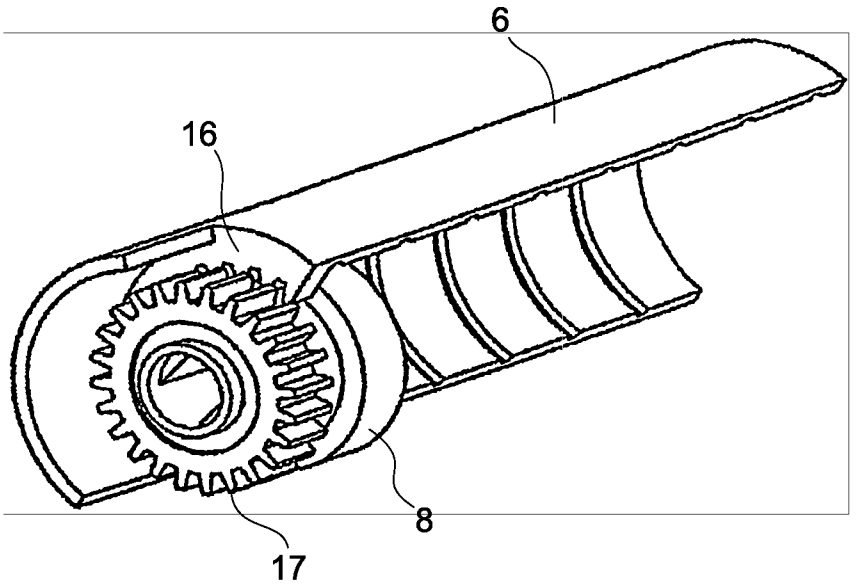

FIG. 5

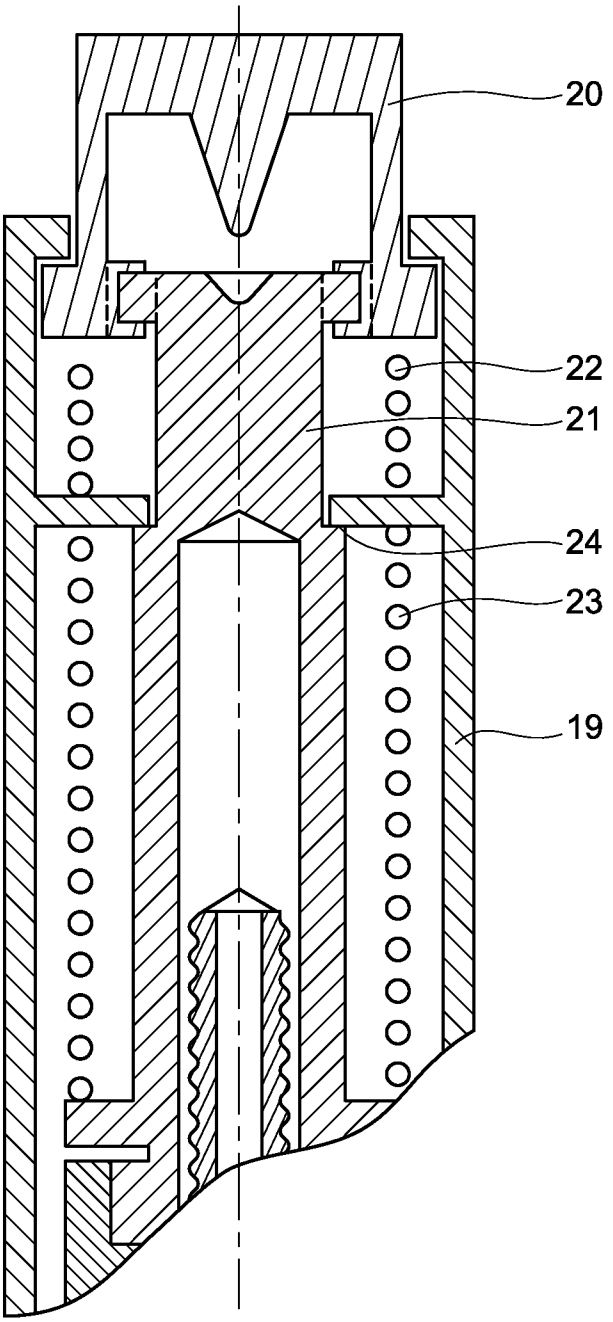

FIG. 6

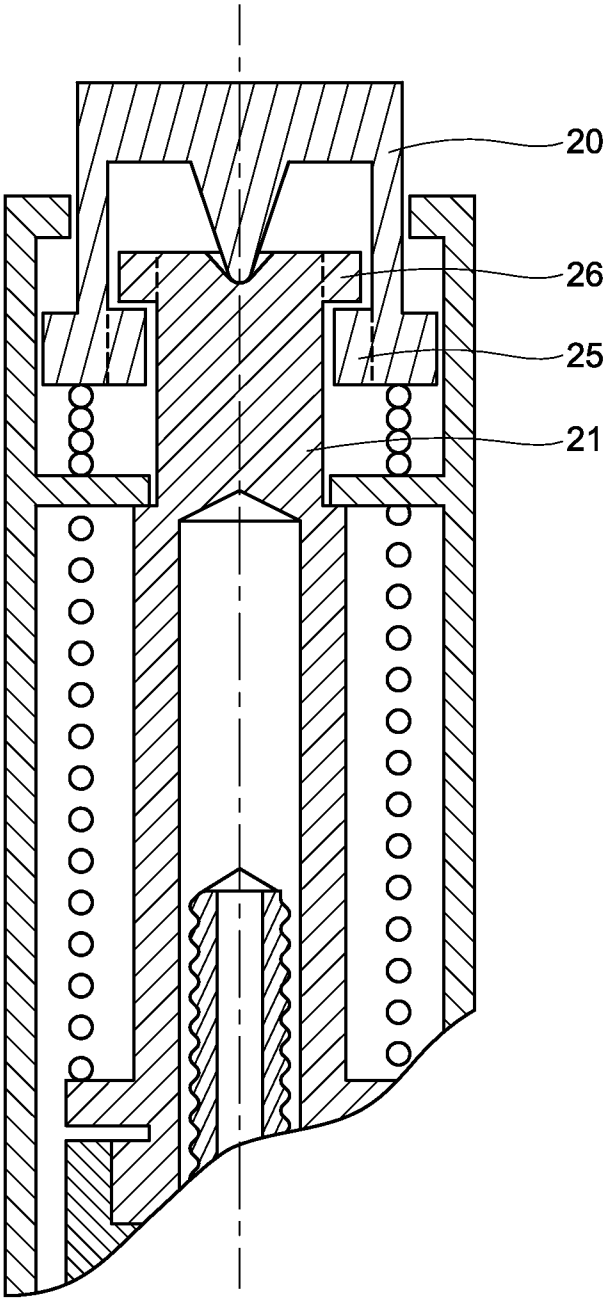

FIG. 7

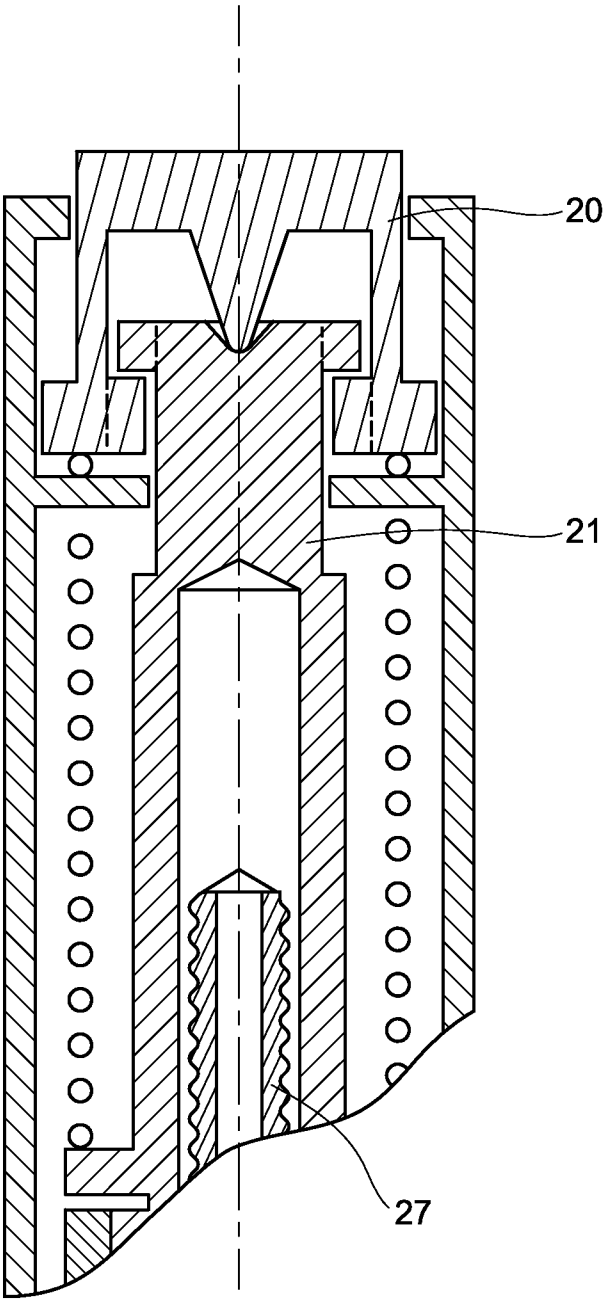

FIG. 8

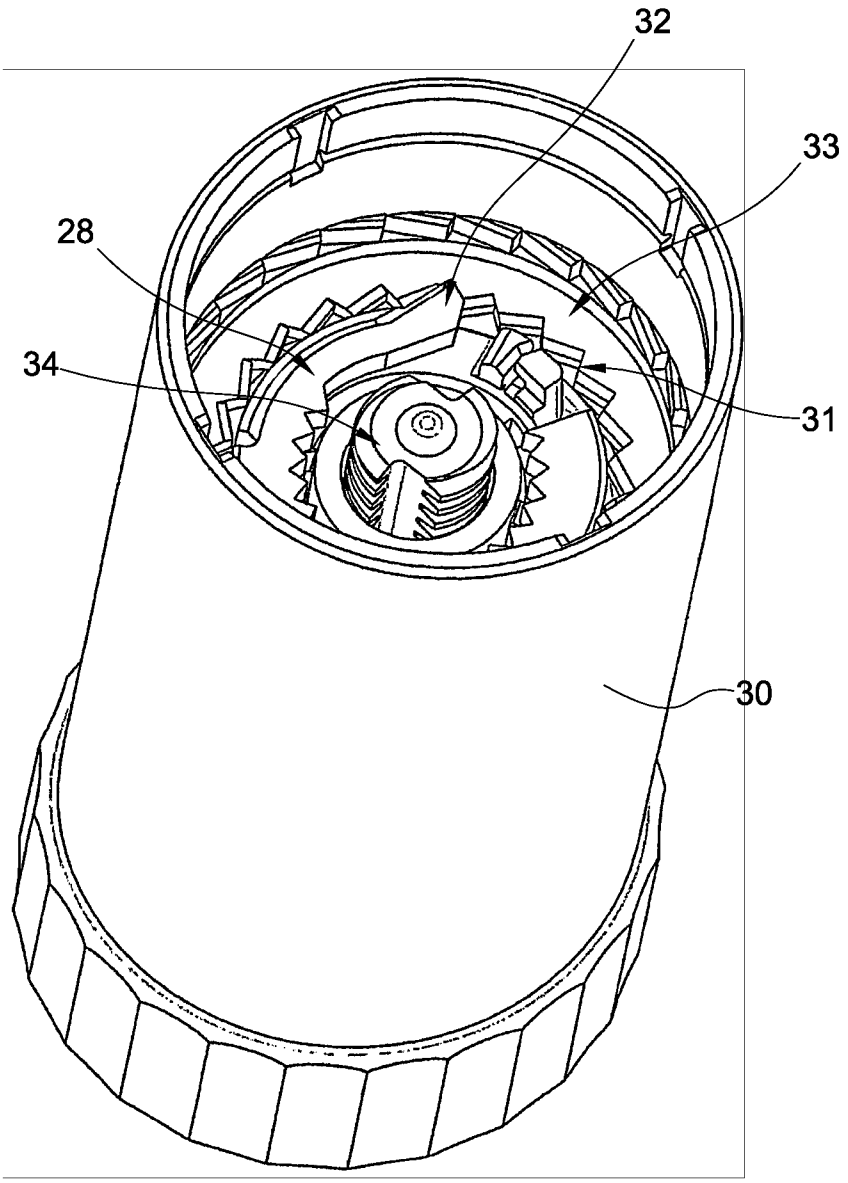

FIG. 9

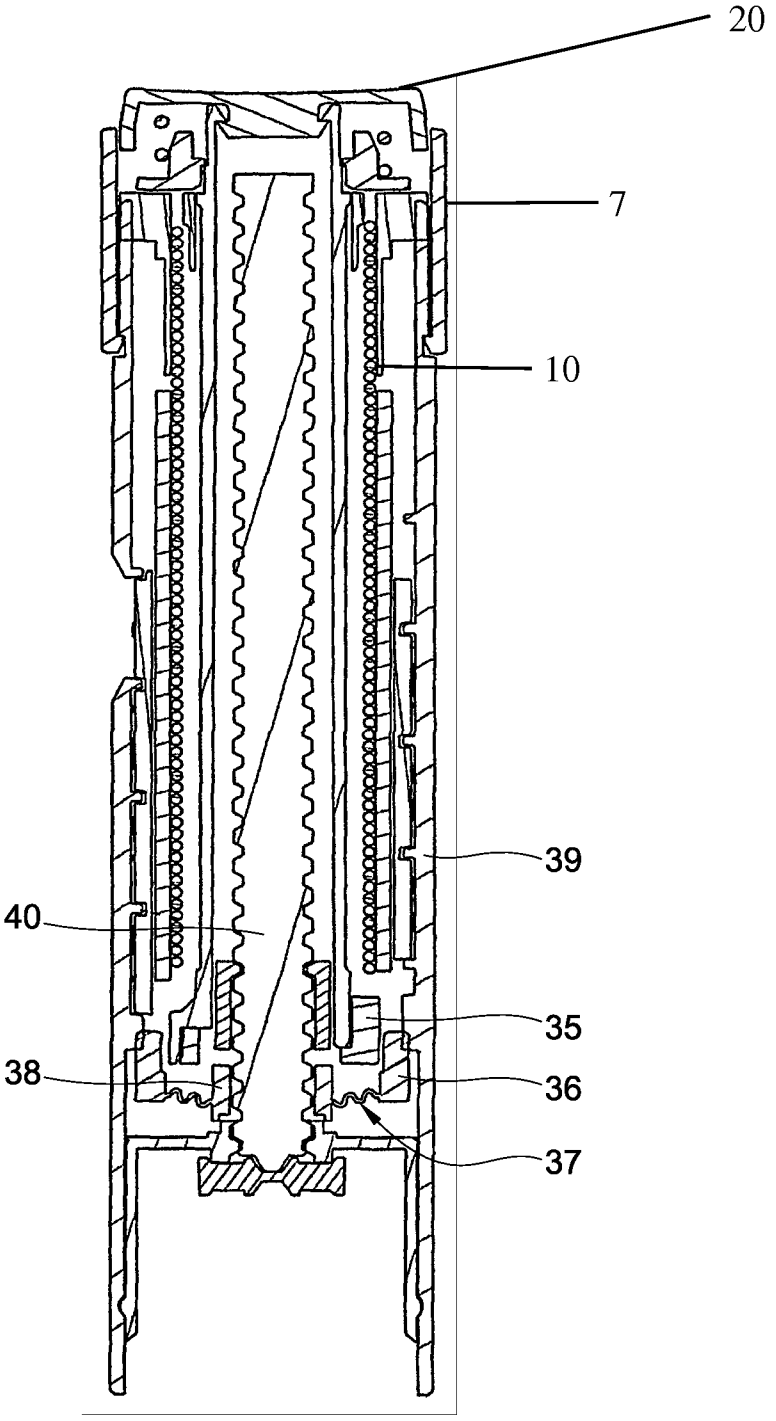

FIG. 10

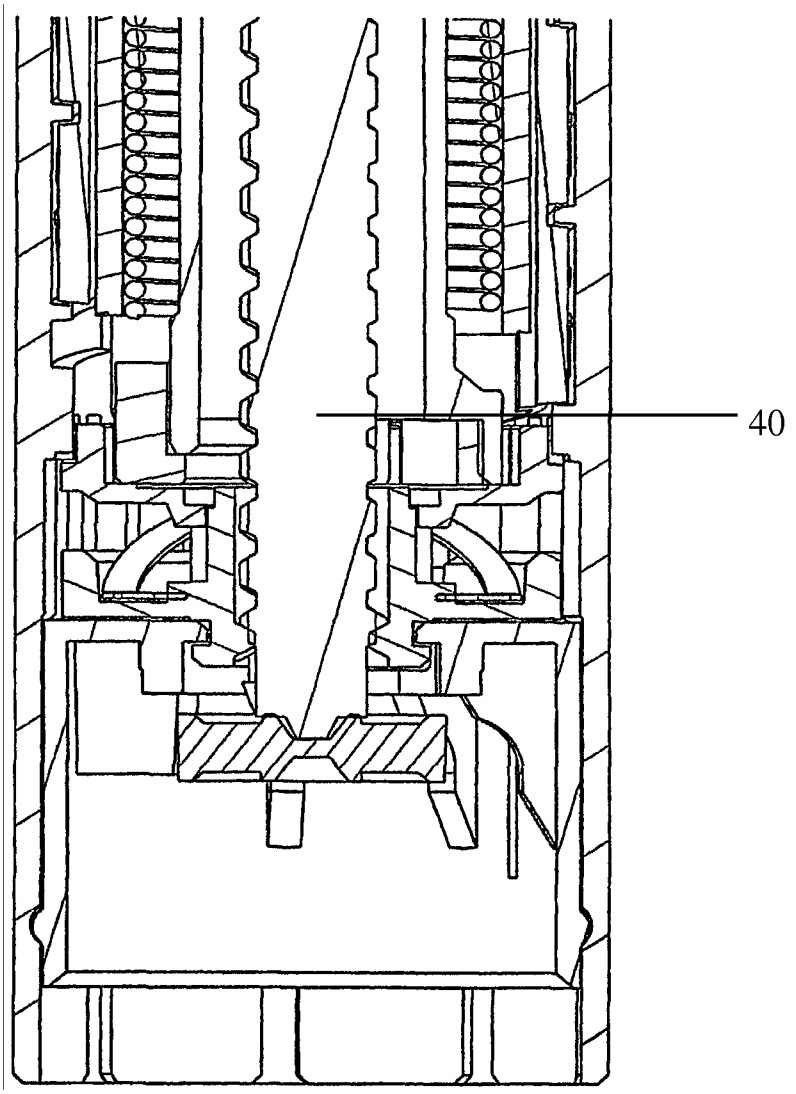

FIG. 11

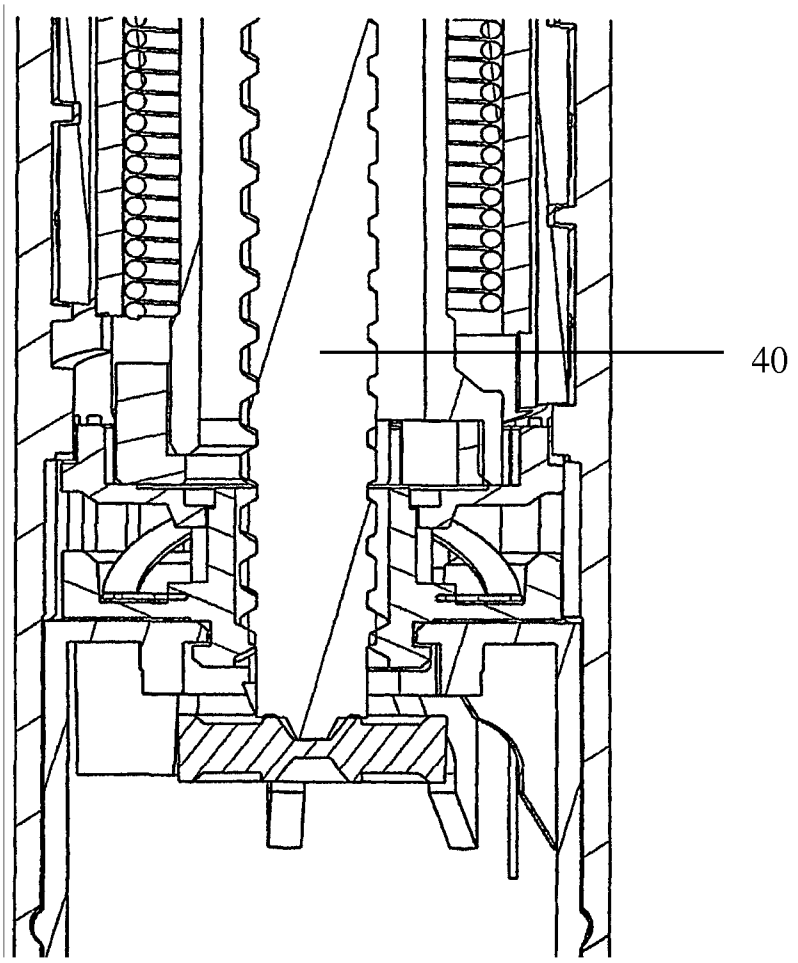

FIG. 12

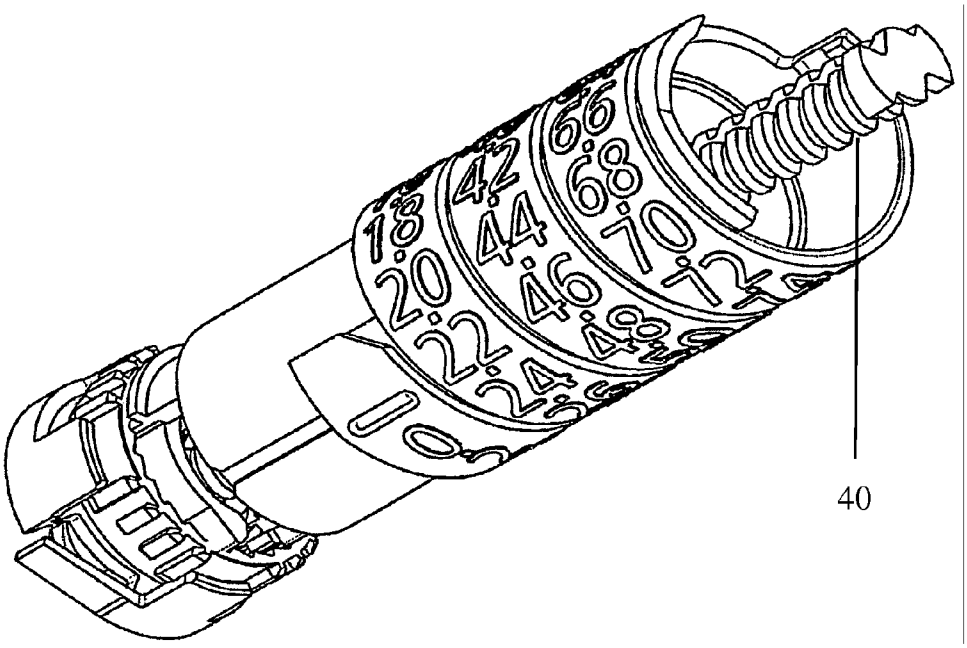

FIG. 13

AUTOMATIC INJECTION DEVICE WITH A TOP RELEASE MECHANISM

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 11/813,435 filed Jun. 2, 2008 (U.S. Pat. No. 8,096,978, issued Jan. 17, 2012) which is a 35 U.S.C. §371 national stage application of International Patent Application PCT/DK2006/000032 (published as WO 2006/076921), filed Jan. 20, 2006, which claimed priority of Danish Patent Application PA 2005 00113, filed Jan. 21, 2005; this application further claims priority under 35 U.S.C. §119 of U.S. Provisional Application 60/647,320, filed Jan. 26, 2005.

The present invention relates to an automatic and handheld mechanical injection device where an injection of a set dose of medicament is initiated by actuating a release member being arranged at or near the top of the injection device.

BACKGROUND OF THE INVENTION

Automatic injection devices have previously been disclosed in the patent literature. Automatic injection devices contain some sort of power reservoir where electrical or mechanical energy can be accumulated. The accumulated energy is easily released by actuating a release mechanism whereby the accumulated energy assists the user in injecting a set dose of medicine and/or assisting needle insertion.

For example, EP 0 516 473 A1 discloses an injection device having a needle which, when the device is operated, is first caused to project, then liquid is forced out through it, and finally the needle is automatically retracted. The needle extends forwardly from a capsule that can slide longitudinally within a barrel-like body, a relatively weak spring normally maintaining the capsule and needle retracted. A more powerful spring acts oppositely on a plunger which, when released, shoots the capsule forward by acting on the liquid therein, and then forces the liquid out through the projecting needle. At the end of the forward stroke the plunger and capsule are decoupled and the weak spring returns the exhausted capsule and its needle to the retracted position. The spring acting on the plunger can be released by a release button positioned on the outer surface of the injection device.

In WO 01/41838 discloses a handheld injection device by which set doses of a liquid medicament can be injected from a medical reservoir, such as cylinder ampoule, by release of a power reservoir in the device. The power reservoir can either be an electric battery by which a motor can be energized to press out a set dose of medicine, or a strained spring maintained in its strained position by a detent which spring when released can press out a set dose of medicine. When the power reservoir is released, the liquid medicine will be pressed out from the cylinder ampoule through an injection needle mounted on the cylinder ampoule or on the injection device carrying the cylinder ampoule. The power reservoir is released fully or partially by activating a release button, such as an electric switch, located on the housing of the injection device and in the distal half of the length of the injection device. By making at least a part of the distal third of the injection device of an ergonomic shaped cross section, the user can grip the injection device as a pencil is gripped by a thumb, an index finger and a long finger.

In both EP 0 516 473 A1 and WO 01/41838 the release buttons are positioned on an outer surface of the injection devices. In EP 0 516 473 A1 the release button is position on the outer side of the cylindrical body, whereas in WO 01/41838 the release button is positioned close to the injection needle of the injection device. However, it may be advantageous to position the release button or mechanism so that the injection device can be activated by providing a force to the upper region of the injection device—preferably to a release button or mechanism arranged axially with the injection device.

It is an object of the present invention to provide an automatic and handheld mechanical injection device having a combined release member and dose setting member.

It is a further object of the present invention to provide an automatic and handheld mechanical injection device where an injection of a set dose can be initiated using the thumb or the index finger of the hand handling the injection device by providing an axial force to an upper region of the injection device.

It is a still further object of the present invention to provide an automatic and handheld mechanical injection device having an exterior design very similar to conventional manual injection devices.

SUMMARY OF THE INVENTION

The above-mentioned objects are complied with by providing, in a first aspect, a handheld injection device by which set doses of a liquid medicament can be injected from a medical reservoir through an injection needle by release of a power reservoir in the device, the power reservoir being adapted to be fully or partially released by actuation of a user operable release member positioned at or near an upper end of the injection device, the upper end being that end of the injection device which is opposite the injection needle, the power reservoir being adapted to be powered by rotation of a rotatably mounted dose setting member.

The amount of power provided to the power reservoir may depend on the angle of rotation of the dose setting member. Thus, a rather limited rotation of the dose setting member provides a relatively small amount energy to the power reservoir, whereas a large rotation of the dose setting member provides a relatively large amount of energy to the power reservoir.

The release member may be positioned less than one fifth or one sixth of the length of the injection device from the upper end. Alternatively, the release member may be axially arranged relative to the injection device so that the release member forms a push button like release member on the top of the injection device.

The release member may be operatively connected to a dose setting member of the injection device in that the release member may engage the dose setting member via a key/keyway connection when the dose setting member is in a dose setting position. The release member may be released from the key/keyway connection with the dose setting member when the dose setting member is in a dose injecting position. With this arrangement, the handheld injection device has no rotating exterior parts or elements.

The power reservoir may be a resilient member, such as a torsion spring or a linear spring, the resilient member being, when released, adapted to press out a set dose of medicine from the medical reservoir through the injection needle. The release member may be operatively connected to a release mechanism adapted to release the resilient member when said release member is actuated. The release member may have a shape which is ergonomic shaped to be activated by a thumb or an index finger of the user.

The medical reservoir may be a cylindrical ampoule comprising a first and a second end of which the first end is closed

by a pierceable membrane which may be pierced by a first end of the injection needle when this needle is mounted on the device. The other end of the injection needle may be sharp so as to be able to pierce the skin at the position where an injection is to be made. The second end of the ampoule may be closed by a piston which may be forced into the ampoule so as to expel medicament through the needle.

The handheld injection device may further comprise a rotatably arranged drive member being adapted to at least partly engage with at least part of a drive track of an associated piston rod, the drive member being adapted to be positioned in a first axial position when the dose setting member is in a dose setting position, the drive member further being adapted to be positioned in a second axial position when the dose setting member is in a dose injection position, the drive member being adapted to release energy accumulated in the power reservoir when the drive member is in its second axial position.

The drive member may be adapted to rotate the associated piston rod upon releasing the accumulated energy in the power reservoir. However, in its first axial position, the drive member is prevented from rotating because the drive member engages at least part of a housing of the injection device. The injection device may further comprise a resilient member, such as a linear spring, for biasing the drive member in a direction towards the dose setting member. The linear spring operatively connects the drive member and the housing.

The dose setting member may be adapted to be moved a distance along an axial direction of the injection device so as to move the drive member between the first and second axial positions. The drive member may be adapted to be moved from the first to the second axial position by applying a force to the dose setting member, the force being applied along the axial direction of the injection device.

The injection device may, as already mentioned, further comprise a push button axially arranged with the dose setting member, the push button being adapted to engage with the dose setting member when the dose setting member is in its dose setting position, and disengage from the dose setting member when the dose setting member is in its dose injection position. By disengage is meant that the push button and the dose setting member are mutually rotatable when this disengaged state is reached. The injection device may further comprise a resilient member, such as a linear spring, for axially biasing the push button in a direction away from the drive member.

The handheld injection device may further comprise a rotatably mounted display member adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member, the rotatably mounted display member being rotatable over an angle corresponding to at least one revolution of the display member. The display member may comprise a dose indicator barrel having numerals arranged along a substantially helical path on an outer surface thereof. Alternatively or in addition, the display member may comprise a counting device having two or more display wheels having numerals arranged on an outer surface thereof.

The handheld injection device may further comprise the associated the piston rod, the piston rod having a threaded outer surface with the drive track arranged in a longitudinal direction of the outer surface of the piston rod. The drive member may be operatively connected to the dose setting member via a ratchet.

The power reservoir may be arranged between the housing and the dose setting member in such a way that when the dose setting member is rotated, energy is accumulated in the power reservoir. The power reservoir may comprise a torsion spring formed as a helical spring extending coaxially with the associated piston rod.

It is to be noted that the interaction between the drive member, the piston rod and the housing may be implemented in various ways. Above, the piston rod has a threaded outer surface and a drive track arranged in the longitudinal direction of the rod. A key arranged on the drive member engages the drive track of the rod and the forward movement of the rod relative to the housing is caused by the threaded outer portion of the rod which meshes with a corresponding threaded portion of the housing. Alternatively, the threaded outer surface of the rod may mesh with a corresponding threaded portion of the drive member whereas the drive track arranged in the longitudinal direction of the rod engages with a key fixedly arranged relative to the housing.

BRIEF DESCRIPTION OF THE INVENTION

The present invention will now be explained in further details with reference to the accompanying figures wherein

FIG. **1** shows an injection device according to the present invention where the release button arranged at the top of the device is activated by the thumb of the user,

FIG. **2** shows an injection device according to the present invention where the release button arranged at the top of the device is activated by the index finger of the user,

FIG. **3** shows an injection device according to the present invention where the release button is arranged on the top surface of the dose setting member, and where the drive member is in its locked position (dial position of dose setting member),

FIG. **4** shows an injection device according to the present invention where the release button is arranged on the top surface of the dose setting member, and where the drive member is in its released position (dosing position of dose setting member),

FIG. **5** shows an expanded view of the drive member in its released position,

FIG. **6** shows an expanded view of the release member in its locked position with the dose setting member,

FIG. **7** shows an expanded view of the release member in its released position with the dose setting member,

FIG. **8** shows an expanded view of the release member in a further released position where the dose setting member is allowed to rotate,

FIG. **9** shows one way of implementing the release mechanism for releasing the energized power reservoir,

FIG. **10** shows another way of implementing the release mechanism for releasing the energized power reservoir,

FIG. **11** shows a third way of implementing the release mechanism for releasing the energized power reservoir,

FIG. **12** shows a fourth way of implementing the release mechanism for releasing the energized power reservoir, and

FIG. **13** shows a fifth way of implementing the release mechanism for releasing the energized power reservoir.

While the invention is susceptible to various modifications and alternative forms, specific embodiments have been shown by way of example in the drawings and will be described in detail herein. It should be understood, however, that the invention is not intended to be limited to the particular forms disclosed. Rather, the invention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the appended claims.

DETAILED DESCRIPTION OF THE INVENTION

FIGS. **1** and **2** show the present invention in its most general aspect. In FIG. **1** a handheld injection device **1** is shown.

The injection device has an injection needle **2** fastened to one of its ends, whereas a release button **3** is arranged at the opposite end of the injection device. When the release button **3** is actuated by provided a force to it along the axial direction of the device energy is released from an internal power reservoir whereby a set dose of medicine is injected from the injection device. In FIG. **1** the release button is actuated by the thumb **4** of the user, whereas in FIG. **2** the release button is actuated by the index finger **5** of the user.

The medicine to be injected is contained in a medical reservoir typically formed as a cylindrical ampoule.

The energy released when the release button **3** is mechanical energy. The power reservoir can be a resilient member, such as a torsion spring, the resilient member being, when released, adapted to press out a set dose of medicine from the medical reservoir through the injection needle. The release button is operatively connected to some sort of release mechanism adapted to release the resilient member when the release button is actuated.

FIG. **3** shows a cross-sectional view of one embodiment of the present invention. The injection device shown in FIG. **3** comprises a housing **6**, a dose setting member **7**, a drive member **8**, a piston rod **9**, a torsion spring **10**, a biasing spring **11**, a cylindrical ampoule **12** and a release member **13**. FIG. **3** shows the injection device in a state where the dose setting member **7** is in its dose setting position.

A dose is set by rotating the dose setting member **7** a certain angle or a certain number of turns. By rotating the dose setting member **7** the torsion spring **10** is strained because the two ends of the torsion spring **10** are fixed to the housing **6** and to the dose setting member **7**, respectively. The dose setting member **7** is operatively connected to the drive member **8** via a ratchet (not shown). This ratchet prevents that the dose setting member **7** returns to its initial position upon straining the torsion spring **10**. Since the drive member **8** engages the housing **6** via a key/keyway connection or a gear wheel, the drive member **8** is not allowed to rotate relative to the housing **6** as long as the dose setting member **7** is in its dose setting position as illustrated in FIG. **3**. In order to keep the dose setting member **7** and the drive member **8** in the dose setting position, the drive member **8** and the dose setting member **7** is biased in a direction towards the top end of the injection device. This biasing is provided by a spring element, such as a linear spring **11**, arranged between the drive member **8** and part of the housing **6**. Thus, in order to release the drive member **8** from its engagement with the housing **6**, a force needs to be provided in order move the dose setting member **7** and the drive member **8** towards the medicine ampoule **12**. A miner cavity **14** ensures that this forward movement of the dose setting member **7** and the drive member **8** can be performed. Similarly, since the drive member **7** and the piston rod **9** engage via a key connection the drive member **8** is allowed to move axially relative to the piston rod **9**.

The drive member **8** has been released from its engagement with the housing **6** in FIG. **4**. In order to achieve this releasing a force, indicated by arrow **15**, has been provided to the release member **13** whereby the release member **13**, the dose member **7** and the drive member **8** have all been moved a distance towards the medicine ampoule **12**. The force indicated by arrow **15** would normally be provided by the thumb or the index finger of the user.

As seen in FIG. **4** the engaging region **16** of the housing is now separated from the engaging region **17** of the drive member **8**. This disengagement allows that the strained torsion spring **10** can release its energy to the dose setting member **7**. The dose setting member **7** and the drive member **8** are fixedly related via the intermediate ratchet (not shown). Thus, when a disengagement between engaging regions **16** and **17** has been established, the dose setting member **7** and the drive member **9** will rotate until the torsion spring **10** reaches an unstrained state. Since the drive member **8** and the piston rod **9** is connected via a key connection the rotation of the dose setting member **7** and the drive member **8** will cause the piston rod **9** to rotate as well. The piston rod **9** has an outer threaded surface which engages with a corresponding threaded portion **18** of the housing whereby the piston rod **9**, upon rotation thereof, will perform a translational movement along the axial direction of the injection device in the direction of the ampoule **12**.

Thus, the force provided to the release member **13** will release accumulated energy in the torsion spring. This energy is converted to a translational movement of the piston rod towards the ampoule whereby a set dose of medicine can be injected from the injection device.

FIG. **5** shows a cut half illustration of the housing **6** of the injection device. As seen, the drive member **8** comprises an engagement region/part **17** formed as gear wheel. Similarly, the housing **6** comprises a corresponding engagement region/part **16** adapted to receive and engage with the teeth of the gear wheel **17**.

FIG. **6** shows another embodiment of the present invention. In contrast to the embodiment shown in FIGS. **3-5** the embodiment shown in FIG. **6** contains no rotating exterior parts or elements. All rotating parts or elements are positioned inside the housing **19**. FIG. **6** shows a release member **20** (formed as a push button) which is mechanically biased towards the end of the injection device by spring element **22**. The release member **20** and dose setting member **21** are forced into engagement as long as the dose setting member **21** is in its dose setting position. The dose setting member **21** is mechanically biased towards the same end of the injection device as the release member **20** due to a spring element (shown as spring element **11** in FIG. **3**) acting on the drive member (shown as drive member **8** in FIG. **3**) which again acts on dose setting member **21**. As seen in FIG. **6** the dose setting member **21** is biased against a mechanical stop **24** where a shoulder formed in the dose setting member **21** abuts a part of the housing **19**.

In FIG. **7** an intermediate stage is illustrated. Here the release member **20** has been pushed an axial distance sufficient to release the release member **20** from the dose setting member **21**. Note that the engagement region **25** and **26** are disengaged, but since the shoulder of the dose setting member still abuts the housing part no axial movement of the dose setting member **21** has been achieved at this stage. Thus, the dose setting member **21** is prevented from rotating since the drive member (not shown) is still engaging the housing.

In FIG. **8** the dose setting member **21** has been moved an axial distance towards the ampoule (not shown) whereby the dose setting member is allowed to rotate freely causing the piston rod **27** push a set dose of medicine out of the ampoule (not shown). Note that the release member **20** and the dose setting member **21** are disengaged in FIG. **8**. This means that the release member **20** is not rotating relative to the housing during injection of a set dose. Then the set dose has been injected the user removes his thumb or index finger from the release member whereby the release member and the dose setting member return to their respective positions as illustrated in FIG. **6**, but now with the spring element **23** being in a relaxed state.

In case the user wants to set a new dose, the user rotates the release member which engages the dose setting member whereby the new dose can be set. Injecting the set dose is achieved by following the steps illustrated in FIGS. **7** and **8**.

FIGS. **9-13** show various embodiments of release mechanisms for releasing the energized power reservoir.

In FIG. **9** a torsion spring (not shown) is energized by rotating a ratchet **28** which is operatively connected to the housing **30** of the injection device when the dose to be injected is being set. In the dose setting position the ratchet **28** is operatively connected with housing part **31** via ratchet arm **32**. Energy accumulated in the torsion spring is released by displacing the ratchet **28** axially whereby it is released from its connection with housing part **31** in that the ratchet arm **32** is moved into housing part **33** whereby the piston rod **34** is allowed to rotate thereby expelling a set dose of medicament.

In the embodiment depicted in FIG. **9** a dose indicator barrel (not shown) moves in the direction away from the push-button (not shown) during setting of a dose. Obviously, the dose indicator barrel may be adapted to move in the opposite direction during setting of a dose, i.e. towards the push-button.

In the embodiment depicted in FIG. **10** the ratchet **35** is only in indirect operation with the housing **39**. The drive member of the embodiment depicted in FIG. **10** is constituted by three part—one part **36** being adapted to corporate with the housing **39**, another part **38** being adapted to drive the piston rod **40** and a flexible member **37** connecting parts **36** and **38**. The flexible member **37** is flexible in the axial direction but establishes a substantially stiff connection between parts **36** and **38** when these parts are rotated relative to each other. Thus, the flexible member **37** ensures that parts **36** and **38** are not rotatably arranged relative to each other. Thus, when the ratchet **35** is moved towards the needle end of the injection device the part **36** is disconnected from the housing **39** whereby parts **36**, **37** and **38** are allowed to rotate thereby rotating the piston rod **40**. The rotating piston rod **40** causes a set dose of medicament to be expelled from the injection device.

The embodiment depicted in FIG. **11** is similar to the embodiment in FIG. **9** except that the piston rod is moved forward by having guiding tracks arranged in the housing (instead of in the drive member) and a threaded engagement between piston rod and the drive member (instead of a threaded engagement between piston rod and housing).

FIGS. **12** and **13** show other release mechanisms between ratchet, drive member and housing.

The invention claimed is:

1. A handheld injection device, comprising:

a rotatable dose setting member that is rotatable about a longitudinal axis of a housing of the injection device;

a power reservoir, comprising a torsion spring for storing energy to expel a dose from the injection device;

a piston rod;

a release member, located at the most proximal portion of the device, opposite an end of the device wherein a needle may be mounted;

the injection device, further comprising a rotatably arranged multi-component driver (**36**, **37**, **38**) having at least a part (**38**) that at least partly engages with at least part of a drive track of an associated piston rod, and a further part (**36**) being axially movable into a position disconnected from the housing thus releasing energy accumulated in the power reservoir, the further part (**36**) being axially movable by the user applying a force onto a generally planar surface of the release member, wherein the generally planar surface is generally perpendicular to a longitudinal direction of the piston rod in the device.

2. An injection device comprising:

a housing;

a drive member;

a piston rod having a longitudinal direction;

a torsion spring for storing energy to drive a dose from the injection device;

a drive mechanism converting relative rotational motion into axial movement of the piston rod;

a release button located at the most proximal end of the device, opposite an end of the device wherein a needle may be mounted, the release button having a generally planar surface that is generally perpendicular to the longitudinal direction of the piston rod.

* * * * *

EXHIBIT E

US009132239B2

(12) **United States Patent**
Møller et al.

(10) **Patent No.: US 9,132,239 B2**
(45) **Date of Patent: Sep. 15, 2015**

(54) **DIAL-DOWN MECHANISM FOR WIND-UP PEN**

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A61M 5/20	(2006.01)

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CPC ***A61M 5/31525*** (2013.01); *A61M 5/20* (2013.01); *A61M 5/3156* (2013.01); *A61M 5/31553* (2013.01)

(58) **Field of Classification Search**
CPC A61M 5/00; A61M 5/3129; A61M 5/24; A61M 5/2033; A61M 5/3287; A61M 5/32; A61M 5/178; A61M 2005/206
USPC 604/187, 136, 272, 164.11
See application file for complete search history.

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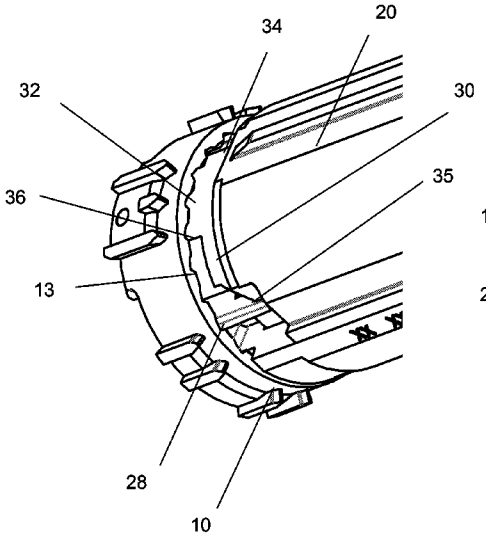
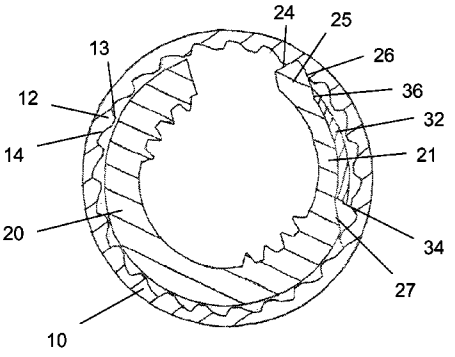
Primary Examiner — Scott Medway
(74) *Attorney, Agent, or Firm* — Wesley Nicolas

(57) **ABSTRACT**

The present invention relates to a dial-down mechanism for an injection device comprising a torsion spring for assisting injection of a dose of medicament from the injection device, the dial-down mechanism comprising a ratchet arm (**21**) engaging a ring element (**10**) and a reset element (**30**) which acts on a knob located on the periphery of the ratchet arm (**21**) to move the ratchet arm (**21**) out of engagement with the ring element (**10**) in order to allow the set dose to be reduced.

3 Claims, 3 Drawing Sheets





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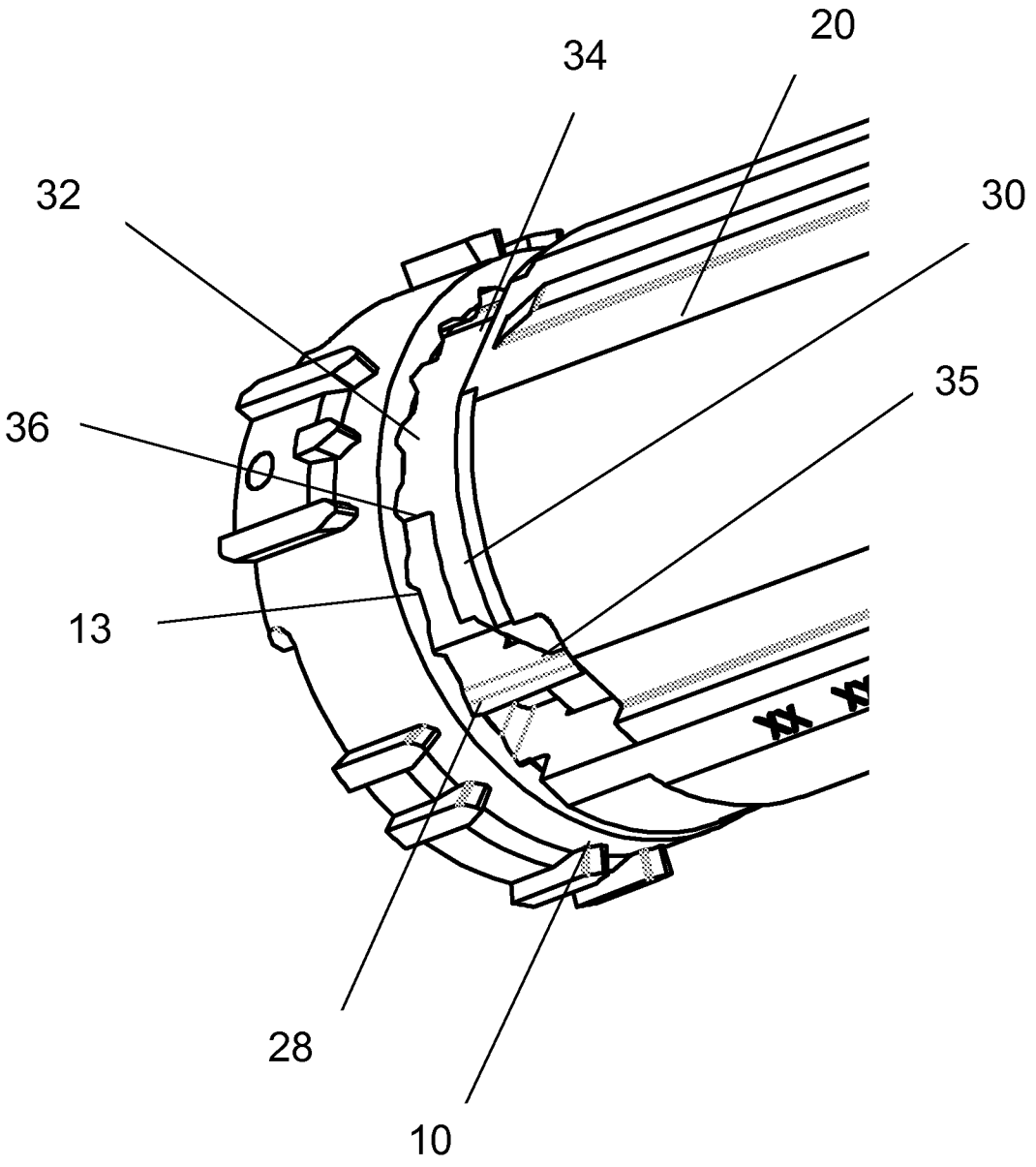

Fig. 1

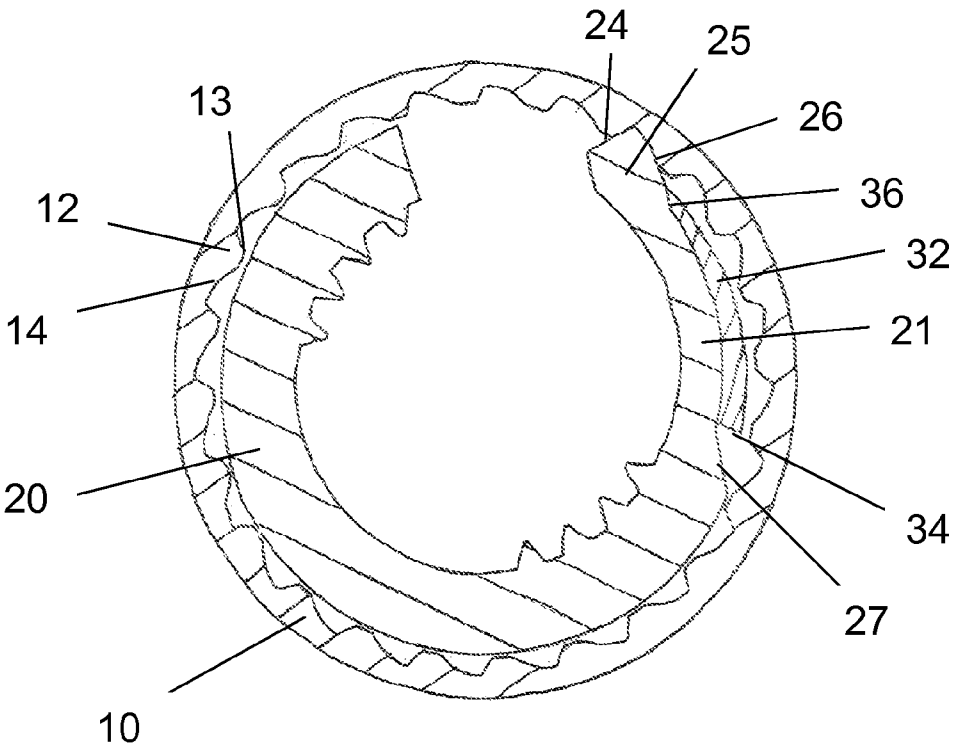

Fig. 2

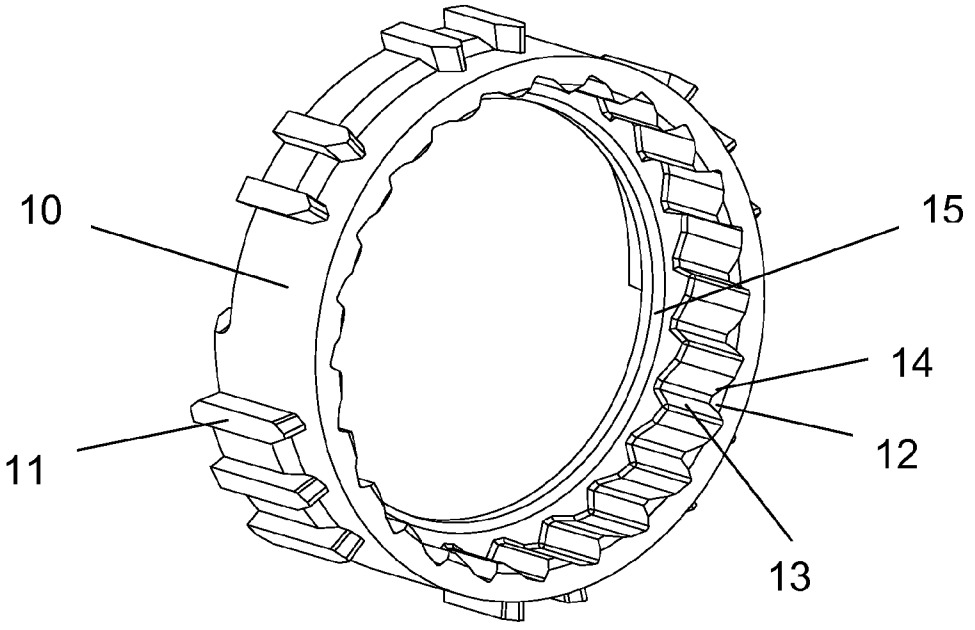

Fig. 3

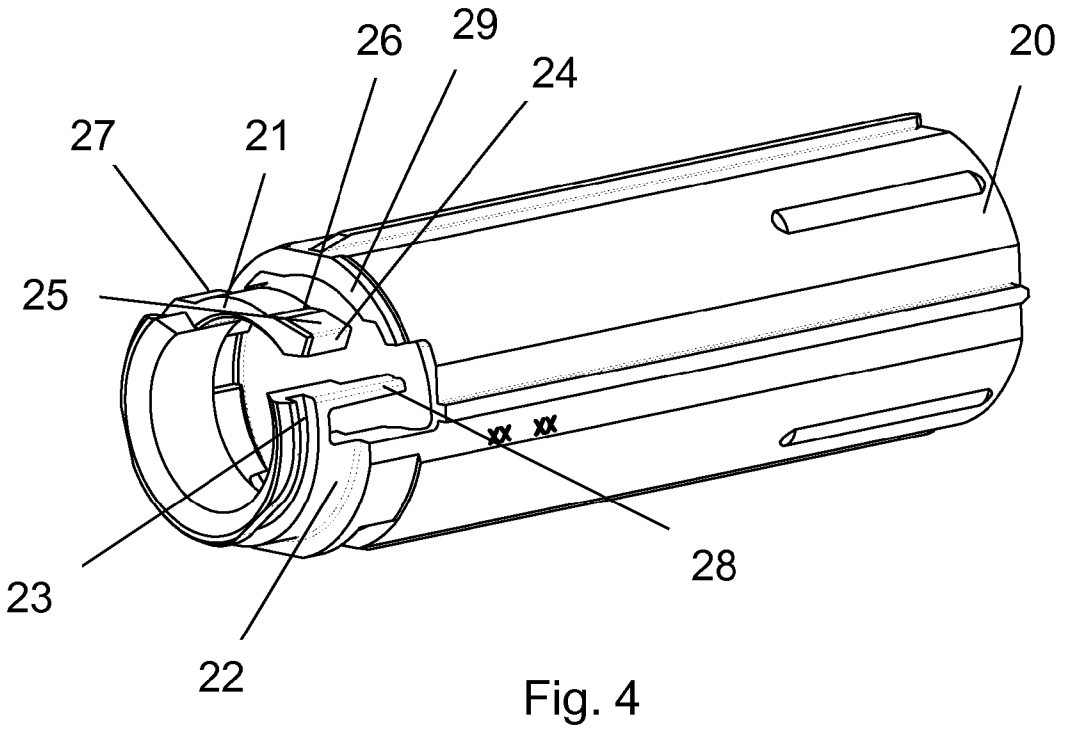

Fig. 4

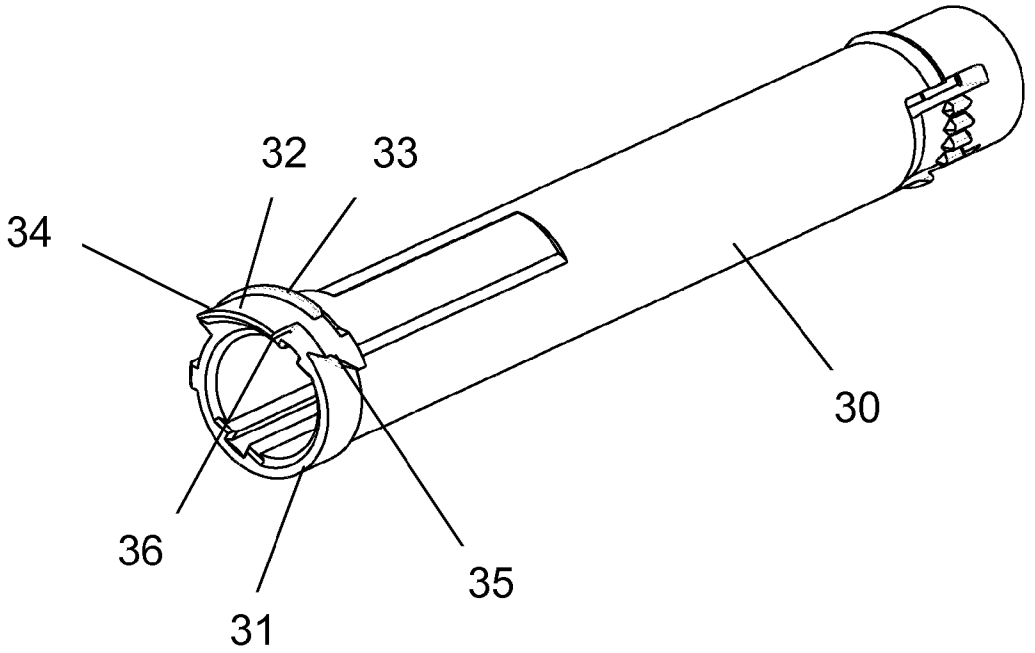

Fig. 5

DIAL-DOWN MECHANISM FOR WIND-UP PEN

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a 35 U.S.C. §371 national stage application of International Patent Application PCT/EP2009/063801 (published as WO 2010/046394), filed Oct. 21, 2009, which claimed priority of European Patent Application EP 08167547.2, filed Oct. 24, 2008; this application further claims priority under 35 U.S.C. §119 of U.S. Provisional Application 61/109,242, filed Oct. 29, 2008.

THE TECHNICAL FIELD OF THE INVENTION

The present invention relates to a dial-down mechanism for automatic wind-up pens. In particular, the present invention relates to an integrated dial-down mechanism for a torsion spring assisted wind-up pen.

DESCRIPTION OF RELATED ART

In known injection devices, such as wind-up pens, based on torsion springs, the user usually strains the torsion spring by rotating a rotatable dose setting member of the injection device. The force thereby applied by the user is stored in the torsion spring for later release.

An example of a known wind-up pen applying a torsion spring may for example be found in U.S. Pat. No. 5,104,380. In this wind-up pen the dose setting member is located at the proximal end and works such that when the user rotates the dose setting member the spring is strained. The wind-up pen disclosed in U.S. Pat. No. 5,104,380 has the disadvantage that if a user sets a dose to large it is not possible to decrease the set dose. The user then has to release the latch mechanism thereby expelling the entire set dose before a new correct dose can be set and delivered.

Modern injection devices as the one e.g. disclosed in U.S. Pat. No. 6,004,297 has the possibility of rotating the dose setting member in an opposite direction and thereby reduce the set dose prior to deliverance of the set dose. Such mechanism is usually referred to as a dial-up/dial-down mechanism since it can both increase and decrease the set dose prior to injection.

Such dial-up/dial-down mechanism for a spring-loaded injection pen is known from WO 02/053214.

A wind-up pen based on a torsion spring and with a dial-up/dial-down mechanism is further disclosed in WO 2006/045526. The mechanism described in this document is based on a number of cam and key engagements. When working within small dimensions as in injection devices it has shown that such small dimensioned cam and key parts has a tendency to break during manufacture or during use.

DESCRIPTION OF THE INVENTION

It is an object of the present invention to provide a dial-down mechanism for automatic wind-up pens which is more robust and less vulnerable to breakage.

The ratchet arm provided on the dose setting tube engages one or more teeth on the fixation element. Further the ratchet arm is provided with a radially extending knob or the like which when moved radial inwardly moves the ratchet arm out of its engagement with the fixation element. The knob on the ratchet arm is moved inwardly by a reset element provided on a reset tube. Once the reset element sweeps over the knob it moves the ratchet arm inwardly. By having the reset element of the reset member work directly on the periphery of the knob and having the knob extend into the orbit described by the reset element small parts engaging each other can be avoided. The reset element can have many different shapes as long as it has the ability to move the ratchet arm out of engagement with the fixation element. Preferably the reset element is a prolongation on the reset tube extending distally from the reset tube such that the predominant part of the reset tube can be housed inside the dose setting tube but with the reset element extending out of the dose setting tube. The engagement between the knob of the ratchet arm and the reset element is designed such that a relative rotation between these two parts results in a inwardly radial movement of the ratchet arm which then is moved out of engagement with the teeth of the fixation element. The fixation element is preferably coupled to the housing of the injection device in a non-rotatable manner through engaging fins located on the external surface of the fixation element. These fins are rotational locked in similar grooves provided on the inside surface of the housing or an element functionally working as a part of the housing, however the fixation element can be moved axially out of its engagement with the housing and into an engagement with a drive element such that the torsional force accumulated in the torsion spring can be delivered to this drive element in order to drive a liquid out of the injection device.

Preferably, the reset element is rotated around the centre axis of the injection pen with a constant radius while the ratchet arm has its knob extending beyond this diameter such that the reset element can be brought into engagement with the knob whereby the ratchet arm is moved out of engagement with the fixation element.

Further the ratchet arm is provided with a steep surface on its free end which engages a steep surface of a tooth of the fixation element. When these two steep surfaces are brought out of engagement, the two elements can rotate relatively to each other.

DEFINITIONS

An "injection pen" is typically an injection apparatus or device having an oblong or elongated shape somewhat like a pen for writing. Although such pens usually have a tubular cross-section, they could easily have a different cross-section such as triangular, rectangular or square or any variation around these geometries.

As used herein, the term "medicament" or "drug" is meant to encompass any drug-containing flowable medicine capable of being passed through a delivery means such as a hollow needle in a controlled manner, such as a liquid, solution, gel or fine suspension. Representative drugs includes pharmaceuticals such as peptides, proteins (e.g. insulin, insulin analogues and C-peptide), and hormones, biologically derived or active agents, hormonal and gene based agents, nutritional formulas and other substances in both solid (dispensed) or liquid form.

All references, including publications, patent applications, and patents, cited herein are incorporated by reference in their entirety and to the same extent as if each reference were individually and specifically indicated to be incorporated by reference and were set forth in its entirety herein.

All headings and sub-headings are used herein for convenience only and should not be constructed as limiting the invention in any way.

The use of any and all examples, or exemplary language (e.g. such as) provided herein, is intended merely to better illuminate the invention and does not pose a limitation on the

scope of the invention unless otherwise claimed. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the invention.

The citation and incorporation of patent documents herein is done for convenience only and does not reflect any view of the validity, patentability, and/or enforceability of such patent documents.

This invention includes all modifications and equivalents of the subject matter recited in the claims appended hereto as permitted by applicable law.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be explained more fully below in connection with a preferred embodiment and with reference to the drawings in which:

FIG. **1** Show an example of the dial-down mechanism.

FIG. **2** Show a sectional view of the dial-down mechanism.

FIG. **3** Show a view of the fixation element in a ring-shaped configuration.

FIG. **4** Show a view of the ratchet tube.

FIG. **5** Show a view of the reset tube.

The figures are schematic and simplified for clarity, and they just show details, which are essential to the understanding of the invention, while other details are left out. Throughout, the same reference numerals are used for identical or corresponding parts.

DETAILED DESCRIPTION OF EMBODIMENT

When in the following terms as "upper" and "lower", "right" and "left", "horizontal" and "vertical", "clockwise" and "counter clockwise" or similar relative expressions are used, these only refer to the appended figures and not to an actual situation of use. The shown figures are schematic representations for which reason the configuration of the different structures as well as there relative dimensions are intended to serve illustrative purposes only.

In that context it may be convenient to define that the term "distal end" in the appended figures is meant to refer to the end of the dial down mechanism including the ring shaped element **10** whereas the term "proximal end" is meant to refer to the opposite end pointing away from the ring shaped element **10**.

The dial down mechanism disclosed in FIG. **1** comprises of three parts, a fixation element or ring **10**, a dose setting element or ratchet tube **20** and a reset tube **30**.

The ring **10** as disclosed in FIG. **3** has on its outside surface a number of engaging means such as fins **11** by which the ring **10** is non-rotatable coupled to a not shown housing of an injection device. The ring **10** could alternatively be attached to the housing in a number of different ways, however, as explained later the ring shaped element **10** must be able to move axially relatively to the housing.

On its inside surface the ring **10** is provided with a plurality of teeth **12** which has a steep edge **13** in one direction and a sloped edge **14** in the opposite direction such that the ratchet arm **21** of the ratchet tube **20** is prevented from rotating in one direction but is allowed to rotate in the opposite direction. This is best seen in FIG. **2**.

The ratchet tube **20** disclosed in details on FIG. **4** has on its distal end a circular part with a peripheral outer surface **22** that fits into the inside of the ring **10**. This outer surface **22** is provided with a circular recess **23** which is engaged with a similar circular element **15** on the ring **10** such that the ring **10** and the ratchet tube **20** is locked to each other in the axial direction but can be rotated relatively to each other.

The peripheral outer surface **22** is provided with a flexible ratchet arm **21** which terminates in a steep surface **24**. The ratchet arm **21** is on its peripheral surface provided with an outwardly pointing protrusion **25** which opposite the steep surface **24** which steep surface **24** also incorporates the protrusion **25** has a sloped surface **26** which slopes down to the ratchet arm **21**.

Once the ratchet tube **20** and the ring **10** is engaged as disclosed in FIG. **1** the steep surface **24** of the ratchet arm **21** engages the steep edge **13** on the ring **10** such that the ratchet tube **20** can only be rotated relatively to the ring **10** in one direction which in FIG. **1** is in the clockwise direction.

The ratchet tube **20** is engaged with a not shown torsion spring which at its opposite end is connected to the housing of the injection device such that when the ratchet tube **20** is rotated in the clockwise direction (seen from a proximal position) the torsion spring is strained and is held in this strained position by the engagement between the steep surface **24** of the ratchet arm **21** and the steep edge **13** of the teeth **12** on the ring **10**.

In this way a user can strain the torsion spring and thereby set a dose by rotating the ratchet tube **20** relatively to the ring **10** in the clockwise direction and the described engagement **24**, **13** makes it impossible for the torsion spring to rotate back the ratchet tube **20**.

In order to provide a possibility for the user to dial down the set dose, a reset tube **30** is provided. In relation to FIG. **5** the reset tube **30** is provided with an extended portion **31** which has a forwardly pointing reset element **32** which follows the periphery of the extended portion **31**.

Once the injection device is assembled the reset tube **30** is fitted inside the ratchet tube **20** such that the reset element **32** is located above the ratchet arm **21** as depictured in FIGS. **1** and **2**. In this position the axial engagement between the ratchet tube **20** and the reset tube **30** is secured by the protrusion **33** of the reset tube **30** engaging in front of the front surface **29** of the ratchet tube **20**.

The extended portion **31** of the reset tube **30** is further provided with a first surface **34** in the clockwise direction and a second surface **35** in the anti-clockwise direction. Further, the reset element **32** is provided with a reset surface **36** in the anti-clockwise direction.

The first surface **34** engages a similar dial-up surface **27** on the ratchet tube **20** such that rotation of the reset tube **30** is clockwise direction is transformed directly to the ratchet tube **20** meaning that when a user dials the reset tube **30** in the clockwise direction to set a dose the ratchet tube **20** follows this rotation and rotates relatively to the ring **10**.

The second surface **35** engages a spring element **28** urging the reset tube **30** in the clockwise direction whereas the reset surface **36** of the reset element **32** engages the sloped surface **26** of the protrusion **25** of the ratchet arm **21**.

When setting a dose as explained above the user rotates the reset tube **30** which rotation is passed on to the ratchet tube **20** which again is allowed to rotate relatively to the ring **10** in the clockwise direction thereby straining the torsion spring.

When a user regrets the set dose and wants to decrease the set dose this is done by rotating the reset tube **30** in the anti-clockwise direction. By doing so—as depictured in FIG. **2**—the reset surface **36** is pressed against the sloped surface **26** of the protrusion **25** which pulls the steep surface **24** out of engagement with the steep edge **13** of the teeth **12**. This allows the torsion spring to be released and force the ratchet tube **20** in the anti-clockwise direction. Due to the size of the torque stored in the torsion spring, the ratchet tube **20** will be

moved faster than the reset tube **30** whereby the sloped surface **26** of the protrusion **25** will no longer have the pressure of reset surface **36** resting on it and the flexible ratchet arm **21** will flex to its initial position and the steep surface **24** will engage the next steep edge **13** of the next teeth **12**. By a continued anti-clockwise rotation of the reset tube **30**, the steep surface **24** will move from teeth **12** to teeth **12** in a continued movement thereby lowering the torque stored in the torsion spring.

Once the correct setting is obtained the torque stored in the torsion spring is released by axially moving the ring **10** out of engagement with the housing, whereby the torsion spring rotates back all three elements **10**, **20**, **30**.

Some preferred embodiments have been shown in the foregoing, but it should be stressed that the invention is not limited to these, but may be embodied in other ways within the subject matter defined in the following claims, e.g. could a needle assembly as herein described be delivered to the user in a rigid and sterile container which further could be shaped as a tool for assisting the user in mounting the needle assembly on to the injection device.

The invention claimed is:

1. A dial-down mechanism for an injection device comprising a torsion spring which is strained when setting a dose by rotating a dose setting member (**20**) relatively to a housing in a first direction, and unstrained when rotating the dose setting member (**20**) in a second direction opposite the first direction, the torsion spring for storing energy to expel a dose from the injection device, the dial-down mechanism comprising:

a fixation element (**10**) coupled to the housing and having a plurality of inwardly pointing teeth (**12**),

at least one ratchet arm (**21**) coupled to the dose setting member (**20**),

wherein the at least one ratchet arm (**21**) engages the teeth (**12**) of the fixation element (**10**) and is shaped such that the dose setting member (**20**) is prevented from rotating in the second direction when the ratchet arm (**21**) engages the teeth (**12**) of the fixation element (**10**),

the dial-down mechanism further comprises a reset member (**30**) configured for movement in a first direction and a second direction opposite the first direction, such that rotation of the reset member (**30**) in the first direction to set a dose is transformed directly to the dose setting member (**20**) and thereby rotates relatively to the fixation element (**10**), and rotation of the reset member (**30**) in the second direction activates the ratchet arm (**21**) to disengage the fixation element (**10**) and thereby allow the dose setting member (**20**) to rotate in the second direction by carrying at least one forward extending reset element (**32**) located distally to the reset member (**30**) and which acts on at least one part (**25**) of the ratchet arm to move the ratchet arm (**21**) out of engagement with the teeth (**12**) of the fixation element (**10**) thereby dialing down the set dose, wherein

the reset member (**30**) is at least partially provided inside the dose setting tube (**20**) and axially retained by the dose setting member (**20**), and

the ratchet arm (**21**) carries at least part (**25**) extending radially from the at least one ratchet arm (**21**) and having an outer radius from the centre axis of the injection device larger than the outer radius of the remaining part of the ratchet arm (**21**).

2. A dial-down mechanism according to claim **1**, characterized in that, the reset element (**32**) travels along a constant radius from the centre axis of the injection device when rotated.

3. A dial-down mechanism according to claim **1**, characterized in that, the ratchet arm (**21**) is provided with a steep surface (**24**) engaging a steep surface (**13**) of the teeth (**12**) of the fixation element (**10**).

* * * * *

EXHIBIT F

US009457154B2

(12) **United States Patent**
Moller et al.

(10) **Patent No.: US 9,457,154 B2**
(45) **Date of Patent: Oct. 4, 2016**

(54) **INJECTION DEVICE WITH AN END OF DOSE FEEDBACK MECHANISM**

(75) Inventors: **Claus Schmidt Moller**, Fredensborg (DK); **Bo Radmer**, Hillerod (DK); **Lars Ulrik Nielsen**, Virum (DK); **Christian Peter Engaard**, Vejby (DK)

(73) Assignee: **Novo Nordisk A/S**, Bagsvaerd (DK)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 615 days.

(21) Appl. No.: **11/813,389**

(22) PCT Filed: **Jan. 20, 2006**

(86) PCT No.: **PCT/EP2006/000486**

§ 371 (c)(1),
(2), (4) Date: **Jul. 9, 2008**

(87) PCT Pub. No.: **WO2006/079481**

PCT Pub. Date: **Aug. 3, 2006**

(65) **Prior Publication Data**

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Related U.S. Application Data

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(30) **Foreign Application Priority Data**

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(51) **Int. Cl.**
A61M 5/315 (2006.01)
A61M 5/24 (2006.01)
A61M 5/20 (2006.01)

(52) **U.S. Cl.**
CPC ***A61M 5/3157*** (2013.01); ***A61M 5/3155*** (2013.01); *A61M 5/20* (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC .. A61M 5/24; A61M 5/31551; A61M 5/315; A61M 5/31541; A61M 5/3155; A61M 5/31593; A61M 5/31535; A61M 2205/582; A61M 2205/583; A61M 5/3157; A61M 5/20; A61M 5/31561; A61M 5/31585; A51M 2205/581
USPC 604/118, 186, 189, 207–211, 232, 246, 604/260
See application file for complete search history.

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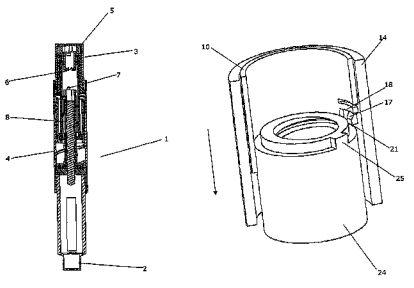
Primary Examiner — Emily Schmidt
Assistant Examiner — Lauren M Peng
(74) *Attorney, Agent, or Firm* — Wesley Nicholas

(57) **ABSTRACT**

An injection device with a dose delivering mechanism being adapted to provide a non-visual, e.g. audible and/or tactile, feedback signal when a set dose has been at least substantially injected. A first and a second part of the injection device are adapted to perform a relative rotational movement with respect to each other. The relative rotational movement causes at least two parts of the injection device to abut or engage, and this abutment or engagement causes the non-visual feedback signal to be generated. A very distinct and precise feedback is provided as compared to prior art axial solutions because the generation of the feedback signal is initiated by the relative rotational movement. Feedback signal may be generated by a change in a rotational velocity of at least one part, e.g. by changing the pitch of a threaded portion or by engaging a non-rotating part and a rotating part, thereby causing the non-rotating part to start rotating. May alternatively be generated by building up and releasing a tension. The injection device is suitable for injecting insulin.

17 Claims, 14 Drawing Sheets



(52) **U.S. Cl.**
CPC *A61M 5/24* (2013.01); *A61M 5/31535* (2013.01); *A61M 5/31551* (2013.01); *A61M 5/31561* (2013.01); *A61M 5/31585* (2013.01); *A61M 2205/581* (2013.01); *A61M 2205/582* (2013.01)

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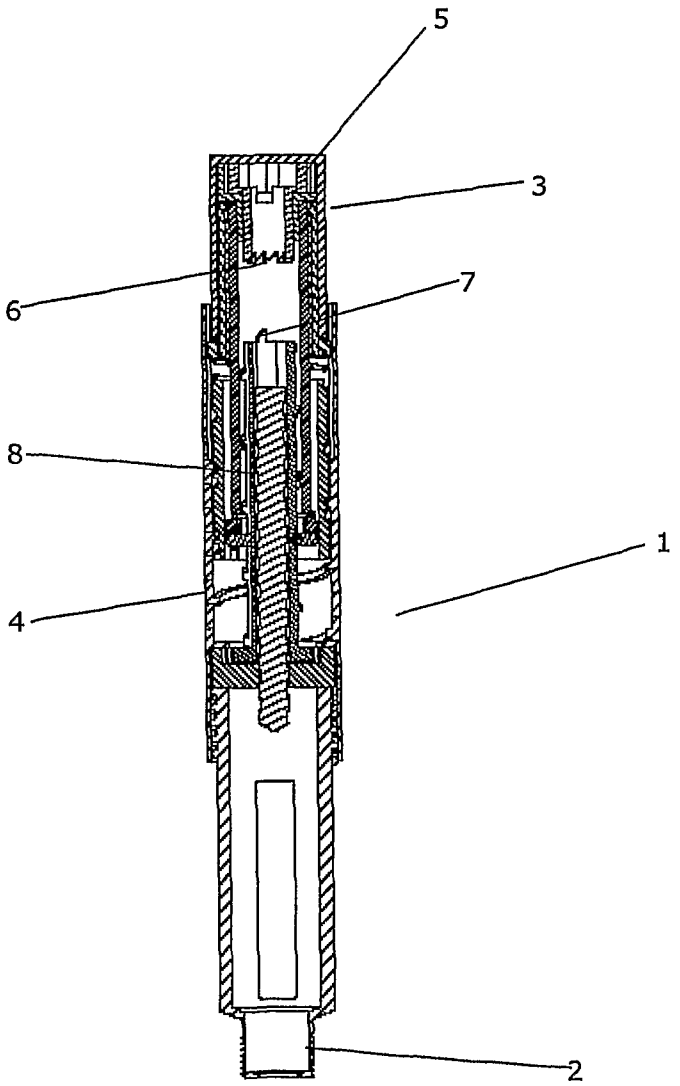

Fig. 1

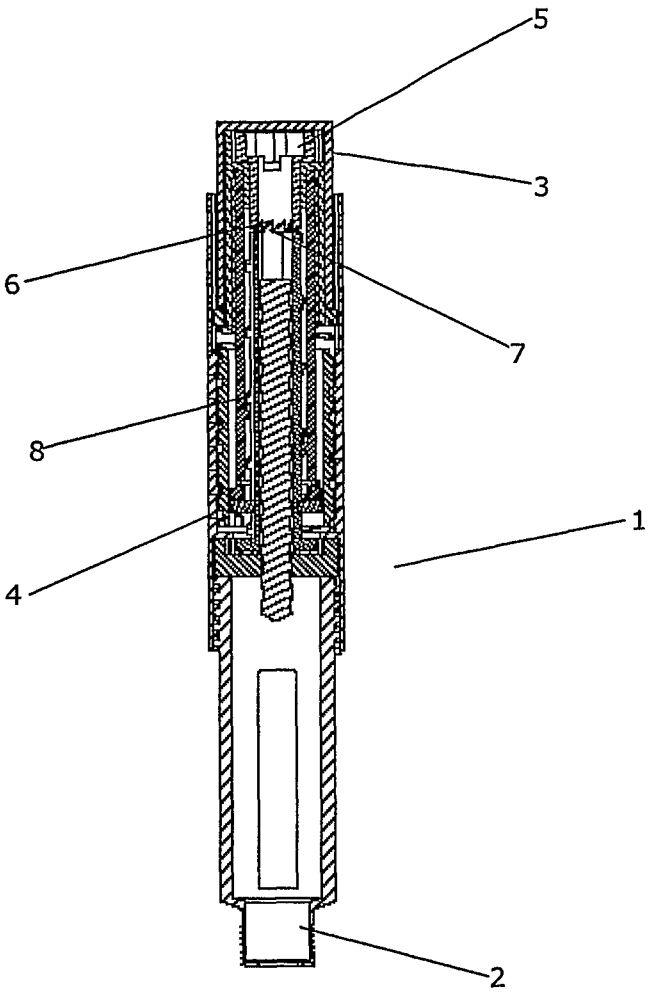

Fig. 2

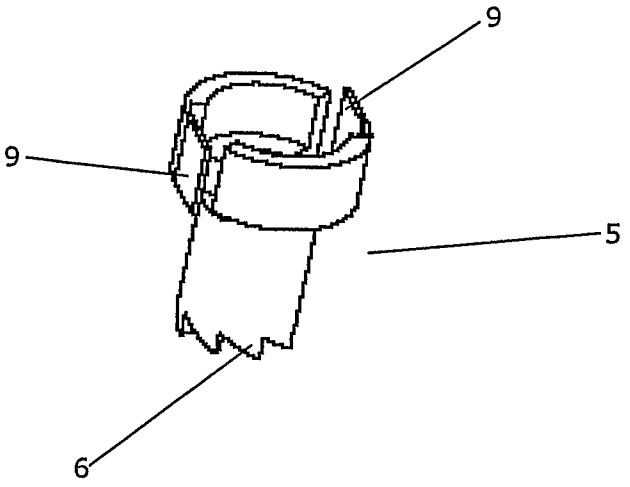

Fig. 3

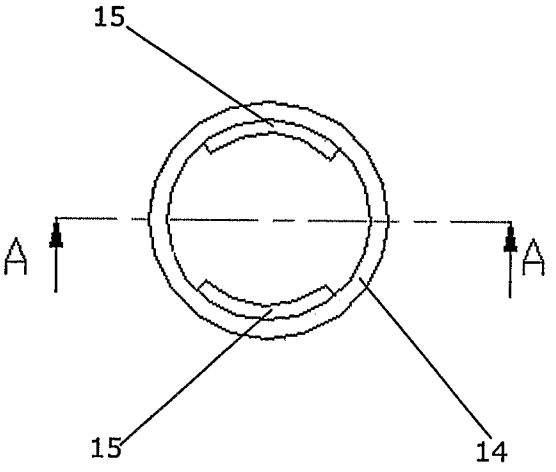

Fig. 5

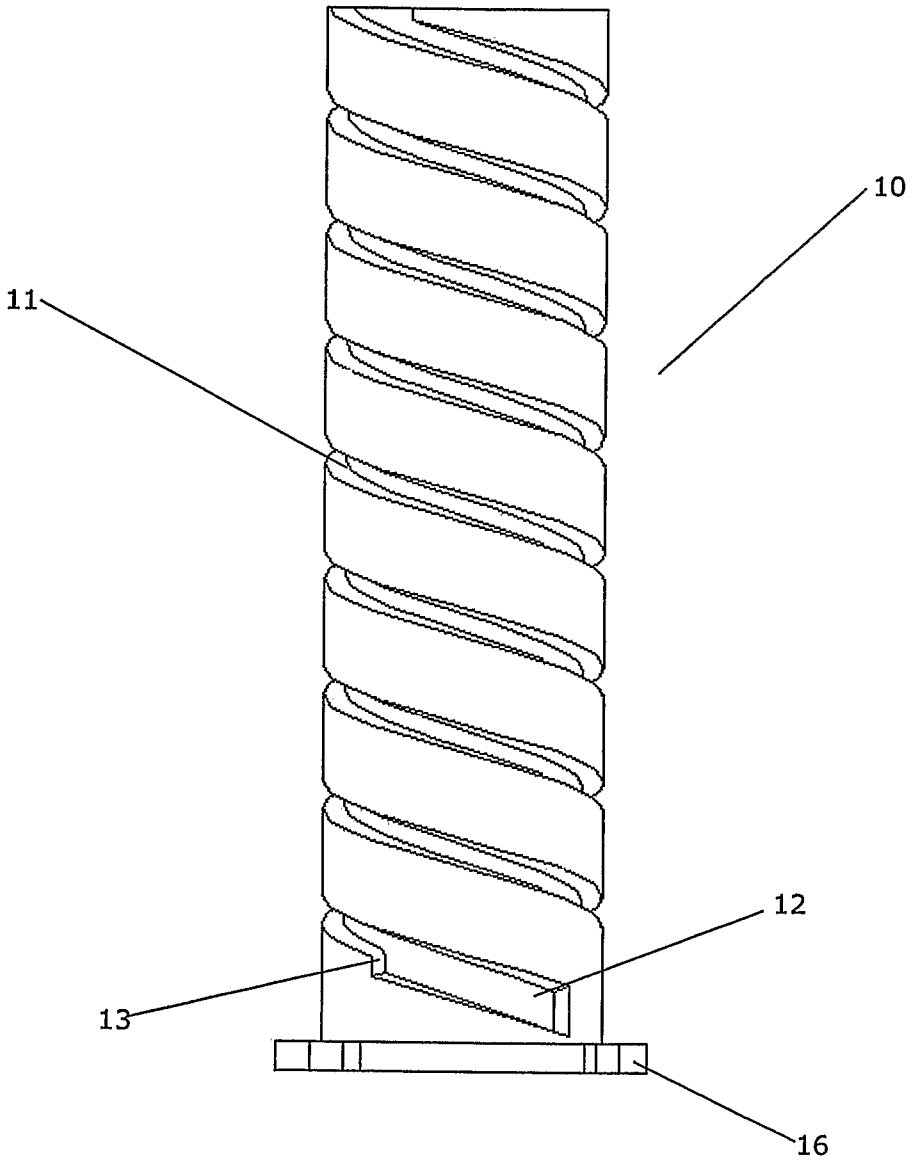

Fig. 4

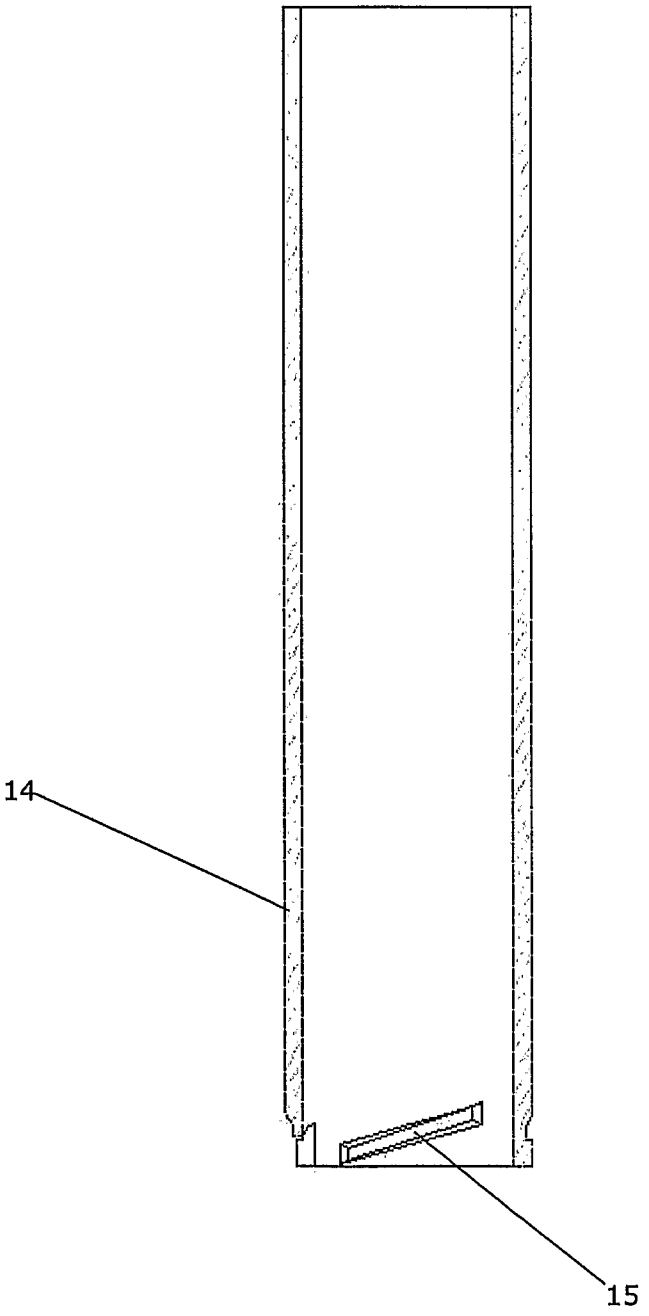

Fig. 6

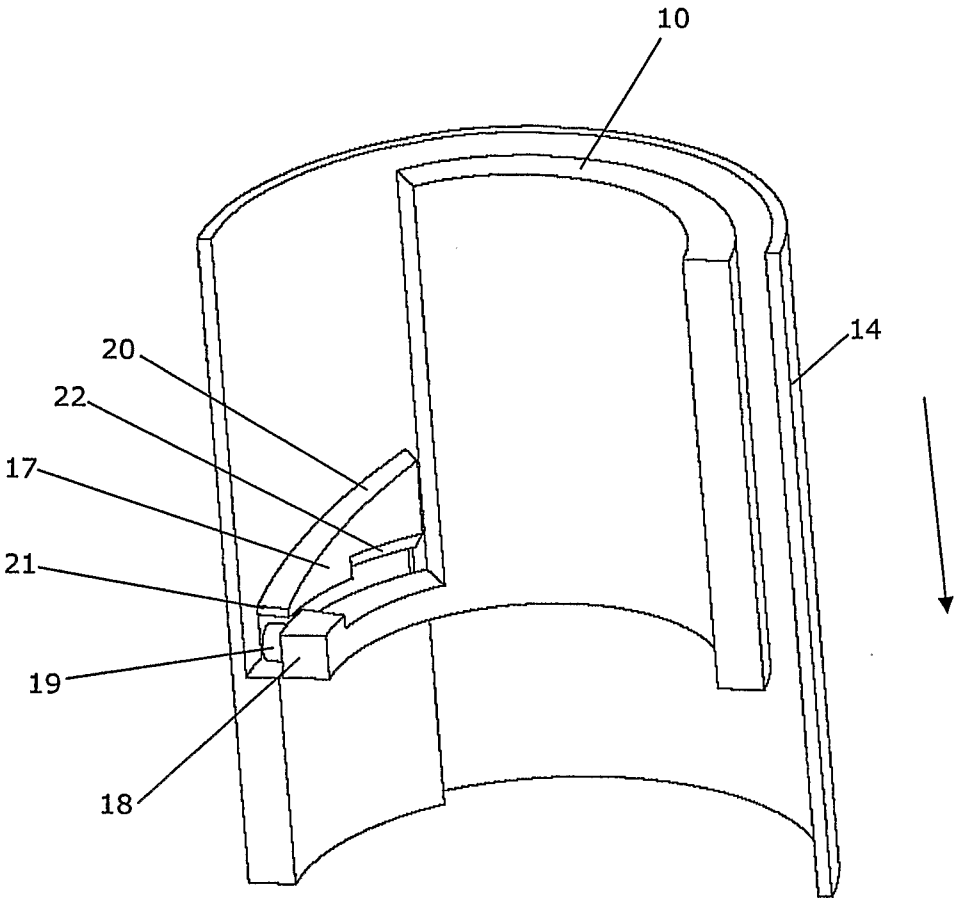

Fig. 7

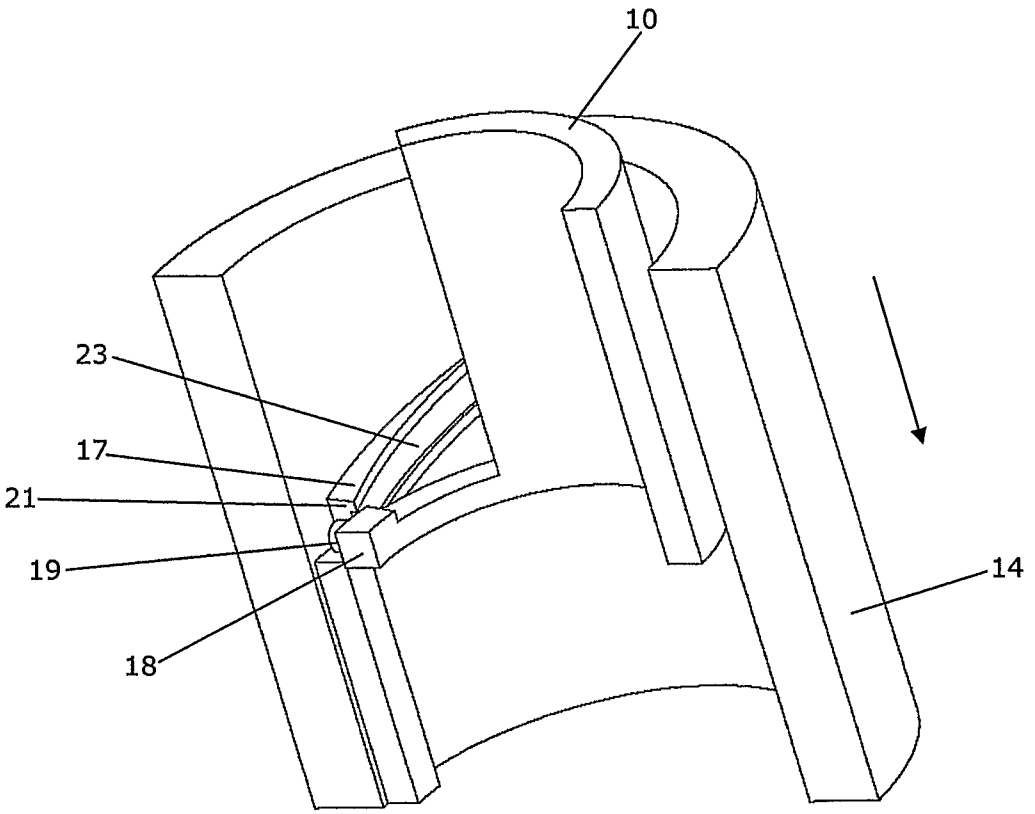

Fig. 8

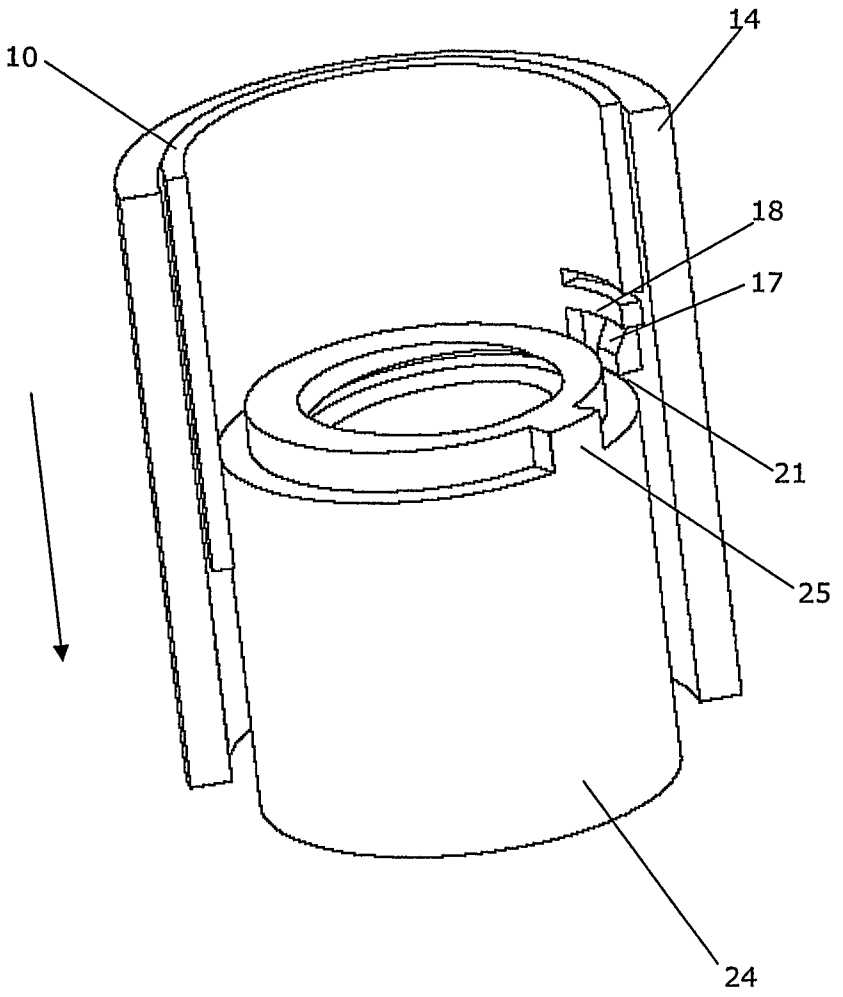

Fig. 9

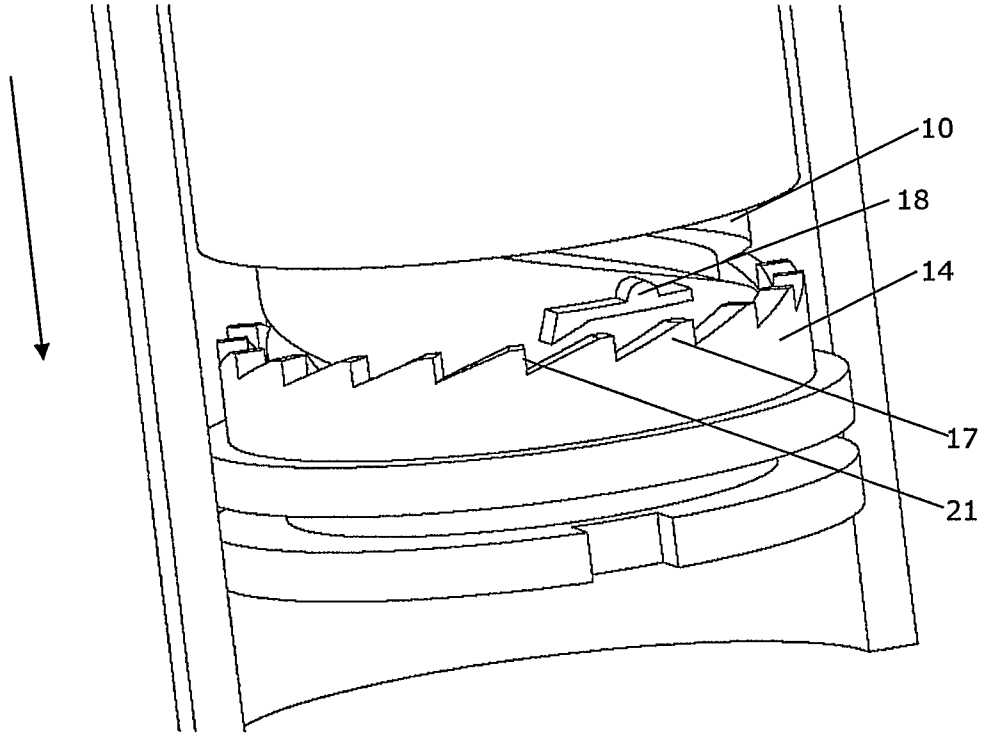

Fig. 10

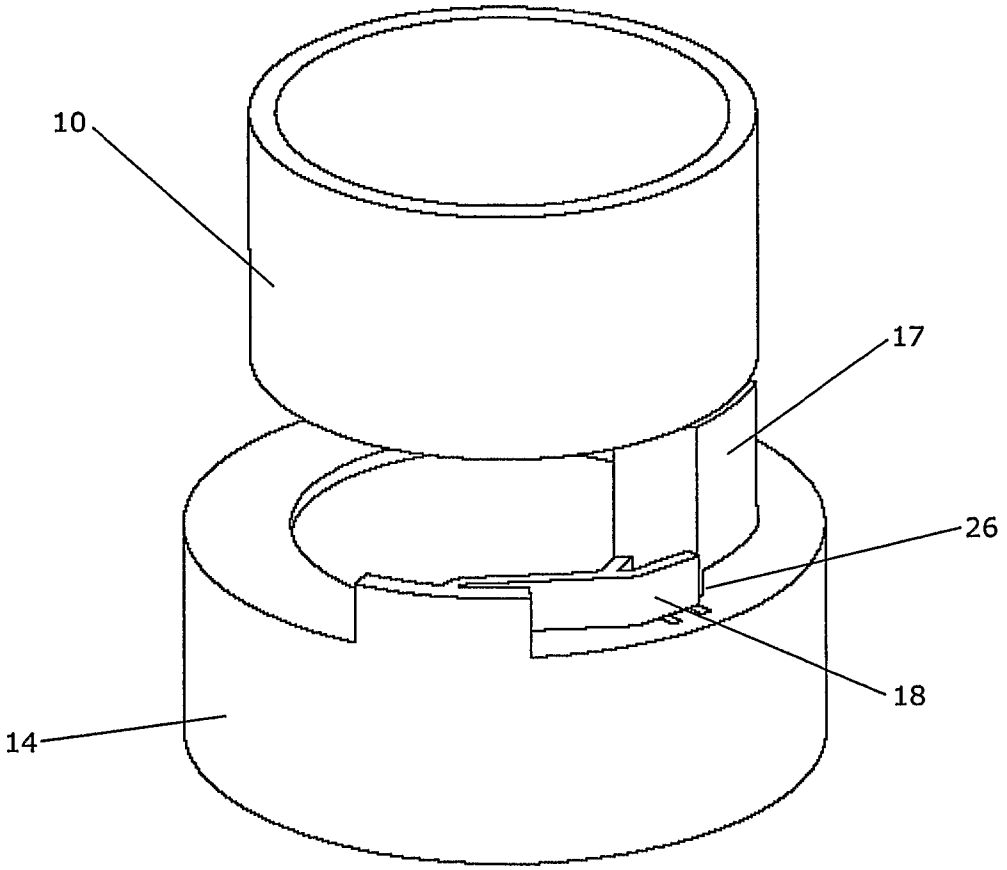

Fig. 11

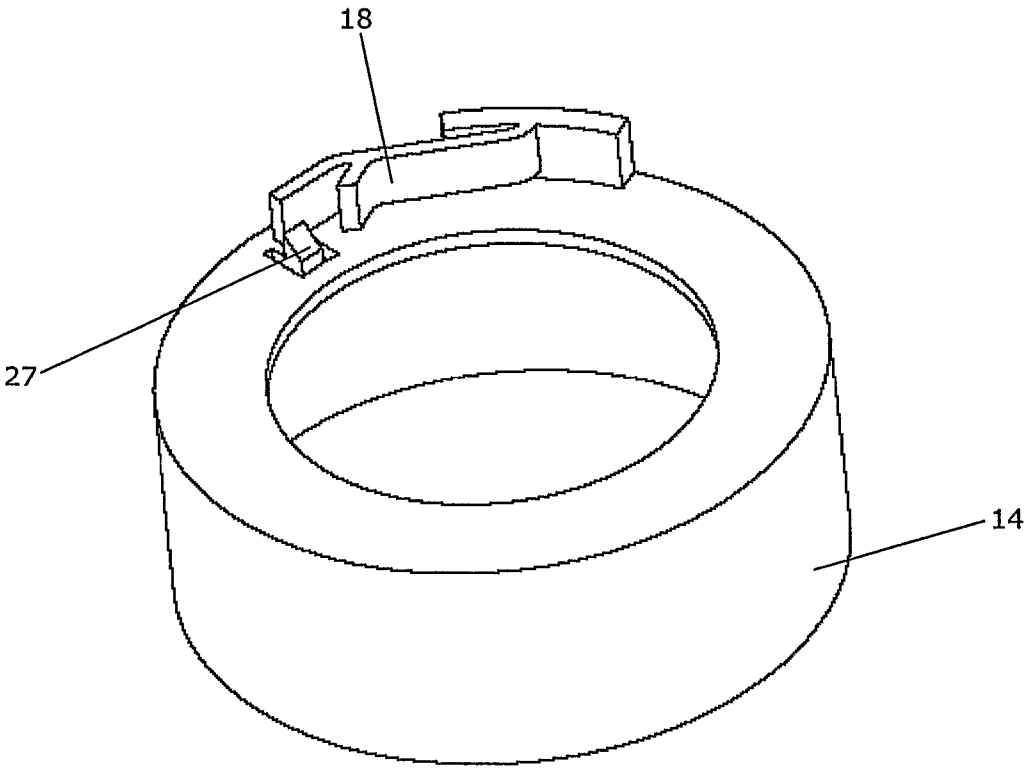

Fig. 12

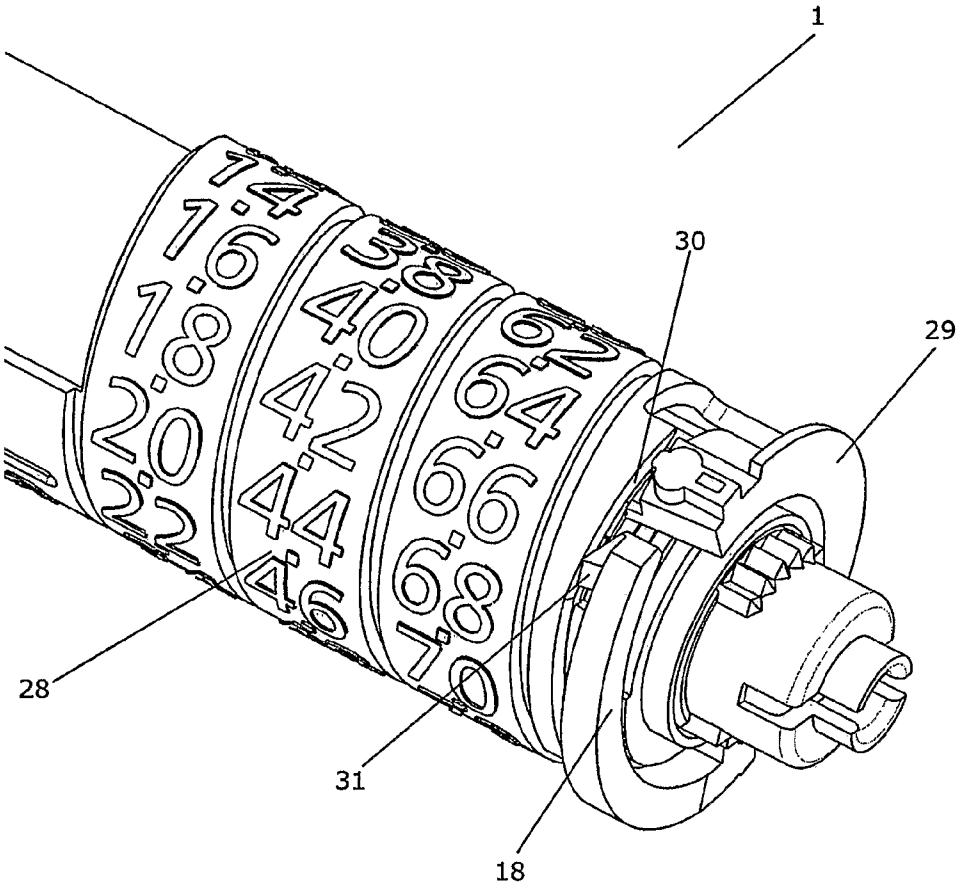

Fig. 13

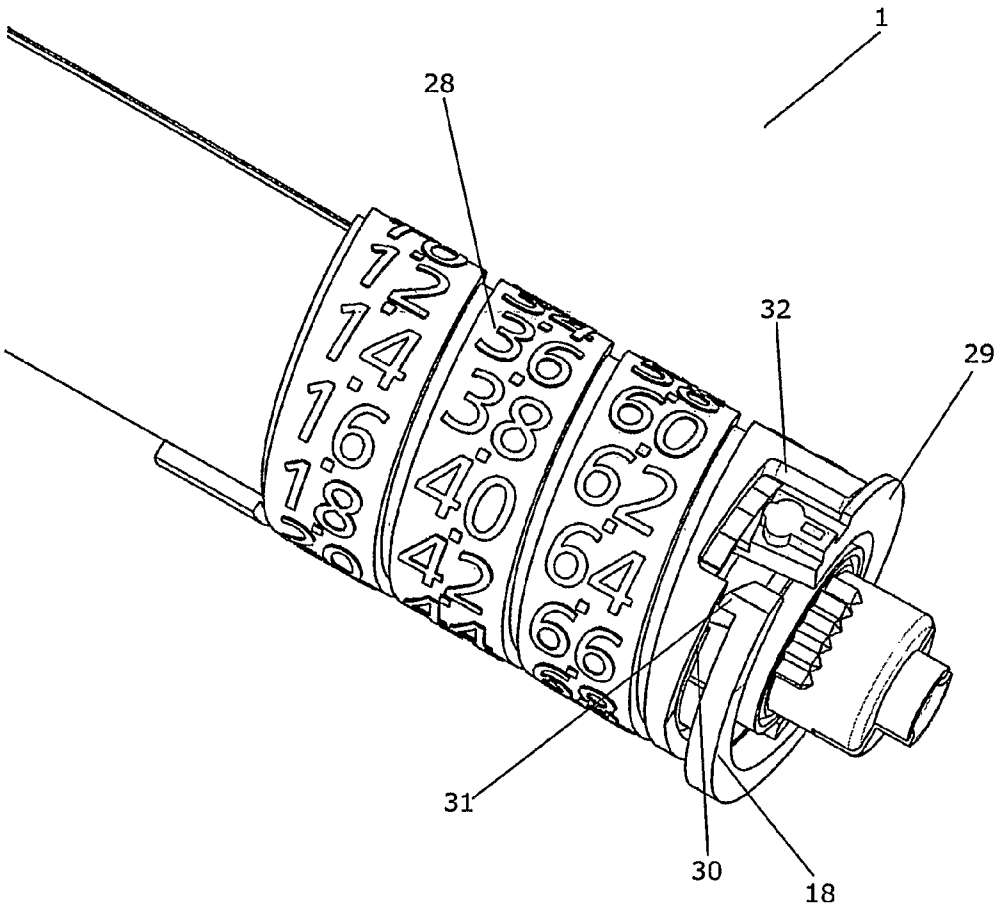

Fig. 14

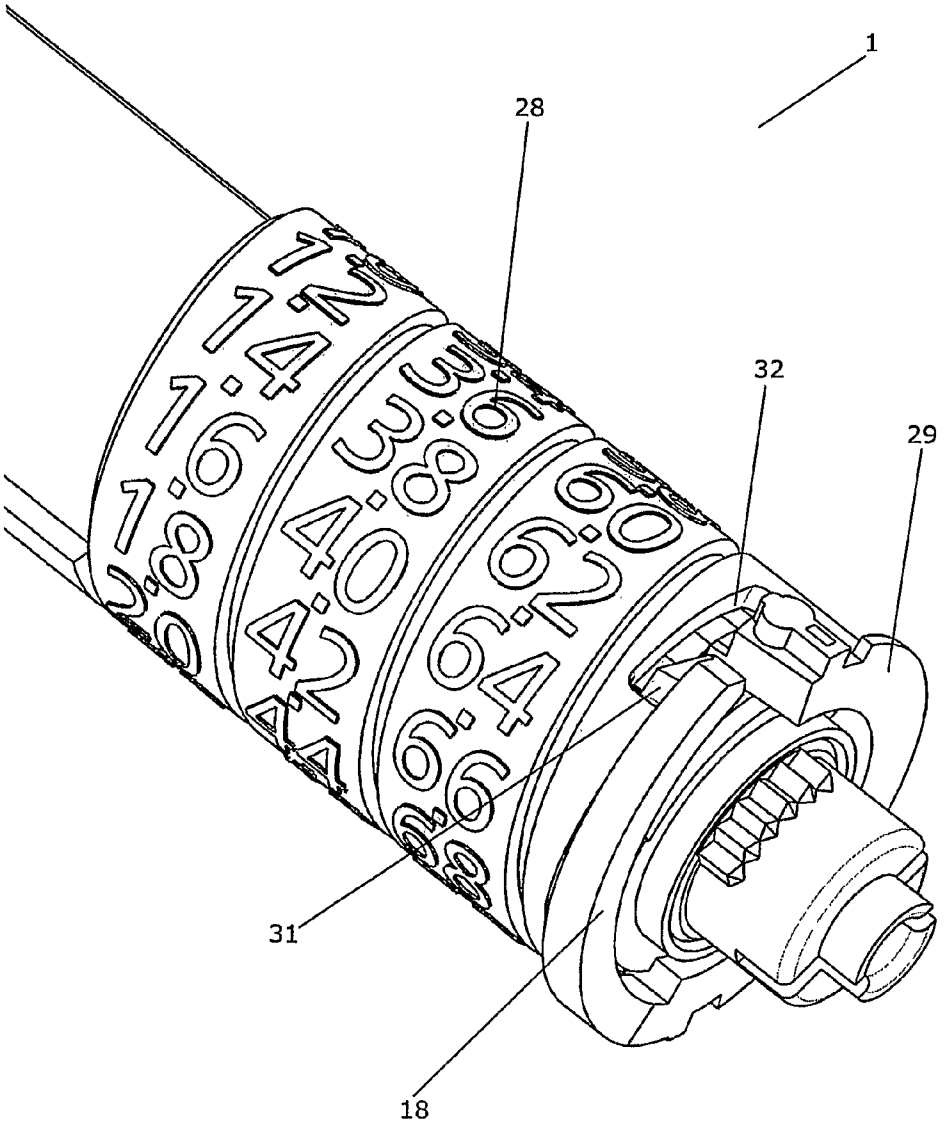

Fig. 15

INJECTION DEVICE WITH AN END OF DOSE FEEDBACK MECHANISM

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a 35 U.S.C. §371 national stage application of International Patent Application PCT/EP2006/000486 (published as WO 2006/079481), filed Jan. 20, 2006, which claimed priority of European Patent Application 05075187.4, filed Jan. 25, 2005; this application further claims priority under 35 U.S.C. §119 of U.S. Provisional Application 60/647,491, filed Jan. 27, 2005.

FIELD OF THE INVENTION

The present invention relates to an apparatus for delivering liquid drugs to a mammal, preferably a human being, preferably in a subcutaneous manner. More particularly, the present invention relates to an injection device which is capable of providing a non-visual feedback signal to a user indicating that a set dose has been injected by the injection device.

BACKGROUND OF THE INVENTION

In the present disclosure reference is mainly made to the treatment of diabetes by injection of insulin. However, this is merely an exemplary use of the present invention. Thus, the present invention may be used for injection of any other suitable kind of drug, e.g. growth hormone.

Injection devices, e.g. in the form of injection pens, are mainly made for users who have to inject themselves frequently, e.g. people having insulin-dependent diabetes or needing treatment by growth hormones. A number of requirements are set to such injection devices. The setting of a dose must be easy and unambiguous and it must be easy to read the set dose. Furthermore, it must be possible, with a minimum of trouble, to cancel or change a wrongly set dose. Finally, when the dose is injected the dose setting mechanism must return to zero. This is very important since it ensures that the set dose is actually injected, thereby allowing the user to keep track of which dose is injected.

Many injection devices work with a threaded piston rod which cooperates with a nut, the nut and the piston being capable of rotating relatively to each other. The dose setting may be obtained by dialing the nut away from a stop to which it is returned during injection by pressing the piston rod forward, either manually or by means of a mechanically biased mechanism, such as a spring, until the nut member abuts the stop. In other injection devices one of the elements, the nut or the piston rod, is kept inrotatable while the other one is allowed to rotate a set angle depending on the set dose, whereby the piston rod is dialed a distance in a forward direction through the nut member.

In such prior art injection devices a dose is normally set by dialing a dose setting member, and the set dose is injected by pushing an injection button. In elongated pen shaped injection devices the dose setting member and the injection button normally form a single member. When the injection button is pushed the set dose is expelled. However, the amount of drug expelled is only equal to the set dose if the injection button has been pushed as far as possible, the dose setting member thereby having been brought back to zero. In order to ensure that the correct dose has actually been injected, the user therefore has to visually inspect the position of the dose setting member during the injection.

This is disadvantageous because the injection in some cases will take place in a part of the body where visual inspection during the injection is very difficult or even impossible. Furthermore, in case the user is visually impaired it may be difficult for the user to visually inspect the dose setting member during or after the injection, regardless of where on the body the injection is performed. Since it is not uncommon for people having diabetes to be visually impaired, this is an important aspect.

It is therefore desirable to provide a feedback signal to the user indicating that the set dose has been injected, the feedback signal being of a kind which makes it unnecessary for the user to visually inspect whether or not the set dose is injected.

Some prior art injection devices have a mechanism which informs the user that a dose is being injected by producing an audible 'click' for each dose unit being injected. However, since these clicks appear during the entire injection they do not provide a feedback signal indicating that the set dose has been injected, and the problem indicated above is therefore not solved by these injection devices. Prior art injection devices of this type are, e.g., described in U.S. Pat. No. 4,592,745, EP 0 688 571 and US 2004/0210199.

In WO 98/57688 an injection device is disclosed which addresses the above mentioned problem. Thus, WO 98/57688 discloses an injection device having a dose setting device. A dose is set by dialing a dose setting member. Apart from setting a dose the dialing action causes an injection button to be moved from a position where it abuts a housing of the injection device to a position where it protrudes from the housing. The set dose is subsequently delivered by pushing the injection button back into abutment with the housing. In one embodiment a lock is activated when the injection button reaches the housing, and the activation of the lock produces an audible click indicating that the injection button is in abutment with the housing and thereby that the set dose has been delivered. During the injection, including the final part when the lock is activated, the injection button is moved linearly. The linear distance traveled by the injection button during the last few doses is relatively short. It may therefore be difficult to determine accurately from the audible click produced by the lock whether or not and when the set dose has been delivered.

EP 0 594 357 discloses another injection device which addresses the above mentioned problem. Thus, EP 0 594 357 discloses an injection device having a top section with resilient legs depending perpendicularly from the top section. The outer surface of the resilient legs has a ridge which rests on a ledge inside of the dose knob. The dose knob may have an elongated section which fits into a cylindrical sleeve such that when the dose knob is pushed into the sleeve, at the end of injection, the top portion of the sleeve touches end of the leg of the resilient legs displacing the ridge from the ledge and causing a snapping noise. As it is the case with the injection device described in WO 98/57688, the dose knob is moved linearly during injection, also during the final part of the injection when the resilient legs are displaced from the ridge causing the snapping noise. Therefore the shortcomings described above are also applicable here.

SUMMARY OF THE INVENTION

It is, thus, an object of the present invention to provide an injection device being capable of precisely and in a non-visual manner indicating to a user when a set dose has been injected.

It is a further object of the present invention to provide an injection device being capable of non-visually indicating to a user when a set dose has been injected, the indication being delivered to the user in a very distinct manner.

It is an even further object of the present invention to provide a dose delivering mechanism for an injection device, the dose delivering mechanism being capable of precisely and in a non-visual manner indicating to a user when a set dose has been injected.

According to the present invention the above and other objects are fulfilled by providing an injection device comprising:

- a housing,
- a dose setting member being operable to set a desired dose to be injected,
- a piston rod being adapted to cooperate with a piston so as to cause a set dose to be injected from an ampoule, and
- a dose delivering mechanism being adapted to operate the piston rod in such a way that a set dose is injected, the dose delivering mechanism further being adapted to provide a non-visual feedback signal to a user only at the end of injection of a set dose,

wherein first and second parts of the injection device are adapted to perform a relative rotational movement with respect to each other during injection of a dose, and wherein said relative rotational movement causes at least two parts of the injection device to abut or engage, said abutment or engagement causing the non-visual feedback signal to be generated.

The injection device of the present invention is very suitable for use by persons which have to frequently inject themselves, e.g. persons having insulin-dependent diabetes or needing treatment by growth hormones. The desired dose being set by means of the dose setting member is, thus, a dose of a specific drug which the person in question needs to inject at that specific point in time. The desired dose may be a fixed dose which the person needs to inject each time an injection is performed, or it may be a varying amount, e.g. varying according to the time of day and/or one or more parameters which may be measured or chosen prior to setting the dose (e.g. blood glucose (BG) level, contents of a meal, etc.).

The piston rod is preferably adapted to push a piston into an ampoule, thereby causing the set dose to be injected. This may be obtained in various ways and is well known and well described in the art.

The dose delivering mechanism is adapted to provide a non-visual feedback signal to a user only at the end of injection of a set dose. Thus, the feedback signal may be generated when the set dose has been injected, e.g. exactly when or immediately after the last unit has been injected. Alternatively, the feedback signal may be generated before the complete dose has been delivered, e.g. when a few units remain to be injected, the remaining units being injected while the feedback signal is sensed by the user. Thus, when the user perceives the feedback signal the set dose will have been delivered, and the user will therefore not be able to tell the difference between a feedback signal being generated after the dose has been completely injected and a feedback signal being generated immediately before the dose has been completely injected. In any event the user can regard the perception of the feedback signal as an indication that the set dose has been delivered, and the user may therefore react correspondingly, e.g. by removing a pressure applied manually to an injection button.

Since the non-visual feedback signal is provided only at the end of injection of a set dose the user will know distinctly that when the feedback signal is received the set dose has been fully injected. This is an advantage compared to prior art injection devices where a click for each injected dose unit is produced. In this case the user would have to count the number of clicks produced and compare this to the number of set dose units in order to tell exactly when the set dose has been fully injected.

A first part and a second part of the injection device are adapted to perform a relative rotational movement with respect to each other during injection of a dose. This may, e.g., be the housing and the piston rod, or it may be a separate member and any other part of the injection device, e.g. the housing and/or the piston rod, the sole purpose of the separate member being to generate the non-visual feedback signal. Three or more parts of the injection device may perform mutual rotational movements during injection of a dose. Furthermore, the relative rotational movement may be performed all through the injection of a dose or it may be performed during only part of the injection. Thus, the relative rotational movement may be started or stopped at the end of injection of a set dose as defined above, in which case this starting or stopping may advantageously cause the non-visual feedback signal to be generated.

The relative rotational movement causes at least two parts of the injection device to abut or engage, and this abutment or engagement causes the non-visual feedback signal to be generated. One or both of the parts which abut or engage may be the first and/or second parts, i.e. the parts performing the relative rotational movement. Alternatively, one or both of the parts which abut or engage may be other parts of the injection device. This will be described in further details below.

Due to the fact that the relative rotational movement initiates the generation of the non-visual feedback signal it is ensured that the movement generating the non-visual feedback signal is much longer than a corresponding movement in an injection device where the feedback signal is generated by a linear movement of one or more parts. Thereby the generated signal will be much more precise and distinct, and a far more accurate feedback signal has thereby been provided. This is very advantageous because it makes it much easier for the person to ascertain that the expected and desired dose has actually been injected.

The non-visual feedback signal may comprise an audible and/or a tactile signal. In this case the person using the injection device will be able to hear and/or feel that the set dose has been injected. Alternatively or additionally, the non-visual feedback signal may comprise any other suitable kind of signal which can be perceived by other senses than sight. Furthermore, the non-visual feedback signal may be followed by a visual signal, e.g. a scale drum showing a 'zero', a lamp or a diode which is turned on or off or starts flashing simultaneously with the generation of the non-visual feedback signal. Thereby the user may, in addition to the non-visual feedback signal, use this visual feedback signal to further ensure that the set dose has actually been injected.

In one embodiment of the present invention the abutment or engagement is caused by a change in a rotational velocity of at least one part of the dose delivering mechanism. This may, e.g., be accomplished by allowing a separate member to start rotating at the end of injection of a set dose, typically in such a way that this member rotates during injection of the last few units of the set dose. The rotation of this separate member will in turn generate a non-visual feedback signal to

the user. Thus, in this case the rotational velocity of this member relatively to, e.g., the housing, changes from zero to a certain velocity, and this change causes the non-visual feedback signal to be generated, e.g. in the form of a clicking sound generated by protruding parts present on the separate member moving against an inner part of the housing or an outer part of the piston rod.

Alternatively or additionally, the change in rotational velocity may cause a tactile feedback signal to be generated. It may, e.g., be possible to feel the rotational movement itself, and thereby it may be possible for the user to detect a substantial change (decrease or increase) in the rotational velocity.

In one embodiment the injection device may further comprise a ratchet operating the piston rod and having a threaded portion being adapted to engage with a part of the dose delivering mechanism, in which case the change in a rotational velocity is generated by a change in the pitch of the threaded portion of the ratchet, said change in the pitch in return causing a change in a translational velocity of said part of the dose delivering mechanism, said change in translational velocity causing at least two parts of the injection device to abut, thereby causing the non-visual feedback signal to be generated.

In this embodiment the non-visual feedback signal preferably comprises a tactile feedback signal. Thus, the part of the dose delivering mechanism which is adapted to engage with the threaded portion of the ratchet is preferably in directly or indirectly contact with the user during injection of a dose. Thus, the part may be, form part of or be operatively connected to an injection button which the user presses during injection. Thereby the user will be able to feel the change in translational velocity.

The pitch may be changed from a certain value used during the main part of the injection to zero, i.e. the threaded portion simply stops at a position corresponding to the end of injection of a set dose. In this case the user will feel a kind of 'axial resistance' during the injection until the ratchet/dose delivery part reaches the position where the threaded portion stops. Then the part will stop rotating and instead increase the velocity of a translational (axial) movement which is also performed while the ratchet/dose delivery part travels the threaded portion, due to the pitch of the threaded portion. The user will be able to feel this increase in translational velocity. Furthermore, the translational movement is preferably eventually stopped, e.g. due to part of the dose delivery mechanism abutting a stop member. This stop will also be very distinctly felt by the user, thereby producing a non-visual feedback signal, and it may further produce a sound, in which case the non-visual feedback signal comprises a tactile as well as an audible signal. In this embodiment the two parts of the injection device which are caused to abut may advantageously be a scale drum and a part of the housing, the scale drum performing a rotational and axial movement defined by the threaded portion. Alternatively, the two parts may be a dose knob and a proximal part of the housing, the dose knob performing an axial movement which follows the axial part of the movement of the scale drum as described above.

Alternatively, the pitch may either increase or decrease from one non-zero value to another. This has the advantage that the engaging part is readily moved back into engagement with the threaded portion when a new dose is to be set.

In another embodiment the dose delivering mechanism may comprise a first dose part and a second dose part, the first dose part being adapted to rotate relatively to the housing during injection of a dose and the first dose part comprising means for engaging the second dose part at the end of injection of a set dose, thereby causing the second dose part to rotate along with the first dose part, in which case the non-visual feedback signal is generated by the resulting rotational movement of the second dose part.

In this embodiment the rotational movement of the second dose part increases from zero to a non-zero value at the end of injection of the set dose. The second dose part may be provided with teeth, protrusions, flexible arms or similar means being adapted to be moved against another part of the device during rotation of the second dose part, thereby producing a sound which at least partly constitutes the non-visual feedback signal.

The second dose part may be positioned between the first dose part and the housing. In case the second dose part is provided with teeth, protrusions, flexible arms or the like as described above, these may advantageously be moved against a part of the housing when the second dose part is rotated along with the first dose part.

Alternatively, the non-visual feedback signal may be generated as a result of an abutment between two parts of the dose delivering mechanism performing a relative rotational movement. The feedback signal may, e.g., be obtained by releasing a tension which has previously been introduced in a part of the injection device, the release of the tension being caused by the abutment between the two parts.

The tensed part may comprise a spring means, such as a separate spring member or at least one resilient portion of at least one of the first and second parts performing the relative rotational movement. In case the spring means is in the form of at least one resilient portion of the part(s) the non-visual feedback signal may be generated in the following manner. First the resilient portion(s) is/are bent into a tensed position. At a later time this tension is released, e.g. by rotating the resilient portion(s) away from a part which holds the resilient portion(s) in the tensed position. Thereby the resilient portion(s) will restore its/their relaxed position(s), and this movement will generate a clicking sound, i.e. a non-visual feedback signal. The resilient portion(s) may be in the form of spring arm(s), in which case a sound may be generated due to moving air caused by sudden release of the tensed spring arm(s). Alternatively, abutment between a moving part and a release mechanism may release the tension of the resilient portion(s).

The tension may be introduced during dose setting, e.g. by tightening a spring member or moving a resilient portion into a tensed position as described above. This may be obtained by letting the dose setting mechanism be connected to a spring member, e.g. in such a way that a spring is tightened when a dose setting member is turned, or in such a way that a part being provided with a resilient portion is rotated along with a dose setting member, thereby causing the resilient part to be moved into a tensed position.

Alternatively, the tension may be introduced during injection of a dose. This may be obtained in a manner very similar to what is described above. However, in this case the tensed part should be operatively connected to the dose delivering mechanism.

The dose delivering mechanism may be adapted to be manually operated, e.g. by means of an injection button which the user must press manually during the injection.

Alternatively, the dose delivering mechanism may be adapted to be operated by means of a mechanically biased mechanism, e.g. comprising at least one spring. The mechanically biased mechanism may, in this case, be biased during setting of a dose. When the injection is subsequently performed this is done by releasing the tension previously

built up in the mechanically biased mechanism, and the stored energy will then cause the set dose to be injected. This kind of injection device does not require a force applied by the user in order to inject a set dose.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will now be further described with reference to the accompanying drawings in which:

FIG. **1** shows a cross section through an injection device according to a first embodiment of the invention and being in a position where a dose has been set,

FIG. **2** shows a cross section through the injection device of FIG. **1** in a position where a dose has been injected,

FIG. **3** shows a click item adapted to be positioned in the injection device of FIGS. **1** and **2**,

FIG. **4** shows a threaded inner part being adapted to be positioned in an injection device according to a second embodiment of the invention,

FIG. **5** shows a top view of an outer part being adapted to engage with the inner part of FIG. **4**,

FIG. **6** is a cross section along line A-A in FIG. **5**,

FIGS. **7-10** show parts of injection devices according to a third, fourth, fifth and sixth embodiment of the invention, respectively, all having a spring arm and a wedge structure,

FIG. **11** shows part of an injection device according to a seventh embodiment of the invention having a spring arm and a release mechanism,

FIG. **12** shows an outer part of the injection device of FIG. **11** from a different angle, and

FIGS. **13-15** show part of an injection device according to an eighth embodiment of the invention having a spring arm, at various points in time.

The Figures are schematic and simplified for clarity, and they only show details which are essential to the understanding of the invention while other details are left out. Throughout the description of the drawings the same reference numerals will be used for identical or corresponding parts.

DETAILED DESCRIPTION OF THE DRAWINGS

When in the following terms as 'upper' and 'lower', 'left' and 'right', 'horizontal' and 'vertical', 'clockwise' and 'counter clockwise' or similar relative expressions are used, these only refer to the accompanying drawings and not to the actual situation of use. The shown Figures are schematic representations for which reason the configuration of the different structures as well as their relative dimensions are intended to serve illustrative purposes only. In that context it may be convenient to define that the term 'distal end' in the accompanying drawings is meant to refer to the end of the injection device carrying an injection needle, whereas the term 'proximal end' is meant to refer to the opposite end pointing away from the injection needle.

FIG. **1** shows a cross section through an injection device **1** according to a first embodiment of the invention. At its distal end the injection device **1** is provided with a portion **2** being adapted to carry an injection needle (not shown). At its proximal end the injection device **1** comprises a combined dose setting and injection button **3**. During dose setting the dose setting and injection button **3** is rotated. This causes the dose setting and injection button **3** to be moved away from a housing **4** to the position shown in FIG. **1**. During injection the user presses the dose setting and injection button **3**, thereby moving it back into the housing **4**. This movement causes the set dose to be injected from the injection device **1**. Inside the dose setting and injection button **3** there is positioned a click item **5** which is provided with a set of teeth **6** being adapted to engage with a corresponding tooth **7** positioned on a ratchet **8**. During injection the ratchet **8** will rotate relatively to the housing **4** while the click item **5** will not rotate.

FIG. **2** shows a cross section of the injection device **1** of FIG. **1**. However, in FIG. **2** a dose has just been injected, i.e. the dose setting and injection button **3** has been pushed to a position inside the housing **4**. Thereby the set of teeth **6** on the click item **5** engage with the tooth **7** on the ratchet **8**. Since the ratchet **8** rotates during the injection, this will cause the click item **5** to be rotated along with the ratchet **8**. This rotational movement will cause the click item **5** to produce a sound in a manner which will be explained further below with reference to FIG. **3**. Since the click item **5** is only rotated during the injection of the last few units of the set dose the produced sound indicates that the set dose has been substantially injected. Thereby a non-visual feedback signal has been generated.

FIG. **3** is a perspective view of a click item **5** adapted to be inserted in the injection device **1** of FIGS. **1** and **2**. The part of the click item **5** positioned opposite the set of teeth **6** is provided with two resilient parts **9**. The resilient parts **9** are resilient due to a reduced thickness of the material making up the parts **9** as compared to the thickness of the material making up the remaining parts of the click item **5**. When the click item **5** is rotated as described above the resilient parts **9** will be moved against the inner part of the housing **4**, and this will cause the resilient parts **9** to be alternatingly tensed and released. Each time the resilient parts **9** are released they will produce a clicking sound, thereby generating the non-visual feedback signal.

FIG. **4** shows a threaded inner part **10** being adapted to be inserted inside a housing of an injection device according to a second embodiment of the invention. The main part of the thread **11** has a constant pitch. However, in the lower part of the thread **12** the pitch is abruptly decreased. This can be seen in the form of an axial edge **13**. Thereby a part engaging with the thread **11**, **12** will be moved abruptly relatively to the inner part **10** along an axial direction when the engaging part reaches the lower part of the thread **12**, i.e. when it reaches the axial edge **13**. This abrupt movement, and not the least the following abrupt stop when this movement stops, can be felt by the user as will be described below. Furthermore, the location of the axial edge **13** towards the end of the threaded portion **12** ensures that the felt abrupt movement indicates the end of injection of a set dose. Thereby a non-visual (tactile) feedback signal has been provided as a result of a change in the pitch of a threaded portion **11**, **12**.

FIG. **5** shows a top view of an outer part **14** being adapted to be positioned around the threaded inner part **10** of FIG. **4**. The outer part **14** is provided with two protruding parts **15** each being adapted to engage with the thread **11**, **12** of the inner part **10**.

FIG. **6** shows a cross section through the outer part **14** shown in FIG. **5** along the line A-A. During injection of a dose the inner part **10** and the outer part **14** will initially be relatively positioned in such a way that the protruding parts **15** engage with the part of the thread **11** being positioned opposite the lower part of the thread **12**. The outer part **14** is then pushed inwards, thereby allowing the protruding parts **15** to travel the threaded portion **11**. Due to the thread **11** the inner part **10** and the outer part **14** perform a relative rotational movement. When the protruding parts **15** reach the axial edge **13** the axial velocity of the outer part **14** will increase abruptly as described above, and because the user

is manually pressing the outer part **14** this abrupt movement, as well as the abrupt stop occurring when the outer part **14** abuts a stop member **16** present on the inner threaded part **10** (see FIG. **4**), will be felt by the user. Thereby a tactile feedback signal is provided. Furthermore, the outer part **14** abruptly abutting the stop member **16** may produce a sound, thereby providing an audible feedback signal in addition to the tactile feedback signal.

FIG. **7** shows part of an injection device according to a third embodiment of the invention. The Figure shows an inner part **10** and an outer part **14**. The inner part **10** and the outer part **14** are adapted to be rotated relatively to each other during injection. The outer part **14** is provided with a wedge structure **17** and the inner part **10** is provided with a spring arm **18**. During injection, in addition to the mutual rotation, the inner part **10** is moved in an axial direction indicated by the arrow. When the spring arm **18** reaches the wedge structure **17** a protruding part **19** of the spring arm **18** will engage an upper part **20** of the wedge structure **17**. This will cause the spring arm **18** to be pressed in a direction opposite to the one indicated by the arrow, thereby introducing a tension in the spring arm **18**. The tension is, thus, built up during injection. The protruding part **19** will subsequently be moved along the upper part **20** of the wedge structure **17** until it reaches the end **21** of the wedge structure **17**. The protruding part **19** will then 'fall over the edge' to the position shown in FIG. **7**, thereby releasing the tension which was previously built up in the spring arm **18**. This sudden release of the tension produces a sound due to air being moved by the spring arm **18** and/or due to the protruding part **19** hitting a stationary part of the outer part **14**. Thereby an audible feedback signal has been produced, and by positioning the wedge structure **17** in an appropriate manner, the feedback signal will indicate to the user that the set dose has been injected.

When a new dose is to be set, the protruding part **19** will pass the wedge structure **17** via a tapered part **22** on the wedge structure **17**.

FIG. **8** shows part of an injection device according to a fourth embodiment of the invention. The fourth embodiment is very similar to the third embodiment shown in FIG. **7**. FIG. **8** also shows an inner part **10** having a spring arm **18** and an outer part **14** having a wedge structure **17**, the inner part **10** and the outer part **14** being adapted to rotate in relation to each other during injection. The spring arm is provided with a protruding part **19**. During injection the inner part **10** moves relatively to the outer part **14** in a direction indicated by the arrow. When the spring arm reaches the wedge structure **17** the protruding part **19** will be caught in a track **23** and moved along this track **23**. Due to the geometry of the wedge structure **17** this movement will result in the spring arm **18** being pressed in a direction away from the outer part **14**, thereby introducing a tension in the spring arm **18**. Thus, the tension is built up during the injection. When the protruding part **19** reaches the end **21** of the wedge structure **17** it will 'fall over the edge', thereby releasing the tension which was previously built up in the spring arm **18**. This will result in an audible feedback signal being generated as described above.

When a new dose is to be set, the protruding part **19** will pass the wedge structure **17** by being lifted in an axial direction along the end **21** of the wedge structure **17**.

FIG. **9** shows part of an injection device according to a fifth embodiment of the invention. FIG. **9** shows an inner part **10** having a spring arm **18** and an outer part **14** having a wedge structure **17**. During injection the inner part **10** will move relatively to the outer part **14** in a direction indicated by the arrow. However, in this embodiment the inner part **10** and the outer part **14** do not rotate relatively to each other. Instead the injection device comprises a rotational part **24** which rotates during injection relatively to the inner part **10** and the outer part **14**. When the spring arm **18** reaches the wedge structure **17** it will be pushed in a direction away from the outer part **14** and towards the rotational part **24**. Thereby it is moved into a path of a protruding part **25** on the rotating part **24**. When the protruding part **25** is rotated to the position of the spring arm **18**, it will therefore push the spring arm **18** out of its path again, thereby introducing a tension in the spring arm **18**. When the protruding part **25** has passed the position of the spring arm **18**, the spring arm **18** will again be free to move into the path of the protruding part **25**, thereby releasing the tension which was previously built up in the spring arm **18**. Thereby an audible feedback signal is generated due to air being moved be the spring arm **18** and/or due to the spring arm **18** hitting a wall of the rotational part **24**, as described above.

FIG. **10** shows part of an injection device according to a sixth embodiment of the invention. The Figure shows an inner part **10** having a spring arm **18** and an outer part **14** having a wedge structure **17**. The inner part **10** and the outer part **14** are adapted to rotate relatively to each other during injection. Furthermore, the inner part **10** moves relatively to the outer part **14** in the direction indicated by the arrow during injection. When the spring arm **18** reaches the wedge structure **17** it will be caught by one of the wedges. Due to the geometry of the wedge structure **17** and to the continued rotational and axial movement (in the direction of the arrow) of the inner part **10**, the spring arm **18** will be pressed in a direction opposite the direction indicated by the arrow, thereby introducing a tension in the spring arm **18**. Subsequently when the spring arm **18** reaches the end **21** of the wedge it will 'fall over the edge', thereby releasing the previously built up tension. This will cause an audible feedback signal to be generated as described above.

FIG. **11** shows part of an injection device according to a seventh embodiment of the invention. The Figure shows an inner part **10** having a wedge structure **17** and an outer part **14** having a spring arm **18** and a locking mechanism (not shown in FIG. **11**). The inner part **10** and the outer part **14** are adapted to rotate in relation to each other during setting of a dose and during injection. The inner part **10** is typically a scale drum or is adapted to rotate along with a scale drum during setting of a dose and during injection. Thus, when a dose is set the inner part **10** is rotated in such a way that the wedge structure **17** presses the spring arm **18** outwards and into engagement with the locking mechanism, thereby introducing a tension in the spring arm **18**. Thus, in this embodiment the tension is introduced during setting of the dose. The locking mechanism will maintain the spring arm **18** in the tensed position during the remaining setting of the dose and during the main part of the injection. However, when the inner part **10** is returning to the initial position a release mechanism **26** on the wedge structure **17** releases the locking mechanism, thereby releasing the tension which was previously built up in the spring arm **18**. Thereby an audible signal is generated as described above, and because the locking mechanism is released when the inner part **10** is returning to the initial position, this audible signal indicates that the set dose has been injected.

FIG. **12** shows the outer part **14** of the injection device of FIG. **11**. The outer part **14** has a locking mechanism **27** which is in a locking position, i.e. it engages the spring arm **18**. Thus, in FIG. **12** the spring arm **18** is tensed. When the inner part (not shown) approaches the outer part **14** as

described above, the release mechanism (not shown) will push the locking mechanism **27** downwards, and the tensed spring arm **18** will then restore its relaxed position, i.e. it will move towards the centre of the outer part **14**. Thereby the tension built up in the spring arm **18** is suddenly released.

FIG. **13** shows part of an injection device **1** comprising a scale drum **28** and a spring arm member **29** positioned at the proximal end of the injection device **1**. The spring arm member **29** is provided with a spring arm **18** which may be deflected in a proximal direction, i.e. away from the scale drum **28**.

During injection of a set dose, the scale drum **28** performs a rotational movement as well as an axial movement towards the spring arm member **29**. This movement will eventually cause an upper portion **30** of the scale drum to abut a protrusion **31** of the spring arm **18**. As the scale drum **28** continues the rotational and axial movement, the spring arm **18** is deflected in a proximal direction, thereby causing a tension to be built up in the spring arm **18**.

FIG. **13** shows a situation where the upper portion **30** of the scale drum **29** and the protrusion **31** of the spring arm **18** abut, and a tension has started to build up in the spring arm **18**.

FIG. **14** shows the injection device of FIG. **13**. In FIG. **14** a tension has been built up in the spring arm **18** as described above. The protrusion **31** of the spring arm **18** is positioned very near a recess **32** formed in the scale drum **28**. Thus, further rotation of the scale drum **28** will cause the protrusion **31** to 'fall over the edge' into the recess **32**. Thereby the tension which has previously been built up in the spring arm **18** is released, and an audible feedback signal is generated by vibrating air and/or by the protrusion **31** hitting a lower edge of the recess **32**.

This situation is illustrated in FIG. **15**, showing the injection device **1** of FIGS. **13** and **14** in a situation where the tension previously built up in the spring arm **18** has been released as described above.

When a new dose is to be set, the feedback mechanism needs to be reset in order to be able to provide an audible feedback signal when the subsequent dose has been injected. This is done by leading the protrusion **31** of the spring arm **18** via a path or track (not visible in FIGS. **13-15**) positioned behind the upper portion **30** of the scale drum **28** during the next dose setting. When the set dose is sufficiently large, the scale drum **28** and the spring arm member **29** will be sufficiently spaced apart to allow the protrusion **31** to be positioned above the upper part **30** of the scale drum **28**. Thereby the feedback mechanism has been reset, i.e. the spring arm **18** is once again ready for being deflected in a proximal direction as described above.

The injection device shown in FIGS. **13-15** is particularly suitable for having a dose delivering mechanism which is adapted to be operated by means of a mechanically biased mechanism, such as a spring.

Some preferred embodiments have been shown in the foregoing, but it should be stressed that the invention is not limited to these, but may be embodied in other ways within the subject matter defined in the following claims.

The invention claimed is:

1. An injection device comprising:

a housing having a longitudinal axis,

a dose setting member being operable by a user to set a desired dose to be injected, the desired dose thereby being a set dose,

a piston rod being adapted to cooperate with a piston so as to cause the set dose to be injected from an ampoule, and

a dose delivering mechanism being adapted to operate the piston rod in such a way that the set dose is injected by means of a mechanically biased mechanism comprising at least one spring, the dose delivering mechanism further being adapted to provide a distinct audible feedback signal to a user only at the end of injection of the set dose,

wherein first and second parts of the injection device are adapted to perform a relative rotational movement around a longitudinal axis with respect to each other during injection of a dose, and wherein said relative rotational movement causes at least the first and the second parts of the injection device to abut or engage, said abutment or engagement causing the audible feedback signal to be generated.

2. An injection device according to claim **1**, wherein the audible feedback signal further comprises a tactile signal.

3. An injection device according to claim **1**, wherein the abutment or engagement is caused by a change in a rotational velocity of at least one part of the dose delivering mechanism.

4. An injection device according to claim **3**, further comprising a ratchet operating the piston rod and having a threaded portion being adapted to engage with a part of the dose delivering mechanism, and wherein the change in a rotational velocity is generated by a change in the pitch of the threaded portion of the ratchet, said change in the pitch in return causing a change in a translational velocity of said part of the dose delivering mechanism, said change in translational velocity causing at least the first and the second parts of the injection device to abut, thereby causing the audible feedback signal to be generated.

5. An injection device according to claim **3**, wherein the dose delivering mechanism comprises a first dose part and a second dose part, the first dose part being adapted to rotate relatively to the housing during injection of a dose and the first dose part comprising means for engaging the second dose part at the end of injection of a set dose, thereby causing the second dose part to rotate along with the first dose part, and wherein the audible feedback signal is generated by the resulting rotational movement of the second dose part.

6. An injection device according to claim **5**, wherein the second dose part is positioned between the first dose part and the housing.

7. An injection device according to claim **1**, wherein the audible feedback signal is generated as a result of an abutment between the first and the second parts of the dose delivering mechanism performing a relative rotational movement.

8. An injection device according to claim **7**, wherein the audible feedback signal is generated by releasing a tension which has previously been introduced in a part of the injection device, the release of the tension being caused by the abutment between the first and the second parts.

9. An injection device according to claim **8**, wherein the tensed part comprises a spring means.

10. An injection device according to claim **8**, wherein the tension is introduced during dose setting.

11. An injection device according to claim **8**, wherein the tension is introduced during injection of a dose.

12. An injection device comprising:

a housing having a longitudinal axis,

a dose setting member being operable to set a desired dose to be injected,

a piston rod being configured to cooperate with a piston so as to cause a set dose to be injected from an ampoule, and

a dose delivering mechanism being configured to operate the piston rod in such a way that a set dose is injected,

wherein the dose delivering mechanism further is configured to provide an audible feedback signal to a user only at the end of injection of a set dose,

wherein first and second parts of the injection device are arranged and configured to perform a relative rotational movement around a longitudinal axis with respect to each other during injection of a dose,

wherein said relative rotational motion is performed in such a manner that one of the first and second parts performs a helical motion accompanying a displacement in the longitudinal direction of the injection device, and

wherein said relative rotational movement causes at least two parts of the injection device to abut or engage, said abutment or engagement causing the audible feedback signal to be generated.

13. An injection device as in claim **12**, wherein the abutment of the first and second parts occurs only after substantially all of the set dose is delivered from the pen.

14. An injection device according to claim **12**, wherein the feedback signal further comprises a tactile signal.

15. An injection device comprising:

a housing having a longitudinal axis,

a dose setting member being operable by a user to set a desired dose to be injected, the desired dose thereby being a set dose,

a piston rod being adapted to cooperate with a piston so as to cause the set dose to be injected from an ampoule, and

a dose delivering mechanism being adapted to operate the piston rod in such a way that the set dose is injected by means of a mechanically biased mechanism comprising at least one spring, the dose delivering mechanism further being adapted to provide a distinct audible feedback signal to a user only at the end of injection of the set dose,

wherein first and second parts of the injection device are adapted to perform a relative rotational movement around a longitudinal axis with respect to each other during injection of a dose, and wherein said relative rotational movement between the first and the second parts causes at least the first and the second parts of the injection device to abut or engage, said abutment or engagement of the first and second parts causing the audible feedback signal to be generated.

16. An injection device comprising:

a housing having a longitudinal axis,

a dose setting member being operable by a user to set a desired dose to be injected, the desired dose thereby being a set dose, wherein the dose setting member is rotatable about a longitudinal axis,

a piston rod being adapted to cooperate with a piston so as to cause the set dose to be injected from an ampoule, and

a dose delivering mechanism being adapted to operate the piston rod in such a way that the set dose is injected by means of a mechanically biased mechanism comprising at least one spring, the dose delivering mechanism further being adapted to provide a distinct audible feedback signal to a user only at the end of injection of the set dose,

wherein first and second parts of the injection device are adapted to perform a relative rotational movement around a longitudinal axis with respect to each other during injection of a dose, wherein the rotation is about the longitudinal axis and wherein said relative rotational movement between the first and the second parts causes at least the first and the second parts of the injection device to abut or engage during the final portion of an injection, said abutment or engagement of the first and second parts causing the audible feedback signal to be generated.

17. An injection device as in claim **16**, wherein the abutment of the first and second parts occurs only after substantially all of the set dose is delivered from the pen.

* * * * *

EXHIBIT G

US009616180B2

(12) **United States Patent**
Markussen

(10) **Patent No.: US 9,616,180 B2**
(45) **Date of Patent: *Apr. 11, 2017**

(54) **AUTOMATIC INJECTION DEVICE WITH A TOP RELEASE MECHANISM**

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(72) Inventor: **Tom Hede Markussen**, Bagsvaerd (DK)

(73) Assignee: **Novo Nordisk A/S**, Bagsvaerd (DK)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **14/797,350**

(22) Filed: **Jul. 13, 2015**

(65) **Prior Publication Data**

US 2015/0314076 A1 Nov. 5, 2015

Related U.S. Application Data

(63) Continuation of application No. 13/326,738, filed on Dec. 15, 2011, now Pat. No. 9,108,002, which is a (Continued)

(30) **Foreign Application Priority Data**

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A61M 5/315 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC ***A61M 5/31551*** (2013.01); ***A61M 5/20*** (2013.01); ***A61M 5/3156*** (2013.01); ***A61M 5/31525*** (2013.01); ***A61M 5/31528*** (2013.01); ***A61M 5/31553*** (2013.01); ***A61M 5/31585*** (2013.01); *A61M 5/24* (2013.01); *A61M 5/31583* (2013.01); *A61M 5/31593* (2013.01); *A61M 2005/202* (2013.01); *A61M 2005/3126* (2013.01)

(58) **Field of Classification Search**
CPC A61M 5/31525; A61M 5/31553; A61M 5/3156; A61M 5/20; A61M 5/24
See application file for complete search history.

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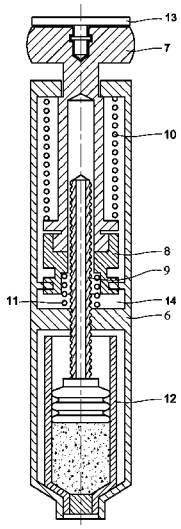
Primary Examiner — Laura Bouchelle
(74) *Attorney, Agent, or Firm* — Wesley Nicolas

(57) **ABSTRACT**

The present invention relates to a handheld mechanical injection device by which set doses of a liquid medicament can be injected from a medical reservoir. The medicament is expelled through an injection needle by release of a power reservoir in the device, the power reservoir being fully or partially released by actuation of a user operable release member being positioned at or near an upper end of the injection device, the upper end being that end of the injection device which is opposite the injection needle.

14 Claims, 13 Drawing Sheets



Related U.S. Application Data

continuation of application No. 11/813,435, filed as application No. PCT/DK2006/000032 on Jan. 20, 2006, now Pat. No. 8,096,978.

(60) Provisional application No. 60/647,320, filed on Jan. 26, 2005.

(51) **Int. Cl.**

A61M 5/20	(2006.01)
A61M 5/24	(2006.01)

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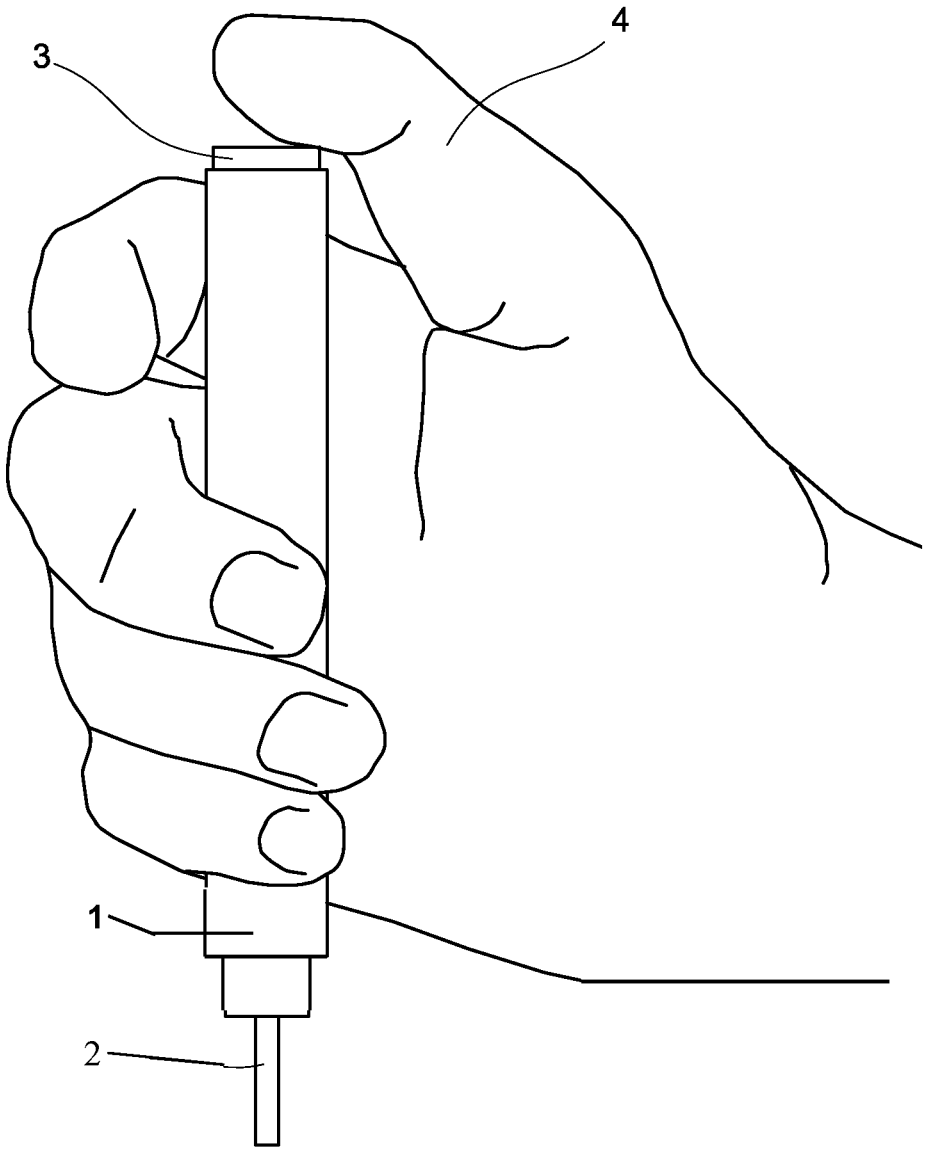

FIG. 1

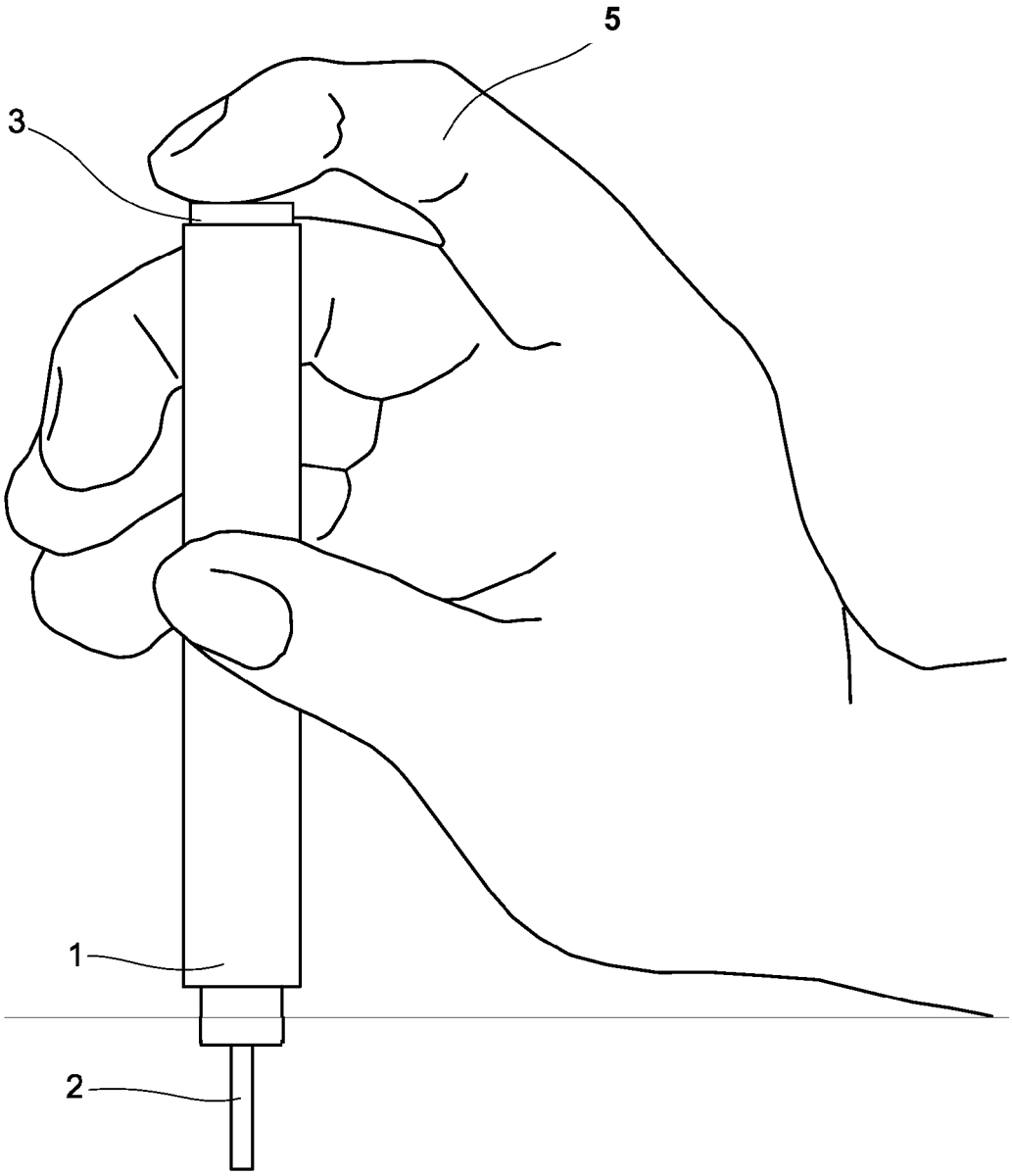

FIG. 2

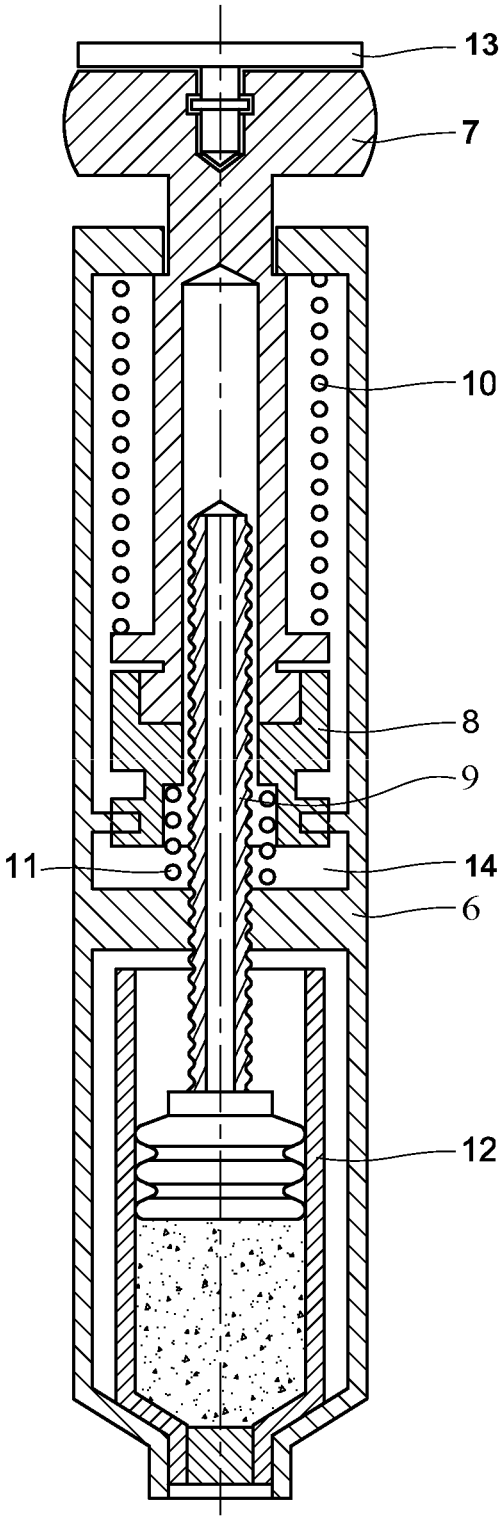

FIG. 3

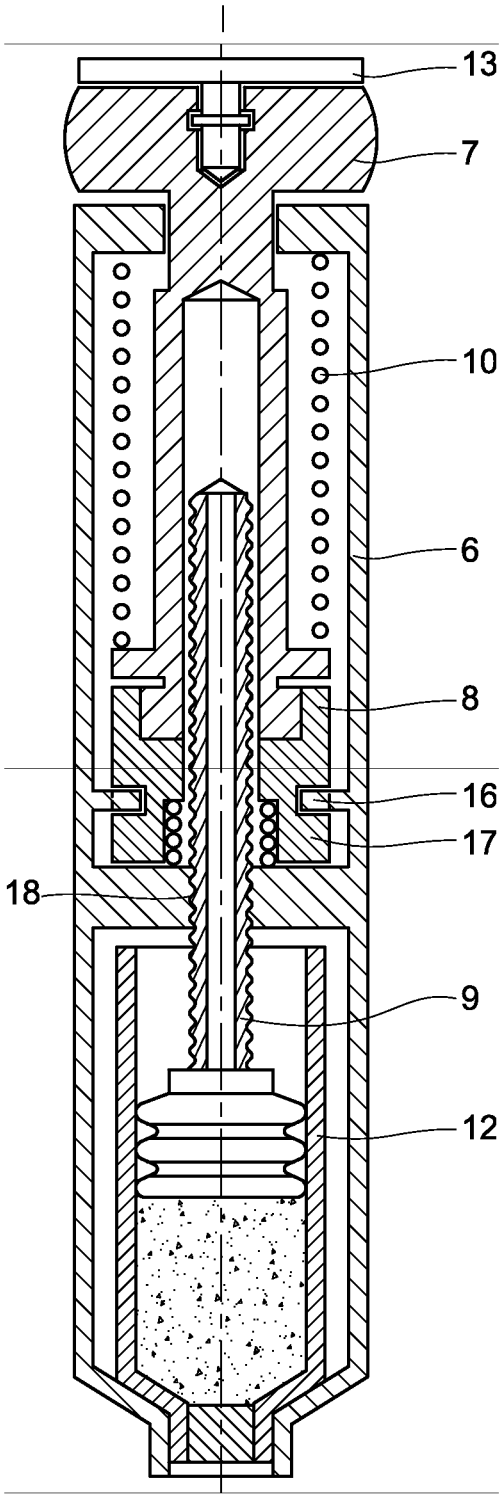

FIG. 4

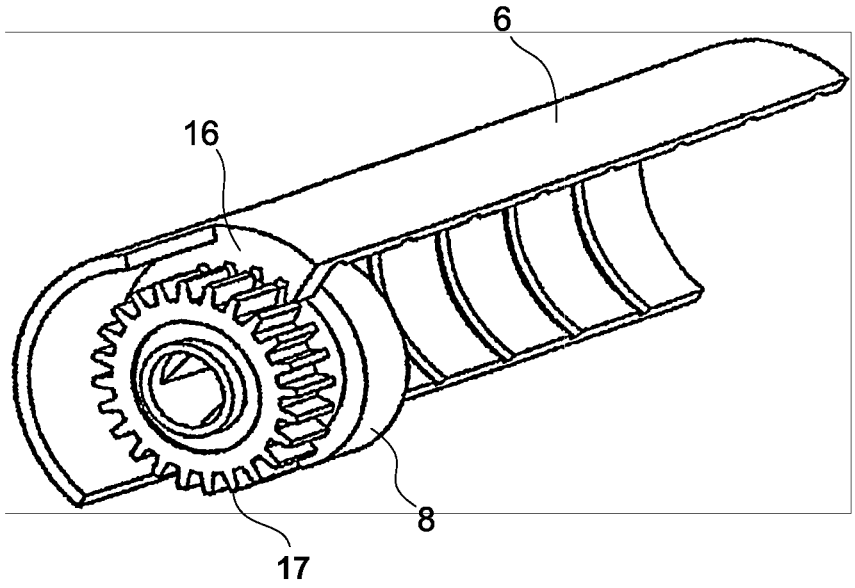

FIG. 5

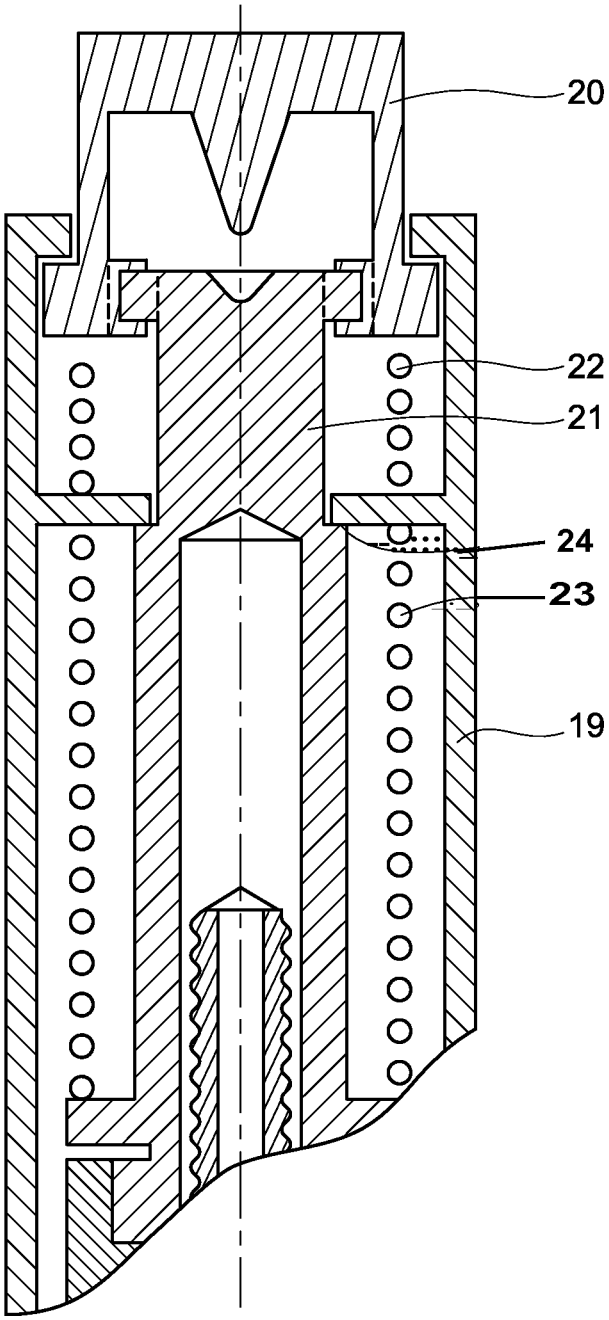

FIG. 6

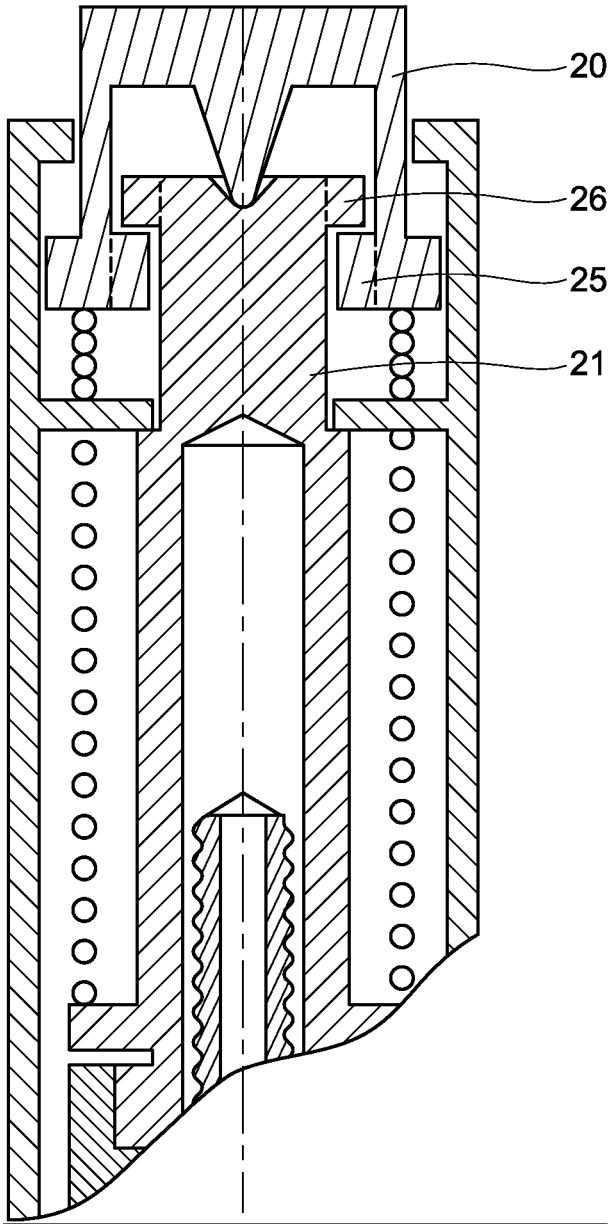

FIG. 7

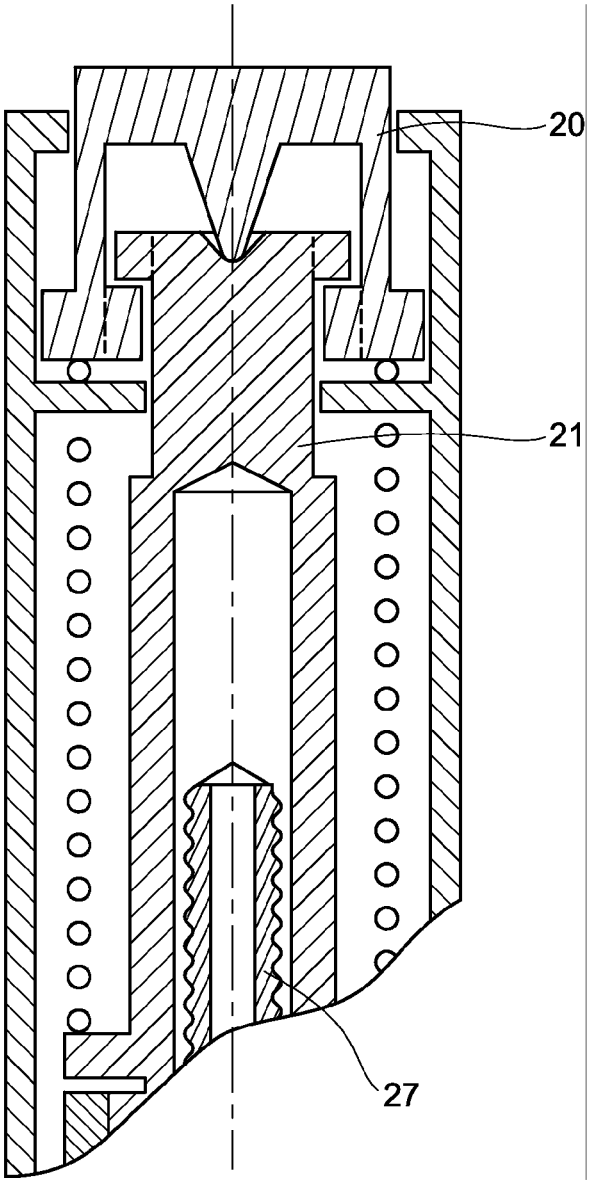

FIG. 8

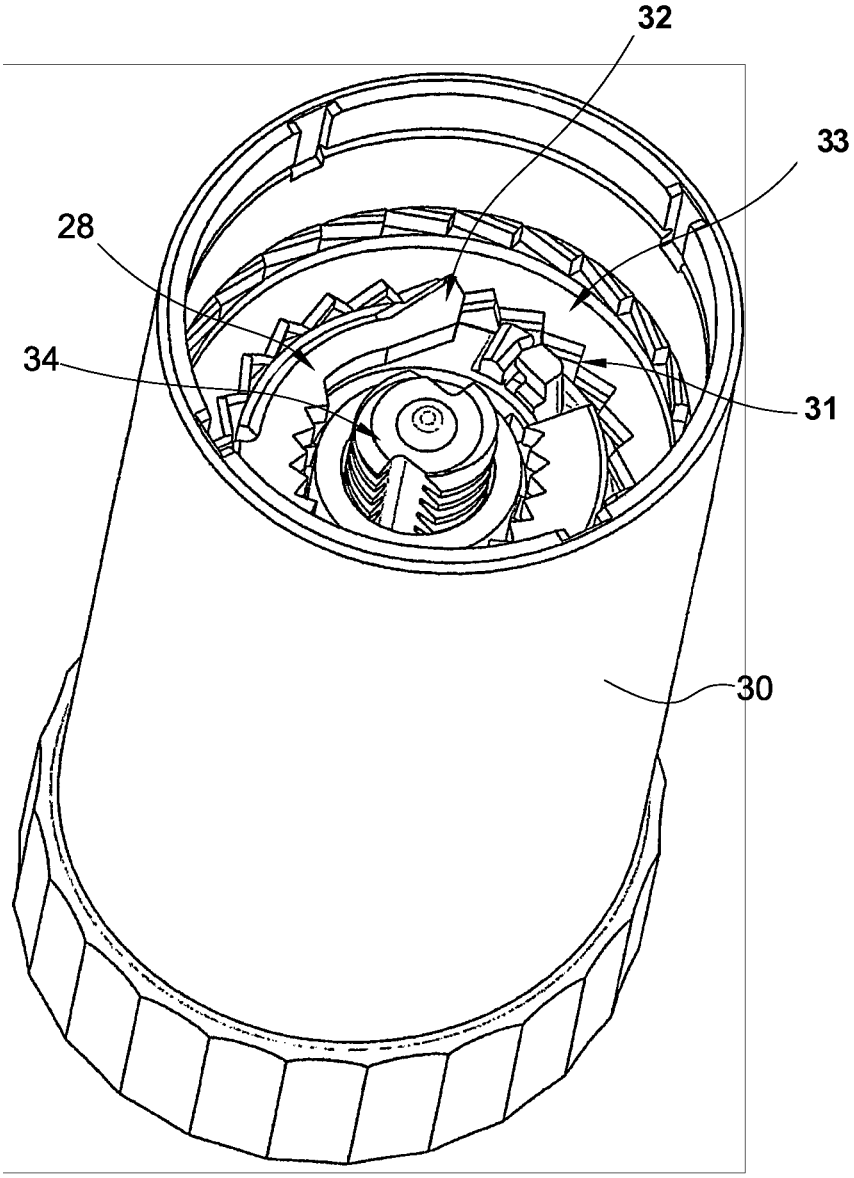

FIG. 9

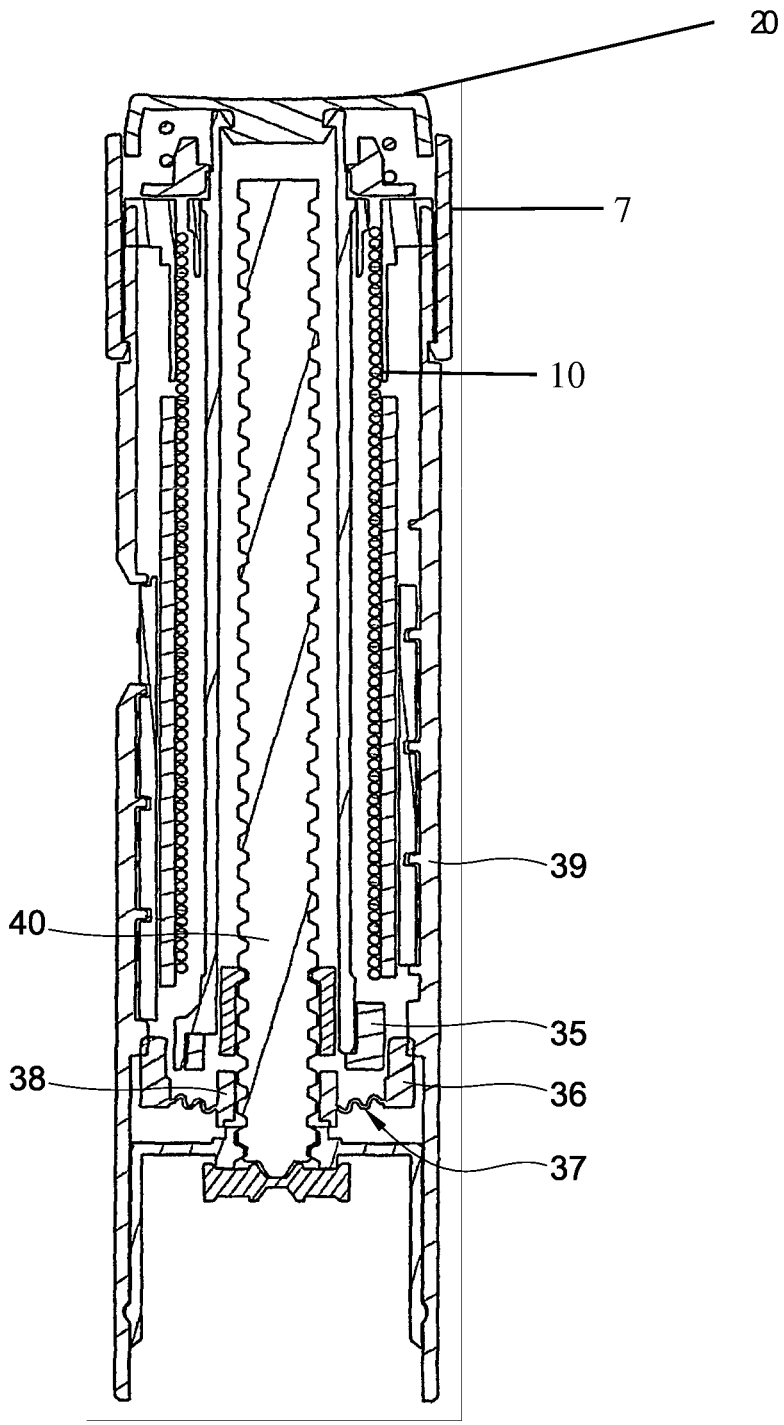

FIG. 10

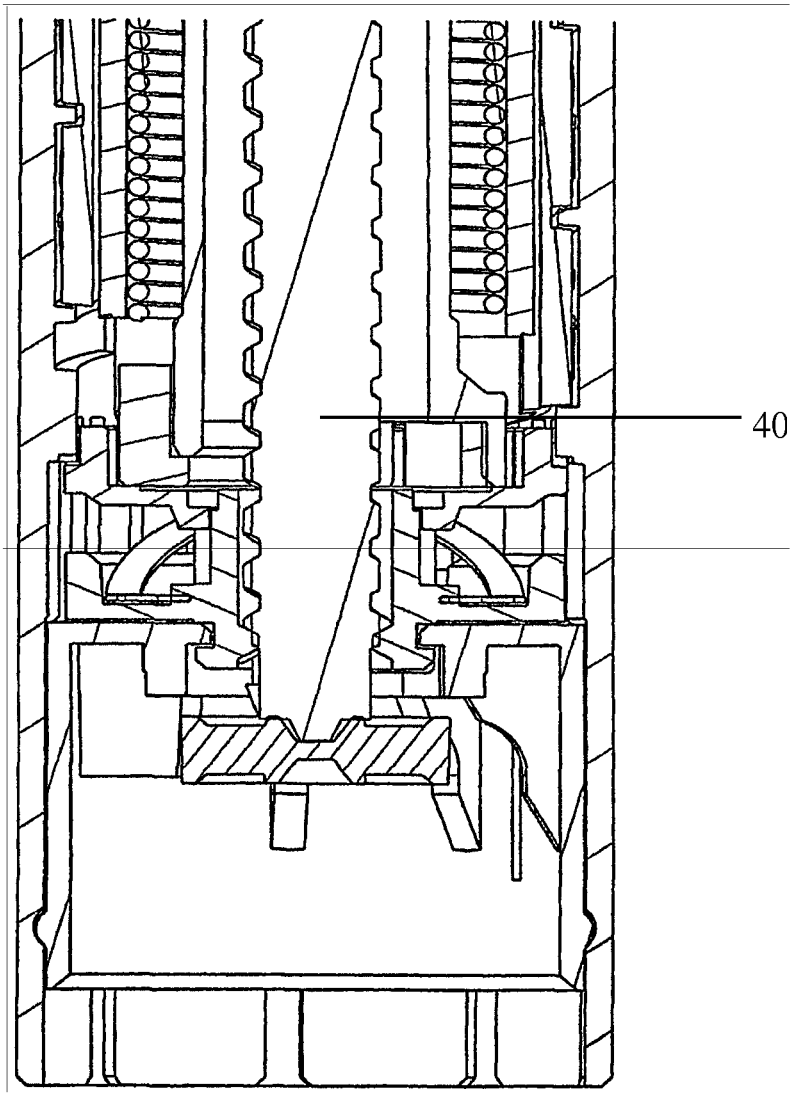

FIG. 11

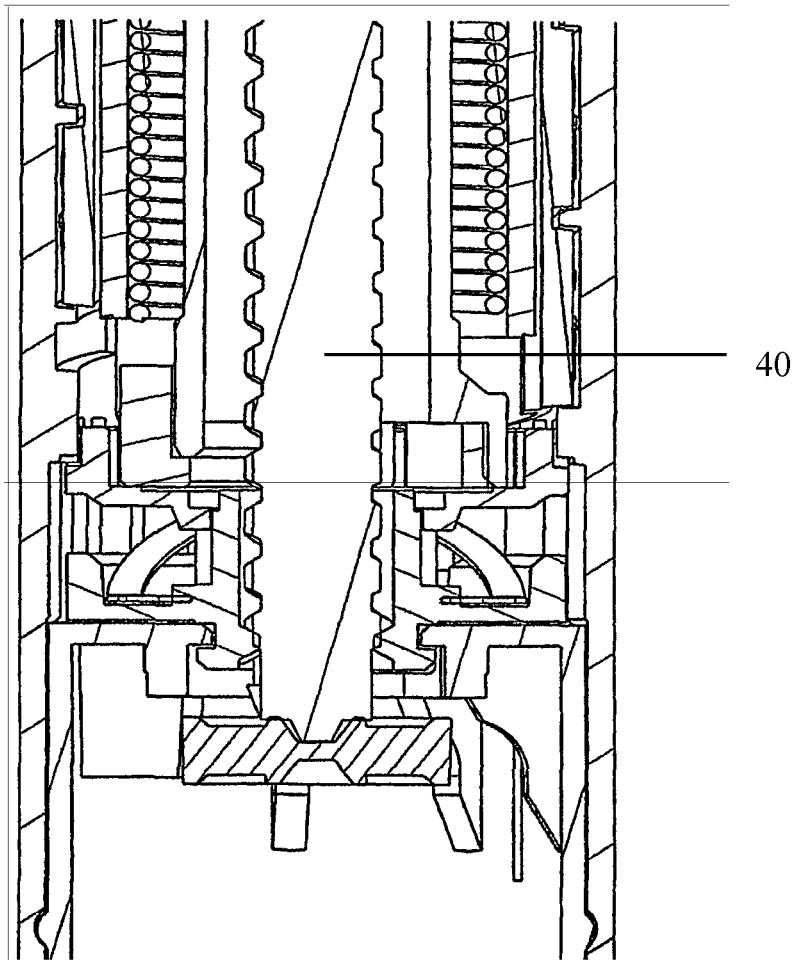

FIG. 12

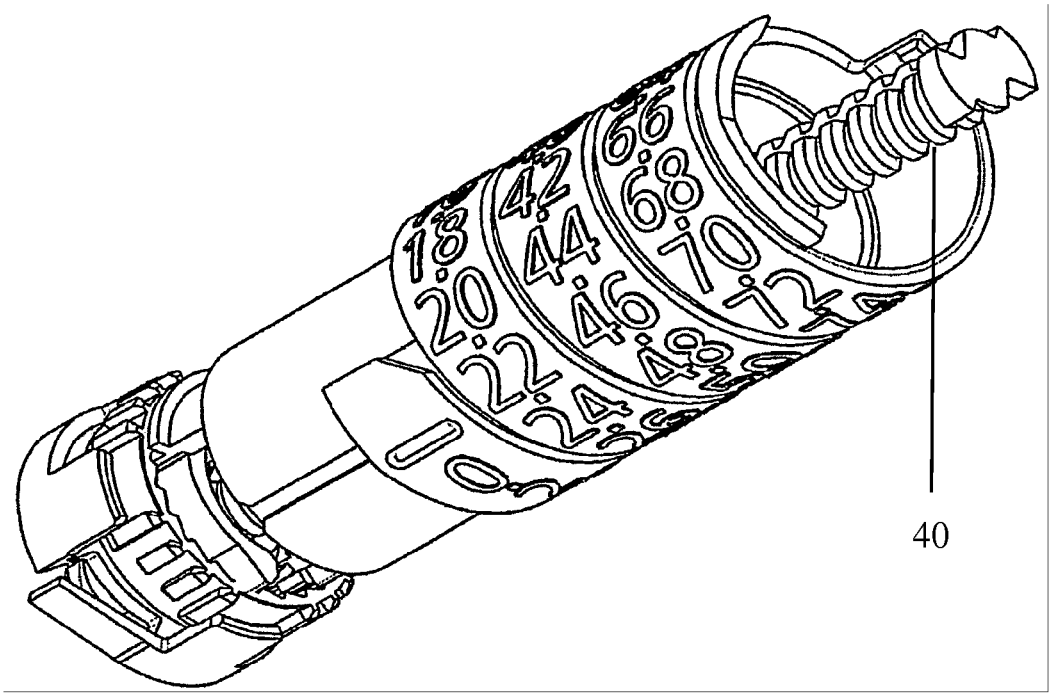
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FIG. 13

AUTOMATIC INJECTION DEVICE WITH A TOP RELEASE MECHANISM

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 13/326,738, filed Dec. 15, 2011 (Issue Fee paid) which is a continuation of U.S. patent application Ser. No. 11/813,435 filed Jun. 2, 2008 (Issued) which is a 35 U.S.C. §371 national stage application of International Patent Application PCT/DK2006/000032 (published as WO 2006/076921), filed Jan. 20, 2006, which claimed priority of Danish Patent Application PA 2005 00113, filed Jan. 21, 2005; this application further claims priority under 35 U.S.C. §119 of U.S. Provisional Application 60/647,320, filed Jan. 26, 2005.

The present invention relates to an automatic and handheld mechanical injection device where an injection of a set dose of medicament is initiated by actuating a release member being arranged at or near the top of the injection device.

BACKGROUND OF THE INVENTION

Automatic injection devices have previously been disclosed in the patent literature. Automatic injection devices contain some sort of power reservoir where electrical or mechanical energy can be accumulated. The accumulated energy is easily released by actuating a release mechanism whereby the accumulated energy assists the user in injecting a set dose of medicine and/or assisting needle insertion.

For example, EP 0 516 473 A1 discloses an injection device having a needle which, when the device is operated, is first caused to project, then liquid is forced out through it, and finally the needle is automatically retracted. The needle extends forwardly from a capsule that can slide longitudinally within a barrel-like body, a relatively weak spring normally maintaining the capsule and needle retracted. A more powerful spring acts oppositely on a plunger which, when released, shoots the capsule forward by acting on the liquid therein, and then forces the liquid out through the projecting needle. At the end of the forward stroke the plunger and capsule are decoupled and the weak spring returns the exhausted capsule and its needle to the retracted position. The spring acting on the plunger can be released by a release button positioned on the outer surface of the injection device.

In WO 01/41838 discloses a handheld injection device by which set doses of a liquid medicament can be injected from a medical reservoir, such as cylinder ampoule, by release of a power reservoir in the device. The power reservoir can either be an electric battery by which a motor can be energized to press out a set dose of medicine, or a strained spring maintained in its strained position by a detent which spring when released can press out a set dose of medicine. When the power reservoir is released, the liquid medicine will be pressed out from the cylinder ampoule through an injection needle mounted on the cylinder ampoule or on the injection device carrying the cylinder ampoule. The power reservoir is released fully or partially by activating a release button, such as an electric switch, located on the housing of the injection device and in the distal half of the length of the injection device. By making at least a part of the distal third of the injection device of an ergonomic shaped cross section, the user can grip the injection device as a pencil is gripped by a thumb, an index finger and a long finger.

In both EP 0 516 473 A1 and WO 01/41838 the release buttons are positioned on an outer surface of the injection devices. In EP 0 516 473 A1 the release button is position on the outer side of the cylindrical body, whereas in WO 01/41838 the release button is positioned close to the injection needle of the injection device. However, it may be advantageous to position the release button or mechanism so that the injection device can be activated by providing a force to the upper region of the injection device—preferably to a release button or mechanism arranged axially with the injection device.

It is an object of the present invention to provide an automatic and handheld mechanical injection device having a combined release member and dose setting member

It is a further object of the present invention to provide an automatic and handheld mechanical injection device where an injection of a set dose can be initiated using the thumb or the index finger of the hand handling the injection device by providing an axial force to an upper region of the injection device.

It is a still further object of the present invention to provide an automatic and handheld mechanical injection device having an exterior design very similar to conventional manual injection devices.

SUMMARY OF THE INVENTION

The above-mentioned objects are complied with by providing, in a first aspect, a handheld injection device by which set doses of a liquid medicament can be injected from a medical reservoir through an injection needle by release of a power reservoir in the device, the power reservoir being adapted to be fully or partially released by actuation of a user operable release member positioned at or near an upper end of the injection device, the upper end being that end of the injection device which is opposite the injection needle, the power reservoir being adapted to be powered by rotation of a rotatably mounted dose setting member.

The amount of power provided to the power reservoir may depend on the angle of rotation of the dose setting member. Thus, a rather limited rotation of the dose setting member provides a relatively small amount energy to the power reservoir, whereas a large rotation of the dose setting member provides a relatively large amount of energy to the power reservoir.

The release member may be positioned less than one fifth or one sixth of the length of the injection device from the upper end. Alternatively, the release member may be axially arranged relative to the injection device so that the release member forms a push button like release member on the top of the injection device.

The release member may be operatively connected to a dose setting member of the injection device in that the release member may engage the dose setting member via a key/keyway connection when the dose setting member is in a dose setting position. The release member may be released from the key/keyway connection with the dose setting member when the dose setting member is in a dose injecting position. With this arrangement, the handheld injection device has no rotating exterior parts or elements.

The power reservoir may be a resilient member, such as a torsion spring or a linear spring, the resilient member being, when released, adapted to press out a set dose of medicine from the medical reservoir through the injection needle. The release member may be operatively connected to a release mechanism adapted to release the resilient member when said release member is actuated. The release

member may have a shape which is ergonomic shaped to be activated by a thumb or an index finger of the user.

The medical reservoir may be a cylindrical ampoule comprising a first and a second end of which the first end is closed by a pierceable membrane which may be pierced by a first end of the injection needle when this needle is mounted on the device. The other end of the injection needle may be sharp so as to be able to pierce the skin at the position where an injection is to be made. The second end of the ampoule may be closed by a piston which may be forced into the ampoule so as to expel medicament through the needle.

The handheld injection device may further comprise a rotatably arranged drive member being adapted to at least partly engage with at least part of a drive track of an associated piston rod, the drive member being adapted to be positioned in a first axial position when the dose setting member is in a dose setting position, the drive member further being adapted to be positioned in a second axial position when the dose setting member is in a dose injection position, the drive member being adapted to release energy accumulated in the power reservoir when the drive member is in its second axial position.

The drive member may be adapted to rotate the associated piston rod upon releasing the accumulated energy in the power reservoir. However, in its first axial position, the drive member is prevented from rotating because the drive member engages at least part of a housing of the injection device. The injection device may further comprise a resilient member, such as a linear spring, for biasing the drive member in a direction towards the dose setting member. The linear spring operatively connects the drive member and the housing.

The dose setting member may be adapted to be moved a distance along an axial direction of the injection device so as to move the drive member between the first and second axial positions. The drive member may be adapted to be moved from the first to the second axial position by applying a force to the dose setting member, the force being applied along the axial direction of the injection device.

The injection device may, as already mentioned, further comprise a push button axially arranged with the dose setting member, the push button being adapted to engage with the dose setting member when the dose setting member is in its dose setting position, and disengage from the dose setting member when the dose setting member is in its dose injection position. By disengage is meant that the push button and the dose setting member are mutually rotatable when this disengaged state is reached. The injection device may further comprise a resilient member, such as a linear spring, for axially biasing the push button in a direction away from the drive member.

The handheld injection device may further comprise a rotatably mounted display member adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member, the rotatably mounted display member being rotatable over an angle corresponding to at least one revolution of the display member. The display member may comprise a dose indicator barrel having numerals arranged along a substantially helical path on an outer surface thereof. Alternatively or in addition, the display member may comprise a counting device having two or more display wheels having numerals arranged on an outer surface thereof.

The handheld injection device may further comprise the associated the piston rod, the piston rod having a threaded outer surface with the drive track arranged in a longitudinal direction of the outer surface of the piston rod. The drive member may be operatively connected to the dose setting member via a ratchet.

The power reservoir may be arranged between the housing and the dose setting member in such a way that when the dose setting member is rotated, energy is accumulated in the power reservoir. The power reservoir may comprise a torsion spring formed as a helical spring extending coaxially with the associated piston rod.

It is to be noted that the interaction between the drive member, the piston rod and the housing may be implemented in various ways. Above, the piston rod has a threaded outer surface and a drive track arranged in the longitudinal direction of the rod. A key arranged on the drive member engages the drive track of the rod and the forward movement of the rod relative to the housing is caused by the threaded outer portion of the rod which meshes with a corresponding threaded portion of the housing. Alternatively, the threaded outer surface of the rod may mesh with a corresponding threaded portion of the drive member whereas the drive track arranged in the longitudinal direction of the rod engages with a key fixedly arranged relative to the housing.

BRIEF DESCRIPTION OF THE INVENTION

The present invention will now be explained in further details with reference to the accompanying figures wherein

FIG. **1** shows an injection device according to the present invention where the release button arranged at the top of the device is activated by the thumb of the user,

FIG. **2** shows an injection device according to the present invention where the release button arranged at the top of the device is activated by the index finger of the user,

FIG. **3** shows an injection device according to the present invention where the release button is arranged on the top surface of the dose setting member, and where the drive member is in its locked position (dial position of dose setting member),

FIG. **4** shows an injection device according to the present invention where the release button is arranged on the top surface of the dose setting member, and where the drive member is in its released position (dosing position of dose setting member),

FIG. **5** shows an expanded view of the drive member in its released position,

FIG. **6** shows an expanded view of the release member in its locked position with the dose setting member,

FIG. **7** shows an expanded view of the release member in its released position with the dose setting member,

FIG. **8** shows an expanded view of the release member in a further released position where the dose setting member is allowed to rotate,

FIG. **9** shows one way of implementing the release mechanism for releasing the energized power reservoir,

FIG. **10** shows another way of implementing the release mechanism for releasing the energized power reservoir,

FIG. **11** shows a third way of implementing the release mechanism for releasing the energized power reservoir,

FIG. **12** shows a fourth way of implementing the release mechanism for releasing the energized power reservoir, and

FIG. **13** shows a fifth way of implementing the release mechanism for releasing the energized power reservoir.

While the invention is susceptible to various modifications and alternative forms, specific embodiments have been shown by way of example in the drawings and will be described in detail herein. It should be understood, however, that the invention is not intended to be limited to the

particular forms disclosed. Rather, the invention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the appended claims.

DETAILED DESCRIPTION OF THE INVENTION

FIGS. **1** and **2** show the present invention in its most general aspect. In FIG. **1** a handheld injection device **1** is shown. The injection device has an injection needle **2** fastened to one of its ends, whereas a release button **3** is arranged at the opposite end of the injection device. When the release button **3** is actuated by provided a force to it along the axial direction of the device energy is released from an internal power reservoir whereby a set dose of medicine is injected from the injection device. In FIG. **1** the release button is actuated by the thumb **4** of the user, whereas in FIG. **2** the release button is actuated by the index finger **5** of the user.

The medicine to be injected is contained in a medical reservoir typically formed as a cylindrical ampoule.

The energy released when the release button **3** is mechanical energy. The power reservoir can be a resilient member, such as a torsion spring, the resilient member being, when released, adapted to press out a set dose of medicine from the medical reservoir through the injection needle. The release button is operatively connected to some sort of release mechanism adapted to release the resilient member when the release button is actuated.

FIG. **3** shows a cross-sectional view of one embodiment of the present invention. The injection device shown in FIG. **3** comprises a housing **6**, a dose setting member **7**, a drive member **8**, a piston rod **9**, a torsion spring **10**, a biasing spring **11**, a cylindrical ampoule **12** and a release member **13**. FIG. **3** shows the injection device in a state where the dose setting member **7** is in its dose setting position.

A dose is set by rotating the dose setting member **7** a certain angle or a certain number of turns. By rotating the dose setting member **7** the torsion spring **10** is strained because the two ends of the torsion spring **10** are fixed to the housing **6** and to the dose setting member **7**, respectively. The dose setting member **7** is operatively connected to the drive member **8** via a ratchet (not shown). This ratchet prevents that the dose setting member **7** returns to its initial position upon straining the torsion spring **10**. Since the drive member **8** engages the housing **6** via a key/keyway connection or a gear wheel, the drive member **8** is not allowed to rotate relative to the housing **6** as long as the dose setting member **7** is in its dose setting position as illustrated in FIG. **3**. In order to keep the dose setting member **7** and the drive member **8** in the dose setting position, the drive member **8** and the dose setting member **7** is biased in a direction towards the top end of the injection device. This biasing is provided by a spring element, such as a linear spring **11**, arranged between the drive member **8** and part of the housing **6**. Thus, in order to release the drive member **8** from its engagement with the housing **6**, a force needs to be provided in order move the dose setting member **7** and the drive member **8** towards the medicine ampoule **12**. A miner cavity **14** ensures that this forward movement of the dose setting member **7** and the drive member **8** can be performed. Similarly, since the drive member **7** and the piston rod **9** engage via a key connection the drive member **8** is allowed to move axially relative to the piston rod **9**.

The drive member **8** has been released from its engagement with the housing **6** in FIG. **4**. In order to achieve this releasing a force, indicated by arrow **15**, has been provided to the release member **13** whereby the release member **13**, the dose member **7** and the drive member **8** have all been moved a distance towards the medicine ampoule **12**. The force indicated by arrow **15** would normally be provided by the thumb or the index finger of the user.

As seen in FIG. **4** the engaging region **16** of the housing is now separated from the engaging region **17** of the drive member **8**. This disengagement allows that the strained torsion spring **10** can release its energy to the dose setting member **7**. The dose setting member **7** and the drive member **8** are fixedly related via the intermediate ratchet (not shown). Thus, when a disengagement between engaging regions **16** and **17** has been established, the dose setting member **7** and the drive member **9** will rotate until the torsion spring **10** reaches an unstrained state. Since the drive member **8** and the piston rod **9** is connected via a key connection the rotation of the dose setting member **7** and the drive member **8** will cause the piston rod **9** to rotate as well. The piston rod **9** has an outer threaded surface which engages with a corresponding threaded portion **18** of the housing whereby the piston rod **9**, upon rotation thereof, will perform a translational movement along the axial direction of the injection device in the direction of the ampoule **12**.

Thus, the force provided to the release member **13** will release accumulated energy in the torsion spring. This energy is converted to a translational movement of the piston rod towards the ampoule whereby a set dose of medicine can be injected from the injection device.

FIG. **5** shows a cut half illustration of the housing **6** of the injection device. As seen, the drive member **8** comprises an engagement region/part **17** formed as gear wheel. Similarly, the housing **6** comprises a corresponding engagement region/part **16** adapted to receive and engage with the teeth of the gear wheel **17**.

FIG. **6** shows another embodiment of the present invention. In contrast to the embodiment shown in FIGS. **3-5** the embodiment shown in FIG. **6** contains no rotating exterior parts or elements. All rotating parts or elements are positioned inside the housing **19**. FIG. **6** shows a release member **20** (formed as a push button) which is mechanically biased towards the end of the injection device by spring element **22**. The release member **20** and dose setting member **21** are forced into engagement as long as the dose setting member **21** is in its dose setting position. The dose setting member **21** is mechanically biased towards the same end of the injection device as the release member **20** due to a spring element (shown as spring element **11** in FIG. **3**) acting on the drive member (shown as drive member **8** in FIG. **3**) which again acts on dose setting member **21**. As seen in FIG. **6** the dose setting member **21** is biased against a mechanical stop **24** where a shoulder formed in the dose setting member **21** abuts a part of the housing **19**.

In FIG. **7** an intermediate stage is illustrated. Here the release member **20** has been pushed an axial distance sufficient to release the release member **20** from the dose setting member **21**. Note that the engagement region **25** and **26** are disengaged, but since the shoulder of the dose setting member still abuts the housing part no axial movement of the dose setting member **21** has been achieved at this stage. Thus, the dose setting member **21** is prevented from rotating since the drive member (not shown) is still engaging the housing.

In FIG. **8** the dose setting member **21** has been moved an axial distance towards the ampoule (not shown) whereby the dose setting member is allowed to rotate freely causing the piston rod **27** push a set dose of medicine out of the ampoule

(not shown). Note that the release member **20** and the dose setting member **21** are disengaged in FIG. **8**. This means that the release member **20** is not rotating relative to the housing during injection of a set dose. Then the set dose has been injected the user removes his thumb or index finger from the release member whereby the release member and the dose setting member return to their respective positions as illustrated in FIG. **6**, but now with the spring element **23** being in a relaxed state.

In case the user wants to set a new dose, the user rotates the release member which engages the dose setting member whereby the new dose can be set. Injecting the set dose is achieved by following the steps illustrated in FIGS. **7** and **8**.

FIGS. **9-13** show various embodiments of release mechanisms for releasing the energized power reservoir.

In FIG. **9** a torsion spring (not shown) is energized by rotating a ratchet **28** which is operatively connected to the housing **30** of the injection device when the dose to be injected is being set. In the dose setting position the ratchet **28** is operatively connected with housing part **31** via ratchet arm **32**. Energy accumulated in the torsion spring is released by displacing the ratchet **28** axially whereby it is released from its connection with housing part **31** in that the ratchet arm **32** is moved into housing part **33** whereby the piston rod **34** is allowed to rotate thereby expelling a set dose of medicament.

In the embodiment depicted in FIG. **9** a dose indicator barrel (not shown) moves in the direction away from the push-button (not shown) during setting of a dose. Obviously, the dose indicator barrel may be adapted to move in the opposite direction during setting of a dose, i.e. towards the push-button.

In the embodiment depicted in FIG. **10** the ratchet **35** is only in indirect operation with the housing **39**. The drive member of the embodiment depicted in FIG. **10** is constituted by three part—one part **36** being adapted to corporate with the housing **39**, another part **38** being adapted to drive the piston rod **40** and a flexible member **37** connecting parts **36** and **38**. The flexible member **37** is flexible in the axial direction but establishes a substantially stiff connection between parts **36** and **38** when these parts are rotated relative to each other. Thus, the flexible member **37** ensures that parts **36** and **38** are not rotatably arranged relative to each other. Thus, when the ratchet **35** is moved towards the needle end of the injection device the part **36** is disconnected from the housing **39** whereby parts **36**, **37** and **38** are allowed to rotate thereby rotating the piston rod **40**. The rotating piston rod **40** causes a set dose of medicament to be expelled from the injection device.

The embodiment depicted in FIG. **11** is similar to the embodiment in FIG. **9** except that the piston rod is moved forward by having guiding tracks arranged in the housing (instead of in the drive member) and a threaded engagement between piston rod and the drive member (instead of a threaded engagement between piston rod and housing).

FIGS. **12** and **13** show other release mechanisms between ratchet, drive member and housing.

The invention claimed is:

1. A handheld injection device, comprising:

a rotatable dose setting member that is rotatable about a longitudinal axis of a housing of the injection device,

a power reservoir comprising a torsion spring for storing energy to expel a dose of medication from the injection device,

a release member axially arranged relative to the injection device, wherein the release member forms a push button like release member,

the injection device further comprising a rotatably arranged multi-component driver (**36**, **37**, **38**) having at least a part (**38**) adapted to drive a piston rod, and a further part (**36**) being axial movable into a position disconnected from the housing releasing the energy accumulated in the power reservoir, the further part (**36**) being axially movable by the user applying a force onto the push button like release member, wherein the release member is located at the most proximal portion of the proximal end of the injection device, opposite an end of the device wherein a needle may be mounted.

2. A handheld injection device according to claim **1**, wherein the amount of power provided to the power reservoir (**10**) depends on the angle of rotation of the dose setting member (**7**).

3. A handheld injection device according to claim **1**, wherein the release member is operatively connected to the dose setting member of the injection device.

4. A handheld injection device according to claim **3**, wherein the release member engages the dose setting member via a key/keyway connection when the dose setting member is in a dose setting position.

5. A handheld injection device according to claim **4**, wherein the release member is released from the key/keyway connection with the dose setting member when the dose setting member is in a dose injecting position.

6. A handheld injection device according to claim **1**, wherein when energy from the torsion spring is released it is adapted to expel a set dose of medicine from a medicine containing reservoir through the injection needle.

7. A handheld injection device according to claim **1**, further comprising a rotatably arranged drive member (**8**) being adapted to at least partly engage with at least part of a drive track of an associated piston rod (**9**), the drive member (**8**) being adapted to be positioned in a first axial position when the dose setting member (**7**) is in a dose setting position, the drive member (**8**) further being adapted to be positioned in a second axial position when the dose setting member (**7**) is in a dose injection position, the drive member (**8**) being adapted to release energy accumulated in the power reservoir (**10**) when the drive member (**8**) is in its second axial position.

8. A handheld injection device according to claim **7**, wherein the drive member is adapted to rotate the associated piston rod upon releasing the accumulated energy in the power reservoir.

9. A handheld injection device according to claim **7**, wherein the drive member is prevented from rotating when it is in its first axial position.

10. A handheld injection device according to claim **7**, further comprising a resilient member, such as a linear spring, for biasing the drive member in a direction towards the dose setting member.

11. A handheld injection device according to claim **7**, wherein the dose setting member is adapted to be moved a distance along an axial direction of the injection device so as to move the drive member between the first and second axial positions, the drive member being movable from the first to the second axial position by applying a force to the dose setting member, the force being applied along the axial direction of the injection device.

12. A handheld injection device according to claim **7**, further comprising a rotatably mounted display member adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member, the rotatably mounted display member being rotatable over an angle corresponding to at least one revolution

of the display member, the display member comprising a dose indicator barrel having numerals arranged along a substantially helical path on an outer surface thereof.

13. A handheld injection device according to claim **7**, further comprising the associated the piston rod, the piston rod having a threaded outer surface with the drive track arranged in a longitudinal direction of the outer surface of the piston rod.

14. A handheld injection device according to claim **7**, wherein the drive member is operatively connected to the dose setting member via a ratchet.

* * * * *

EXHIBIT H

US009687611B2

(12) **United States Patent**
Moeller et al.

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(54) **INJECTION DEVICE WITH TORSION SPRING AND ROTATABLE DISPLAY**

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This patent is subject to a terminal disclaimer.

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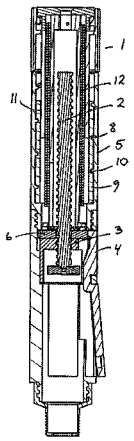
(74) *Attorney, Agent, or Firm* — Wesley Nicolas

(57) **ABSTRACT**

The present invention relates to an injection device comprising a torsion spring operatively connected to a dose setting member being adapted to set a dose to be ejected from the injection device. A rotatably mounted display member adapted to display the dose to be ejected in accordance with a setting of the dose setting member is also provided. The rotatably mounted display member is adapted to be rotated over an angle corresponding to at least one revolution of the display member. The display member may be implemented as a dose indicator barrel having numerals arranged along a helical path on an outer surface thereof, or alternatively, as a counting device having two or more display wheels having numerals arranged on an outer surface thereof.

15 Claims, 5 Drawing Sheets



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continuation of application No. 11/665,571, filed as application No. PCT/EP2005/011287 on Oct. 20, 2005, now Pat. No. 8,357,120.

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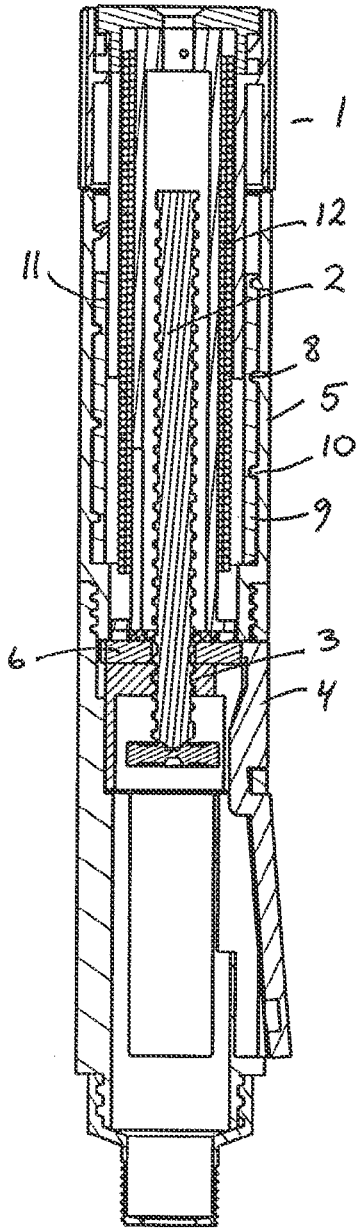

Fig. 1

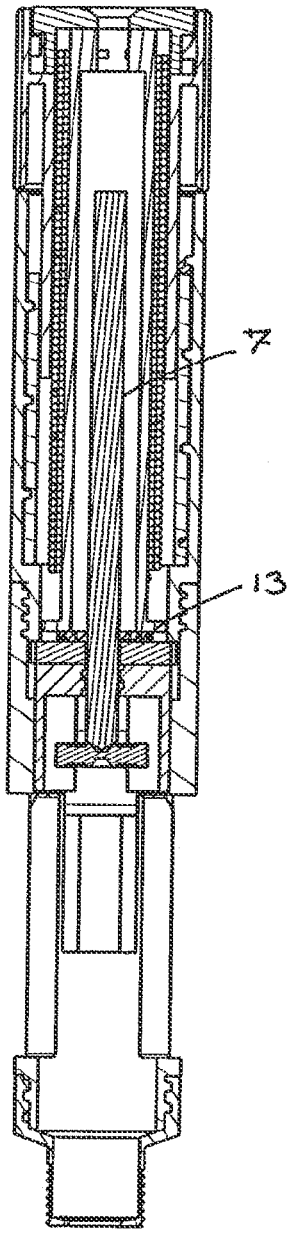

Fig. 2

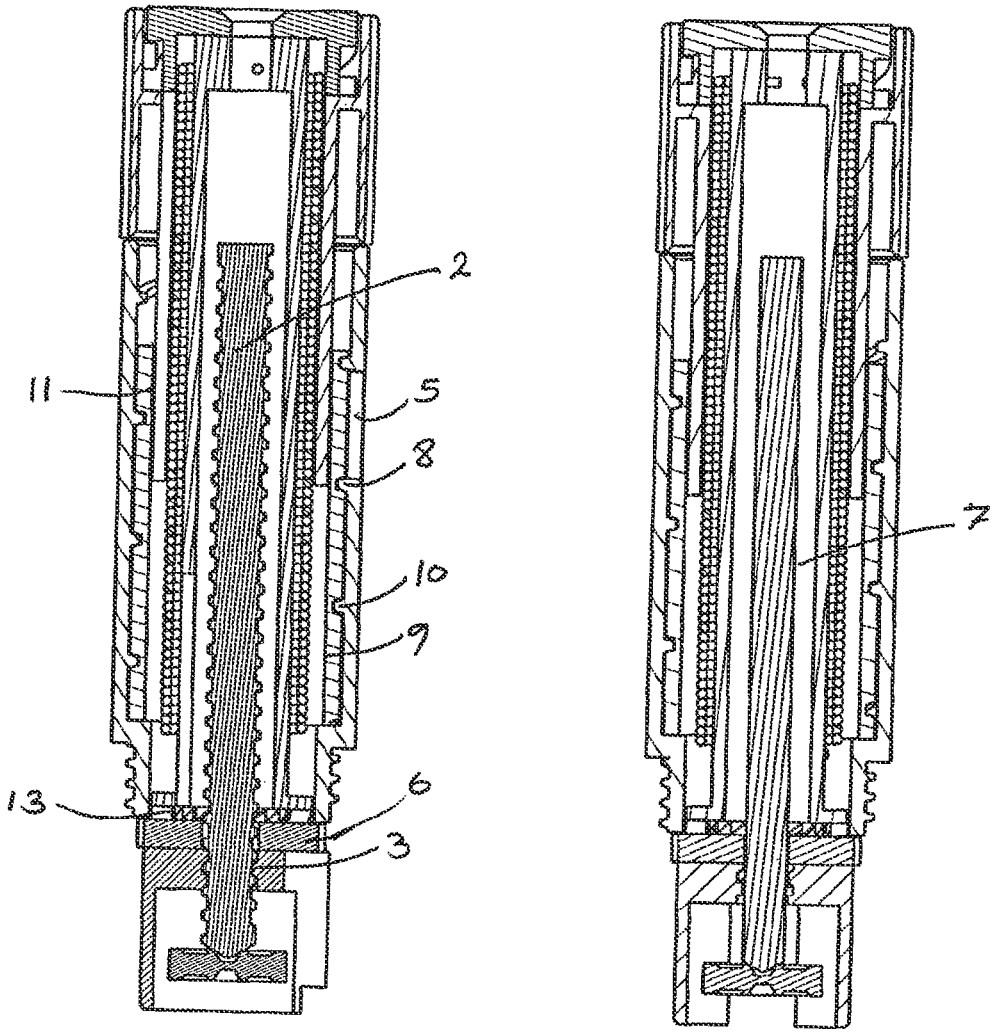

Fig. 3

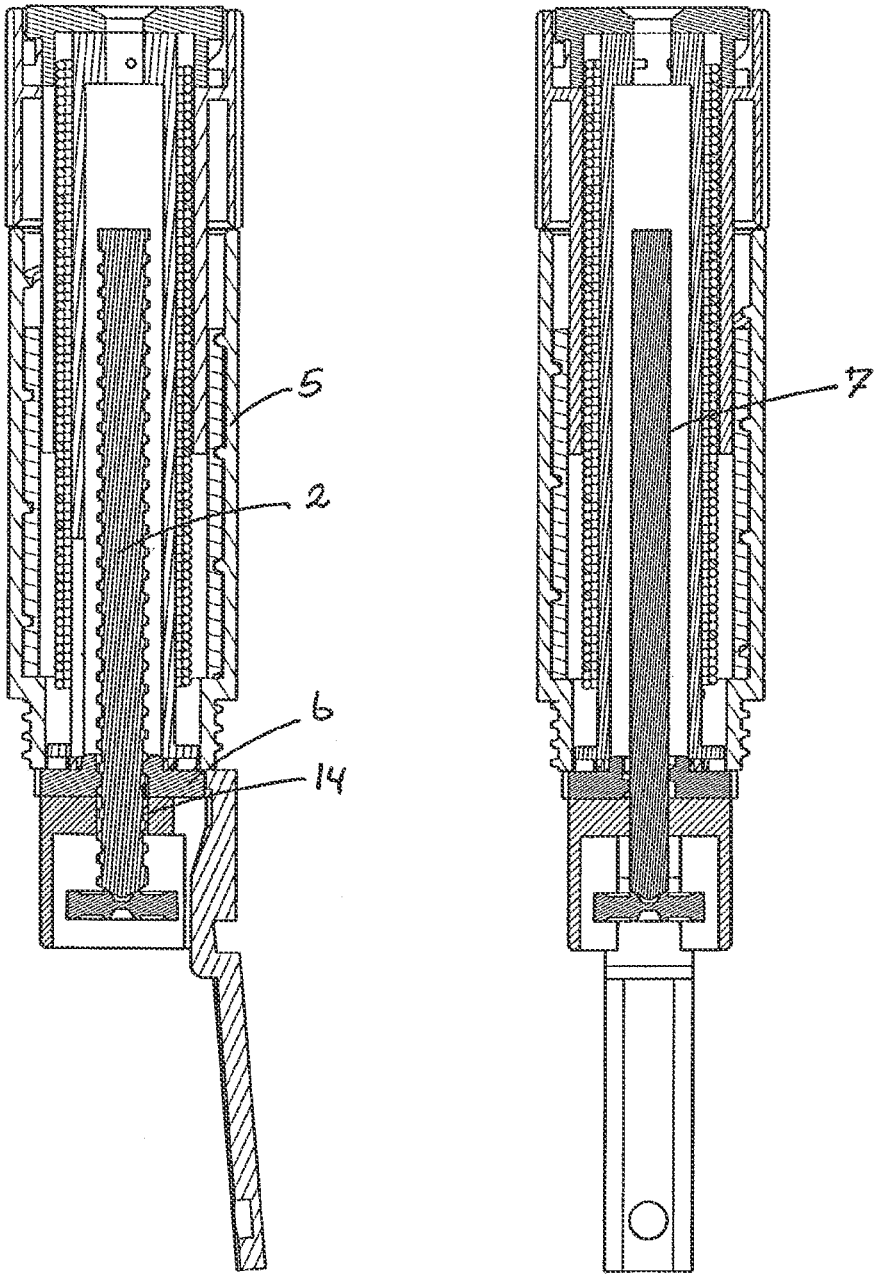

Fig. 4

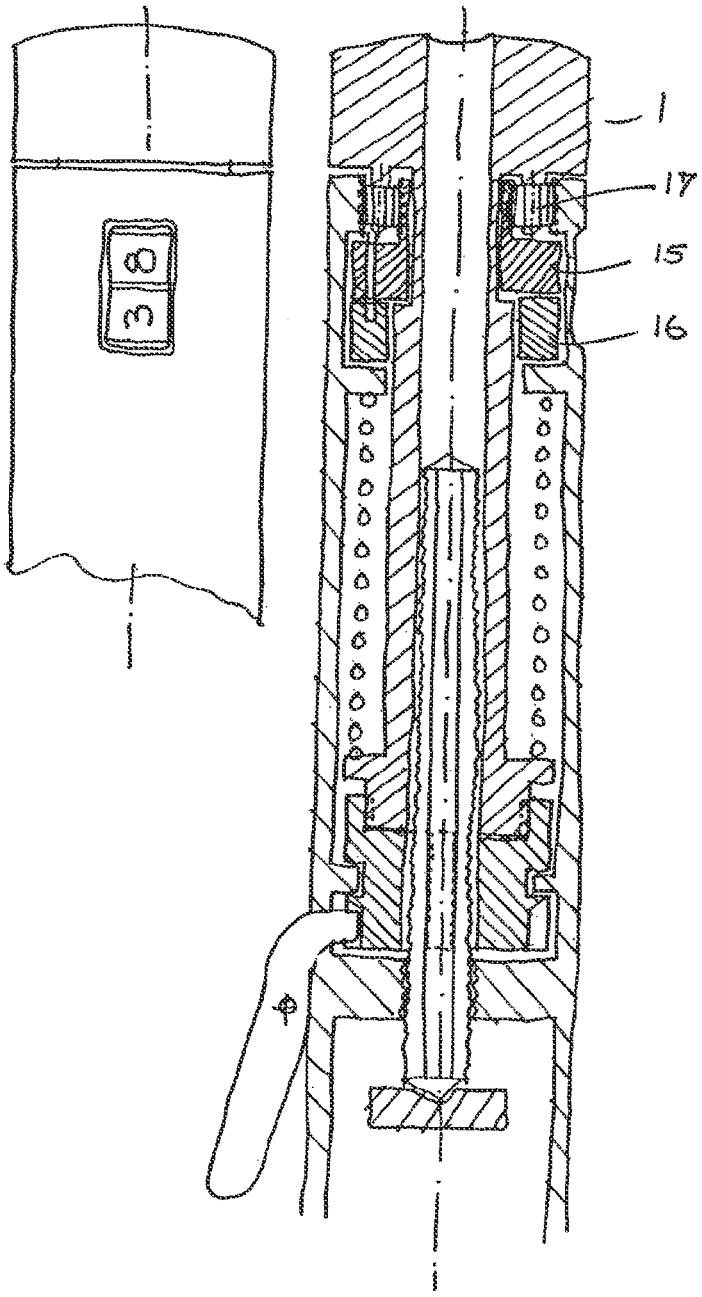

Fig. 5

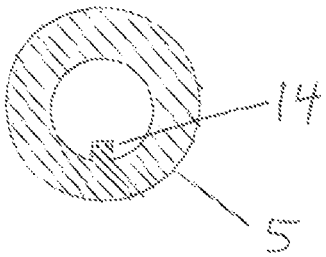

Fig. 6

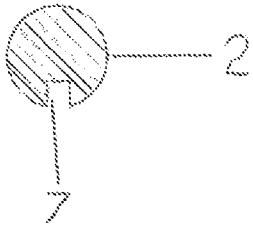

Fig. 7

INJECTION DEVICE WITH TORSION SPRING AND ROTATABLE DISPLAY

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. application Ser. No. 13/626,541, filed Sep. 25, 2012, which is a continuation of U.S. application Ser. No. 11/665,571, filed Dec. 5, 2007, which is a 35 U.S.C. §371 national stage application of International Patent Application PCT/EP2005/011287 (published as WO 2006/045528), filed Oct. 20, 2005, which claims priority of European Patent Application 04077899.5, filed Oct. 21, 2004; this application further claims priority under 35 U.S.C. §119 of U.S. Provisional Application 60/626,271, filed Nov. 9, 2004, all of which are hereby incorporated by reference.

FIELD OF THE INVENTION

The present invention relates to an injection device, such as a wind-up pen, wherein numerals indicating the dose to be ejected from the injection device are displayed over an angle of rotation exceeding one revolution. In particular, the numerals indicating the dose to be ejected are arranged along a helical path, or alternatively, numerals indicating the dose to be ejected are displayed on a counting device. The present invention ensures that an increased accuracy in dose setting may be obtained.

BACKGROUND OF THE INVENTION

Various types of automatic injection devices have been described in the literature. A majority of these automatic injection devices apply dose indicator barrels, dose indicator wheels or the like which, during dose setting, are only allowed to rotate less than one single revolution. The fact that the dose indicator barrel is only allowed to rotate less than one revolution during dose setting puts a limit to the obtainable angular resolution. This limited angular resolution also limits the accuracy of the dose setting procedure.

In prior art injection devices the dose setting scale arranged on the outer surface of the barrels or wheels contains only up to 42 scale units with an incremental of 2. Thus, the accuracy when setting a dose is limited by this rather rough incremental.

Examples of "one revolution" barrels or wheel may for example be found in U.S. Pat. No. 5,725,508, EP 0 338 806 or U.S. Pat. No. 5,104,380.

WO 02/053214 discloses an automatic injection device having a dose indicator barrel capable of rotating more than one revolution. However, the injection device according to WO 02/053214 applies a linear spring to move a piston rod in the distal direction of the injection device. Evidently, an injection device applying a linear spring has a built-in axial displacement due to compressions and extensions of the linear spring along the axial direction of the injection device. This linear movement may easily be utilized to provide axial movements of the dose indicator barrel. However, it is a disadvantage that linear springs are highly non-linear in terms of force vs. compression. In addition, a linear spring exhibits relative high mechanical looses. Thus, due to the problems relating to the non-linear properties and relatively high looses there is a need for injection devices having linear and more efficient injection assisting systems.

The above-mentioned problems may be solved by applying a torsion spring instead of the linear spring. An injection device applying a torsion spring is conceptually different from linear spring-based devices in that torsion-based systems do not have a built-in axial movement of the spring assisting the user in injecting a dose of medicament from the injection device. The advantages of torsion-based injection devices are many, the greatest of these probably being that torsion springs respond in a linear manner over a large working range.

Thus, there is a need for a torsion spring-based injection device providing an improved and more user friendly dose setting procedure. It is an object of the present invention to provide such torsion spring-based injection device having an expanded dose scale with a high resolution.

SUMMARY OF THE INVENTION

The above-mentioned object is complied with by providing, in a first aspect, an injection device comprising

- a torsion spring operatively connected to a dose setting member, the dose setting member being adapted to set a dose to be ejected from the injection device, and
- a rotatably mounted display member adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member, the rotatably mounted display member being rotatable over an angle corresponding to at least one revolution of the display member.

The display member may be adapted to be moved between two end positions. These two end positions may define or set an axial operation range of the display member. The axial operation range of the display member may be associated with a substantially linear working range of the torsion spring. The working range of the torsion spring utilized to move the display member between the two end positions may constitute only a fraction of the available working range provided by the torsion spring. Thus, by applying a torsion spring only a small and linear working range of the available working range is utilized.

The display member may comprise a dose indicator barrel having numerals arranged along a helical path on an outer surface thereof.

According to a first embodiment of the present invention, the injection device may further comprise

- a housing,
- a piston rod having a threaded outer surface with a drive track arranged in a longitudinal direction of the outer surface of the piston rod,

wherein the dose setting member is rotatably mounted and defines a passage for the piston rod, the dose setting member further having a guiding track arranged on an inner surface thereof,

- a rotatable drive member being adapted to at least partly engage with at least part of the drive track of the piston rod so as to drive the piston rod,

wherein the dose indicator barrel has a part engaging at least part of the guiding track of the dose setting member, the dose setting member and the dose indicator barrel being movable in relation to each other, the dose indicator barrel further having a threaded outer surface cooperating with a threaded inner portion of the housing whereby the dose indicator barrel undergoes a combined translational and rotational movement in relation to the housing upon rotation of the dose setting member, and

wherein the injection device has a threaded portion cooperating with the threaded outer surface of the piston rod so that rotation of the piston rod relative to the housing results in a longitudinal movement of the piston rod.

It is to be understood that the drive track dose not necessarily extend over the full length of the piston rod. For example, the drive track may in some cases only extend over a part of the full length of the piston rod. Also, the drive track arranged in the piston rod may be an indentation or groove in the longitudinal direction of the piston rod. Alternatively, it may also be a planar surface or two opposing planar surfaces.

Similarly, it is to be understood that other arrangements in terms of the positioning of the threaded portion of for example the dose indicator barrel may be arranged differently.

According to a second embodiment of the present invention, the injection device further comprises

a housing,

a piston rod having a threaded outer surface with a track arranged in a longitudinal direction of the outer surface of the piston rod,

wherein the dose setting member is rotatably mounted and defines a passage for the piston rod, the dose setting member further having a guiding track arranged on an inner surface thereof,

a rotatable drive member having a threaded portion cooperating with at least part of the threaded outer surface of the piston rod,

wherein the dose indicator barrel has a part engaging at least part of the guiding track of the dose setting member, the dose setting member and the dose indicator barrel being movable in relation to each other, the dose indicator barrel further having a threaded outer surface cooperating with a threaded inner portion of the housing whereby the dose indicator barrel undergoes a combined translational and rotational movement in relation to the housing upon rotation of the dose setting member, and

wherein the injection device has a portion at least partly engaging the track of piston rod so that rotation of the drive member relative to the housing results in a longitudinal movement of the piston rod.

The drive member may be adapted to be connected to the dose setting member via a ratchet. This ratchet allows the dose setting member to be rotated in both directions so that a given dose may be either increased or reduced. Due to the force provided by the torsion spring onto the ratchet, the dose setting member will remain in any position—i.e. dose value—to which it has been brought.

The dose setting member may be adapted to be separated from the driving member. This separation may be achieved in several ways. In one way the separation may be obtained by a retraction of the dose setting member in the axial direction of the injection device. The retraction of the dose setting member must be over a distance sufficient to detach the dose setting member or the drive member from the teeth of the ratchet. Other separation mechanisms, such as pushing the dose setting member or twisting the dose setting member are also applicable.

The torsion spring may be arranged between the housing and the dose setting member in such a way that when the dose setting member is rotated around the piston rod, the torsion spring is strained. The torsion spring may be a helical spring which extends coaxially with the piston rod, and which interconnects the housing and the dose setting member in such a way that rotation of the dose setting member, in order to set the dose, strains the torsion spring.

The injection device may further comprise a locking member adapted to fixate the piston rod in such a way that no relative rotation of the piston rod and the housing is possible when the locking member is in its locking position.

This fixation may be provided by a direct engagement of the locking member into the track of the piston rod, or via the drive member. The injection device may further comprise a release button adapted to release the locking member from its locking position. Preferably, the release button is positioned in the distal half of the length of the injection device.

The injection device may further comprise a first stopping member for defining an outer position of the dose indicator barrel. This outer position of the dose indicator barrel may correspond to a maximum obtainable dose. Another outer position of the dose indicator barrel, given by a second stopping member, may define a stop for providing further doses. The stopping members may form integral parts of the inner surface of the housing.

In a third embodiment, the display member may comprise a counting device having two or more display wheels having numerals arranged on an outer surface thereof. In this second embodiment the counting device may have a first and a second wheel. When the dose setting member is rotated, the first wheel is rotated via an optional gear mechanism, such as a planet gear. This first wheel may contain numerals with an incremental of one. The total scale on this wheel may be from 0 to 9. The second wheel next to the first wheel also contains numerals with an incremental of 1. However, this second wheel "counts" the number of revolutions of the first wheel, or alternatively, it "counts" the tens of the first wheel with an incremental of one.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will now be described in further details with reference to the accompanying figures, wherein

FIG. **1** shows a cross-sectional view of a first embodiment of the injection device according to the present invention,

FIG. **2** shows a cross-sectional view (rotated **90** degrees compared to FIG. **1**) of a first embodiment of the injection device according to the present invention,

FIG. **3** shows a detailed cross-sectional view of a first embodiment of the present invention,

FIG. **4** shows a detailed cross-sectional view of a second embodiment of the present invention, and

FIG. **5** shows a detailed cross-sectional view of a third embodiment of the present invention.

FIG. **6** shows a cross-section of a key in a housing component.

FIG. **7** shows a cross-section view of a piston rod with a track.

While the invention is susceptible to various modifications and alternative forms, specific embodiments have been shown by way of example in the drawings and will be described in detail herein. It should be understood, however, that the invention is not intended to be limited to the particular forms disclosed. Rather, the invention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the appended claims.

DETAILED DESCRIPTION OF THE INVENTION

In its most general aspect the present invention relates to an injection device comprising a torsion spring in combination with a rotatable dose indicator mechanism capable of being rotated at least one revolution i.e. over an angle larger than 360 degrees. For example, the dose indicator mechanism may be implemented as a barrel (see FIGS. **1-4**) or as interconnected wheels (see FIG. **5**), the latter being operated

as a counting device. In order to increase the angular resolution compared to known dose indicator mechanisms the dose indicator mechanism of the present invention is rotatable over an angle of rotation corresponding to at least one revolution. The fact that the dose to be ejected is displayed over at least one revolution allows that the dose setting scale may contain at least 50, 60, 70, 80, 90, 100 units with an incremental of one.

FIGS. **1-3** show a cross-sectional view of the injection device according to a first embodiment of the present invention. The dose of medicament to be ejected from the injection device is set by rotating dose setting member **1**. The dose setting member **1** is attached to the housing **5** of the injection device via torsion spring **12**. When the dose setting member **1** is rotated in order to set a dose to be ejected from the injection device, energy is accumulated in torsion spring **12**. This energy may be released by releasing locking member **4** whereby the piston rod **2** will rotate and move in the distal direction of the injection device. The distal movement of the piston rod **2** is caused by a rotational movement of the piston rod **2** itself in that the piston rod **2** has a threaded outer surface. The threads of the piston rod **2** engage and co-operate with a threaded portion **3** of the injection device causing the piston rod **2** to perform the distal and axial movement.

The inner surface of housing **5** of the injection device is provided with threads **10**. These threads are adapted to engage and co-operate with outer threads **8** of a dose indicator barrel **9**. The dose indicator barrel **9** engages with sliding track **11** of the dose setting member **1** in such a way that the dose indicator barrel **9** is able to slide in said sliding track **11** in an axial direction of the injection device.

When the dose setting member **1** is rotated in order to set a dose, the dose indicator barrel **9** rotates with the dose setting member **1** causing the dose indicator barrel **9** to be axially displaced relative to the housing **5**. A window is provided in the housing **5** of the injection device. Through this window, the user of the injection device may view the actual dose setting level from numerals (not shown) provided on an exterior surface of the dose indicator barrel **9**. The numerals are arranged along a helical path.

An advantage of having the numerals arranged along a helical-like path is that a higher angular resolution is obtainable when a dose is to be set. Due to this higher angular resolution a dose can be set with a significantly higher accuracy. This greater accuracy is obtained since the helical-like path allows for more numerals to be arranged on the dose indicator barrel **9** compared to numerals arranged at the same height on the surface of the dose indicator barrel **9**.

When a dose has been ejected from the injection device, the dose indicator barrel **9** is adapted to be rotated back to its initial position and it is thereby ready to be set to a new dose. The same applies for an injection device applying a counting device as a dose meter.

As already mentioned, the piston rod **2** has a threaded outer surface. This threaded outer surface engages and co-operates with a threaded portion **3** of the injection device. The piston rod **2** is driven by the drive member **6** that engages a track in piston rod **2**. The axial movement of the piston rod **2** is provided by rotating piston rod **2** in the threaded portion **3** of the injection device. Drive member **6** may be locked by the locking member **4**. In its locked position, drive member **6** is prevented from rotating. In order to release the drive member **6**, the user of the injection device may activate a spring-loaded push button **15** whereby drive member **6** causes the piston rod **2** to rotate in threaded part **3** of the housing whereby the piston rod **2** rotates and travels in the distal direction of the injection device. Thus, when the drive member **6** is released, the injection device ejects automatically. During ejection, the dose indicator barrel returns to zero dose.

The dose setting member **1** and the drive member **6** are mechanically connected via a self-tightening ratchet **13**. Preferably, the self-tightening ratchet **13** has saw-toothed teeth with approximately vertical oriented flanks as the self-tightening flanks.

In order to reset or reduce an already set dose, the dose setting member **1** is arranged to be axially retractable over a distance corresponding to the height of the teeth of the one-way ratchet **13**. Thus, by pulling the dose setting member **1** back, and thereby disengage the dose setting member **1** from the drive member **6**, an already set dose can be reduced or even reset. The amount of reduction obviously depends on the angle of rotation (in the opposite rotation direction as when a dose is set) of the dose setting member **1**.

The self-tightening ratchet may be formed as a separate component having first and second engaging parts. Alternatively, one of these parts may form an integral part of the dose setting member **1**, or alternatively, an integral part the drive member **6**.

FIG. **4** shows a second embodiment of the present invention. Compared to the first embodiment, the drive member **6** has a threaded portion cooperating with the threaded outer surface of the piston rod **2**. The main difference compared to the first embodiment is that the piston rod **2** is no longer rotatable relative to the housing **5**. This non-rotatable relationship is ensured in that the housing of the injection device has a key **14** which at least partly engages the track **7** of piston rod **2**. Thus, when the drive member **6** is free to rotate relative to the housing **5** the piston rod **2** will undergo a translational movement along the axial direction of the injection device.

FIG. **5** shows a third embodiment of the present invention. In this embodiment the dose indicator barrel of the first and second embodiment has been replaced by a counting device having two wheels **15**, **16**. In principle the number of wheels may be chosen arbitrary, but for simplicity, a counting device having only two wheels is illustrated in FIG. **5**. The counting device is operated as follows: When the dose setting member **1** is rotated, the wheel closest to the dose setting member **15** is rotated via an optional planet gear **17**. This wheel contains numerals with an incremental of one. The total scale on this wheel may contain **10** units distributed over a scale from 0 to 9, or alternatively, the total scale may contain for example 20 units distributed over two scales each having a scale from 0 to 9.

The second wheel **16** next to the first wheel **15** also contains numerals with an incremental of 1. However, this second wheel "counts" the number of revolutions of the first wheel, or alternatively, it "counts" the tens of the first wheel with an incremental of one. Alternatively, the second wheel "counts" the number of half resolutions of the first wheel in case the first wheel contains a scale having 20 units.

The invention claimed is:

1. An injection device comprising:

a torsion spring (**12**) operatively connected to a dose setting member (**1**), the dose setting member (**1**) being adapted to set a dose to be ejected from the injection device, the torsion spring storing energy necessary to drive a dose of medication from the injection device, wherein energy is accumulated in the spring during a dose setting operation, and

a rotatably mounted display member adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member (**1**), the rotatably mounted display member being rotatable over an angle corresponding to at least one revolution of the display member, wherein the display member is a barrel that is threadedly engaged with a device housing and wherein the barrel moves axially and in a proximal direction during the setting of a dose and moves distally during injection of a dose and wherein the barrel rotates toward a zero position during injection.

2. An injection device according to claim **1**, wherein the display member is adapted to be moved between two end positions, said two end positions defining an operation range of the display member, said operation range being associated with a substantially linear working range of the torsion spring.

3. An injection device according to claim **1**, wherein the display member comprises a dose indicator barrel (**9**) having numerals arranged along a helical path on an outer surface thereof.

4. An injection device according to claim **1**, wherein the display member comprises a counting device having two or more display wheels having numerals arranged on an outer surface thereof.

5. An injection device according to claim **2**, further comprising:

a housing (**5**),

a piston rod (**2**) having a threaded outer surface with a drive track (**7**) arranged in a longitudinal direction of said outer surface,

wherein the dose setting member (**1**) is rotatably mounted and defines a passage for the piston rod (**2**), the dose setting member (**1**) further having a guiding track (**11**) arranged on an inner surface thereof,

a rotatable drive member (**6**) being adapted to at least partly engage with at least part of the drive track (**7**) of the piston rod (**2**) so as to drive the piston rod,

wherein the dose indicator barrel (**9**) has a part engaging at least part of the guiding track (**11**) of the dose setting member (**1**), the dose setting member (**1**) and the dose indicator barrel (**9**) being movable in relation to each other, the dose indicator barrel (**9**) further having a threaded outer surface (**8**) cooperating with a threaded inner portion (**10**) of the housing (**5**) whereby the dose indicator barrel (**9**) undergoes a combined translational and rotational movement in relation to the housing (**5**) upon rotation of the dose setting member (**1**), and

wherein the injection device has a threaded portion (**3**) cooperating with the threaded outer surface of the piston rod (**2**) so that rotation of the piston rod (**2**) relative to the housing (**5**) results in a longitudinal movement of the piston rod (**2**).

6. An injection device according to claim **1**, further comprising a threaded piston rod that moves distally during injection of a dose and a release that releases energy from the spring, the energy from the spring driving a dose from the injection device.

7. An injection device according to claim **5**, wherein the drive member (**6**) is adapted to be connected to the dose setting member (**1**) via a ratchet (**13**).

8. An injection device according to claim **5**, wherein the torsion spring (**12**) is arranged between the housing (**5**) and the dose setting member (**1**) in such a way that when the dose setting member (**1**) is rotated around the piston rod (**2**), the torsion spring (**12**) is strained.

9. An injection device according to claim **8**, wherein the torsion spring (**12**) is a helical spring which extends coaxially with the piston rod (**2**).

10. An injection device according to claim **5**, further comprising a locking member (**4**) adapted to fixate the piston rod (**2**) in such a way that no relative rotation between of the piston rod (**2**) and the housing (**5**) is possible when the locking member (**4**) is in its locking position.

11. An injection device according to claim **10**, further comprising a release button adapted to release the locking member (**4**) from its locking position.

12. An injection device according to claim **11**, wherein the release button is positioned in the distal half of the length of the injection device.

13. An injection device according to claim **5**, further comprising a stopping member for defining an outer position of the dose indicator barrel (**9**), the outer position of the dose indicator barrel (**9**) corresponding to a maximum obtainable dose.

14. An injection pen comprising:

a housing;

a dose setting member for setting a dose, the dose setting member mounted to the housing so that it may rotate relative to the housing, the dose setting member being capable of rotated in two directions, one direction to increase the size of a dose and another to decrease the size of the dose;

a dose indicator barrel having a helical scale, wherein the dose indicator barrel rotates when the dose setting member is rotated and is capable of rotating over more than one revolution; wherein the dose indicator barrel moves axially relative to both the housing the dose setting member when setting a dose;

a torsion spring that store energy when a user rotates the dose setting member to set a dose, the torsion spring supplying the energy to drive a dose of medication from the injection pen; and a release button;

wherein when the release button is activated by the user, the release button causes the torsion spring to drive the set dose from the injection pen and the dose indicator barrel rotates during injection back to a zero position.

15. An injection device comprising:

a housing (**5**) with an inner surface provided with threads (**10**),

a dose setting member (**1**) adapted to set a dose to be ejected from the injection device,

a piston rod (**2**) having a threaded outer surface with a track (**7**) arranged in a longitudinal direction of its outer surface,

a rotatable drive member (**6**) that engages with the track (**7**) or with the threaded outer surface of the piston rod to drive the piston rod (**2**),

a torsion spring (**12**) for accumulating energy that is releasable to rotate the drive member (**6**) whereby the piston rod moves in the distal direction of the injection device to eject the set dose automatically,

wherein,

a rotatably mounted display member is threadedly engaged with the threads (**10**) of the housing (**5**) and operatively connected with the dose setting member (**1**) such that when the dose setting member (**1**) is rotated in order to set a dose,

the display member rotates with the dose setting member (**1**) causing the display member to be axially displaced relative to the housing (**5**) and is adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member (**1**),

the rotatably mounted display member is rotatable over an angle corresponding to at least one revolution, and the display member further returns to return to zero during ejection.

* * * * *

EXHIBIT I

US009775953B2

(12) **United States Patent**
Enggaard et al.

(10) **Patent No.: US 9,775,953 B2**
(45) **Date of Patent: *Oct. 3, 2017**

(54) **DOSE MECHANISM FOR AN INJECTION DEVICE FOR LIMITING A DOSE SETTING CORRESPONDING TO THE AMOUNT OF MEDICAMENT LEFT**

(71) Applicant: **Novo Nordisk A/S**, Bagsvaerd (DK)

(72) Inventors: **Christian Peter Enggaard**, Vejby (DK); **Claus Schmidt Moller**, Fredensborg (DK); **Tom Hede Markussen**, Bagsvaerd (DK)

(73) Assignee: **Novo Nordisk A/S**, Bagsvaerd (DK)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 92 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **14/550,085**

(22) Filed: **Nov. 21, 2014**

(65) **Prior Publication Data**

US 2015/0080812 A1 Mar. 19, 2015

Related U.S. Application Data

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(Continued)

(30) **Foreign Application Priority Data**

Jul. 27, 2005 (EP) 05016291

(51) **Int. Cl.**

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A61M 5/315	(2006.01)
A61M 5/20	(2006.01)

(52) **U.S. Cl.**
CPC ***A61M 5/31551*** (2013.01); ***A61M 5/31505*** (2013.01); ***A61M 5/31526*** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC A61M 5/31526; A61M 5/31528; A61M 5/31541; A61M 5/31551; A61M 5/3156;
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Assistant Examiner — Deanna K Hall
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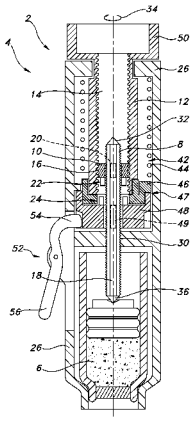
(57) **ABSTRACT**

A mechanism for preventing setting of a dose, which exceeds the amount of a medicament in a reservoir in an injection device. The device can contain a threaded piston rod, a limiter and a driver. The three elements can be arranged such that during dose setting, the limiter is moved towards an end-of-content position, wherein dose setting is limited. The invention contains an accumulative and a non-accumulative embodiment. The invention further relates to a mechanism for preventing ejection of a dose exceeding the set dose.

25 Claims, 7 Drawing Sheets



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(52) **U.S. Cl.**
CPC ***A61M 5/31528*** (2013.01); ***A61M 5/31553*** (2013.01); ***A61M 5/31583*** (2013.01); ***A61M 5/31586*** (2013.01); *A61M 5/20* (2013.01); *A61M 5/3156* (2013.01); *A61M 5/31541* (2013.01); *A61M 5/31571* (2013.01); *A61M 5/31593* (2013.01); *A61M 2005/202* (2013.01); *A61M 2005/3151* (2013.01)

(58) **Field of Classification Search**
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USPC 604/207–211
See application file for complete search history.

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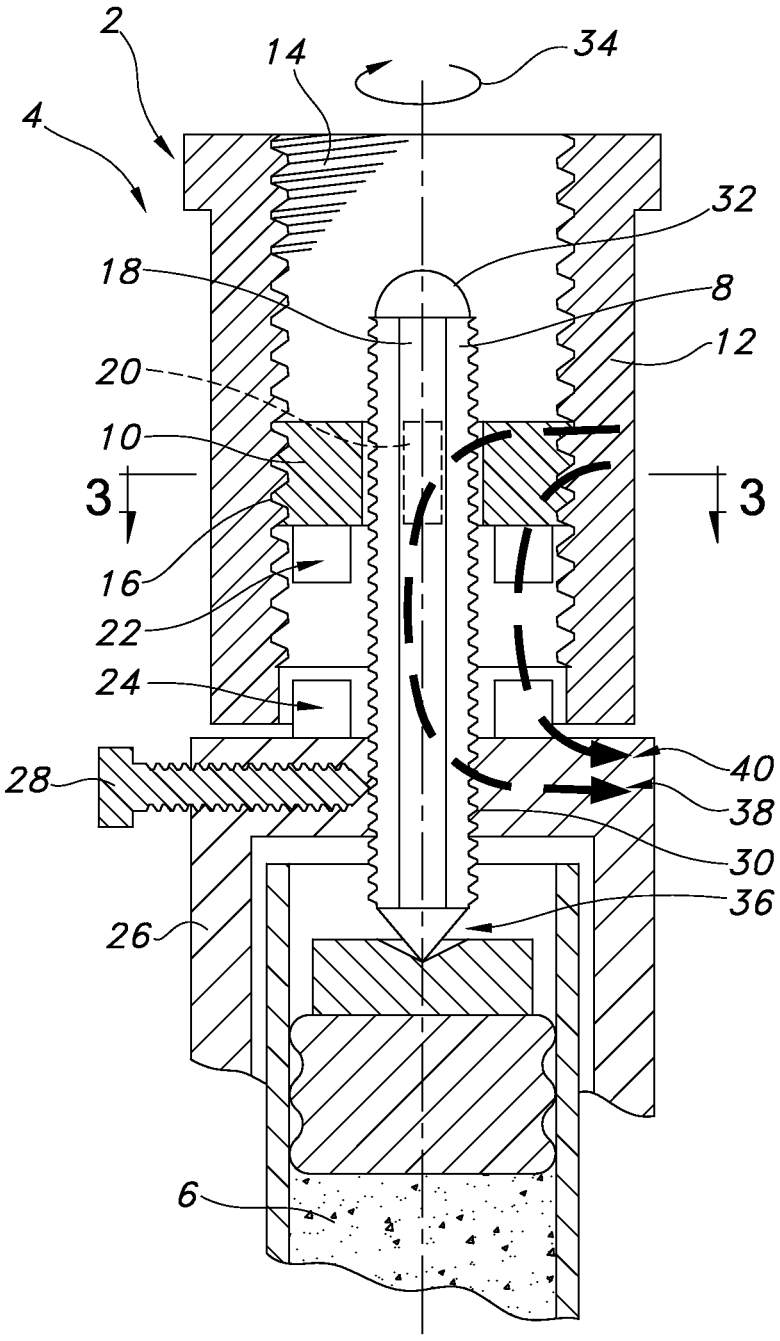

FIG. 1

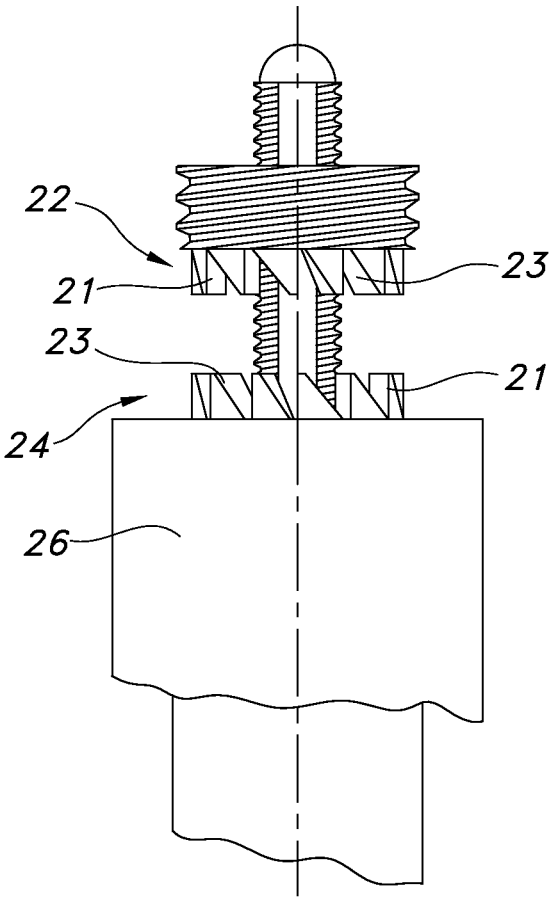

FIG. 2

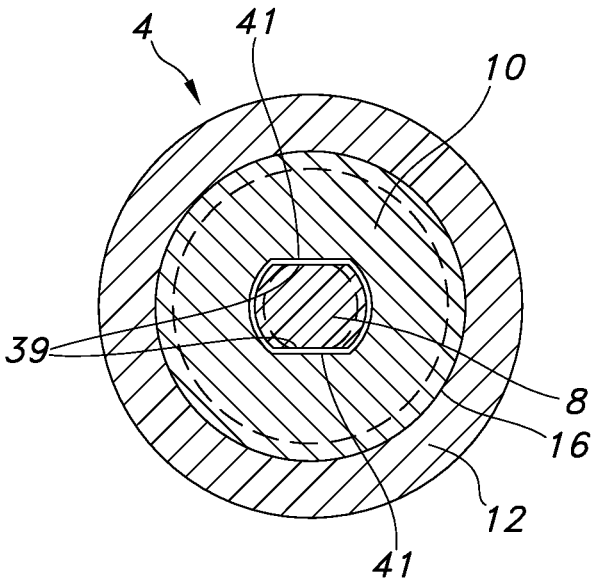

FIG. 3

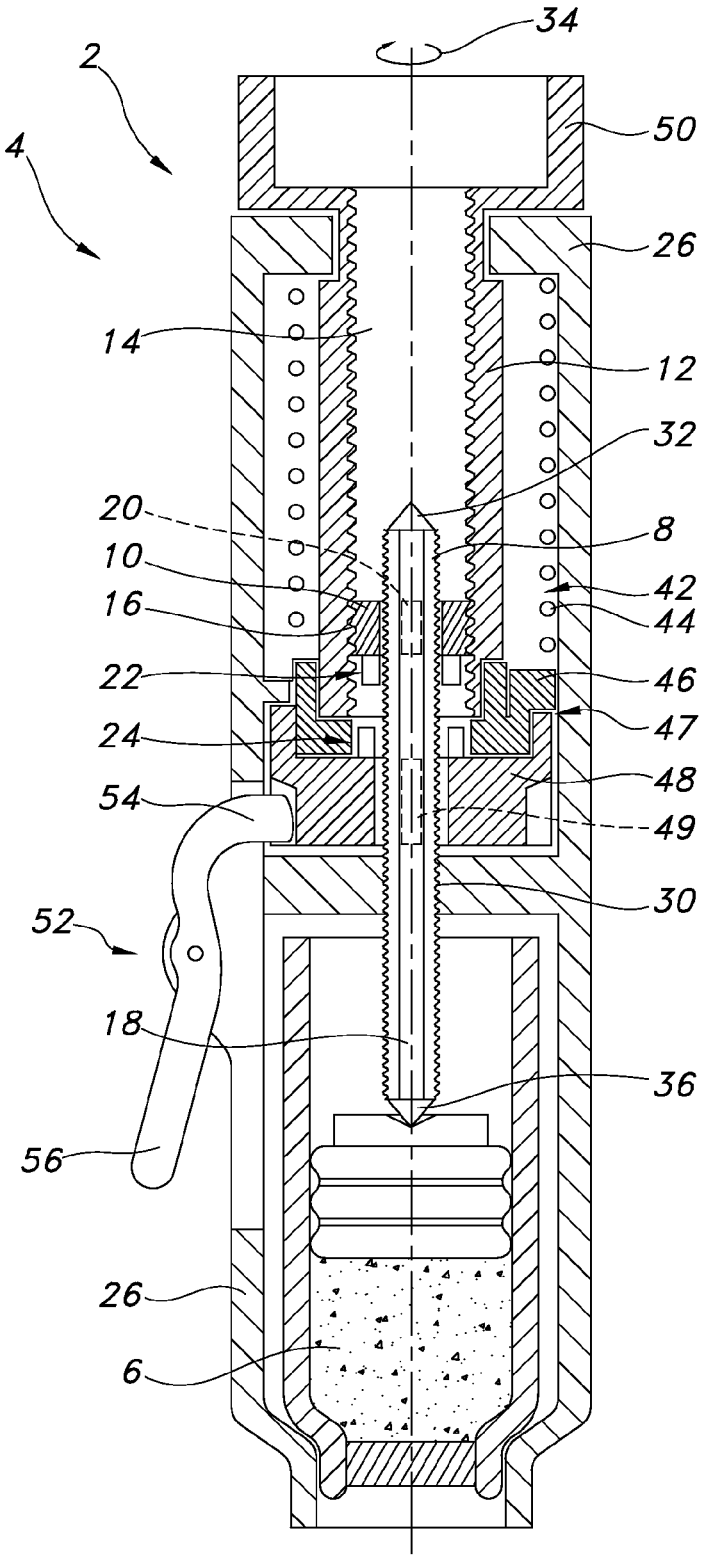
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FIG. 4

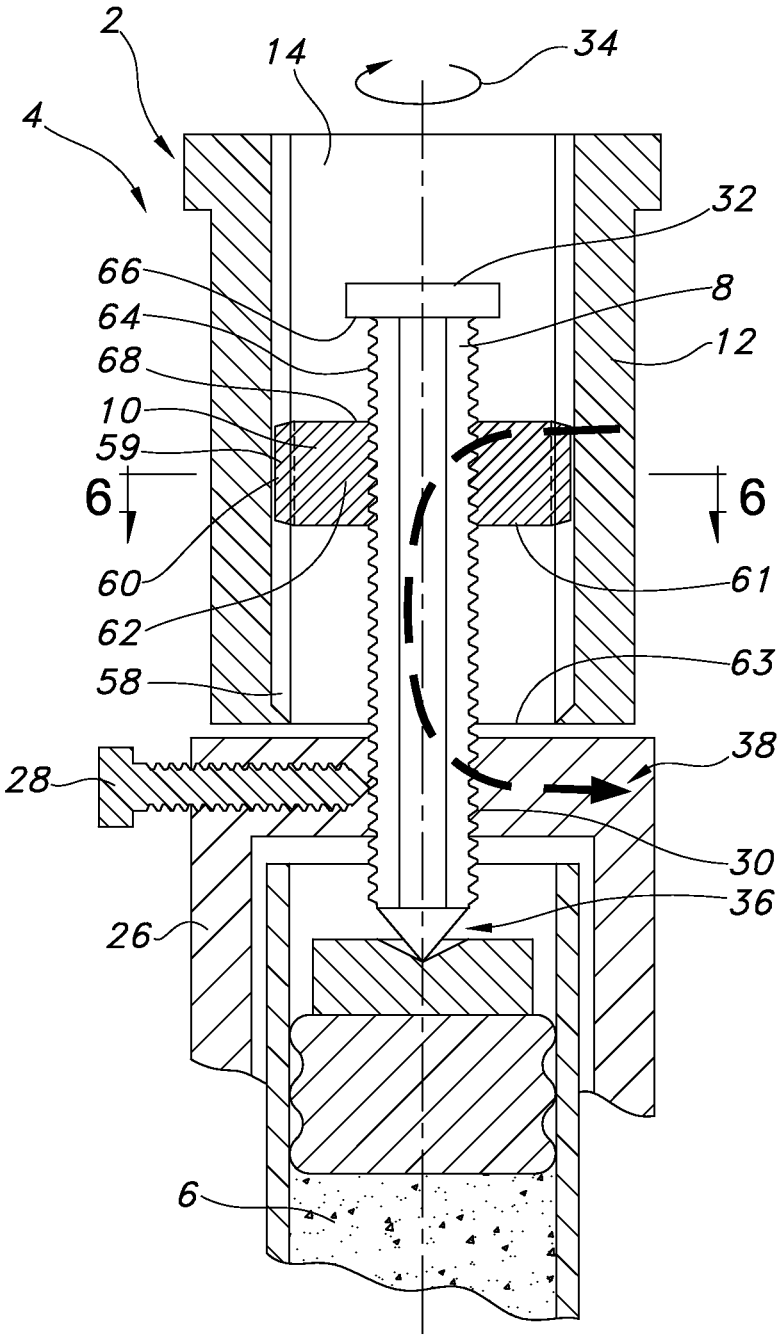

FIG. 5

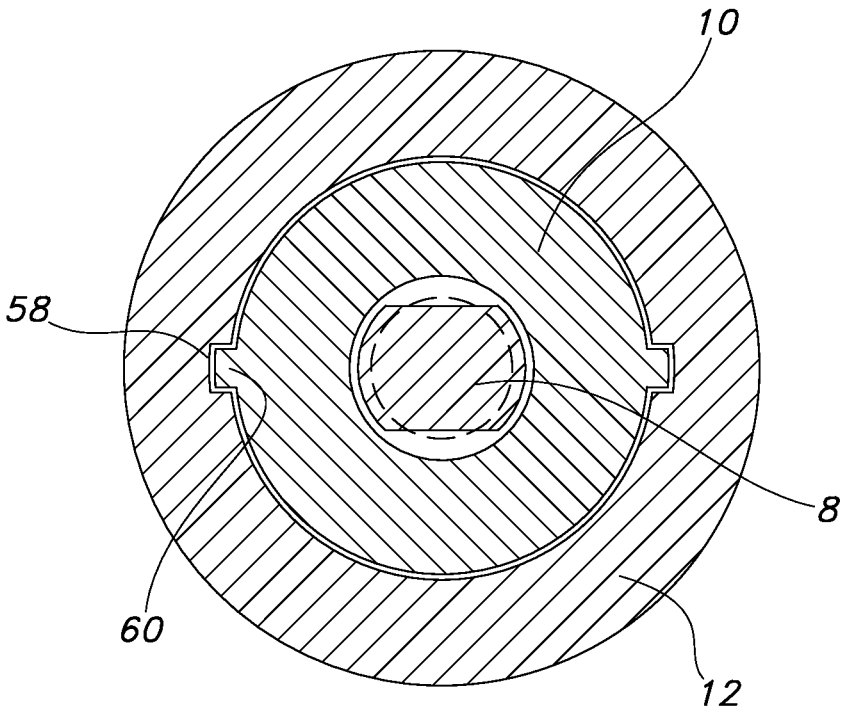

FIG. 6

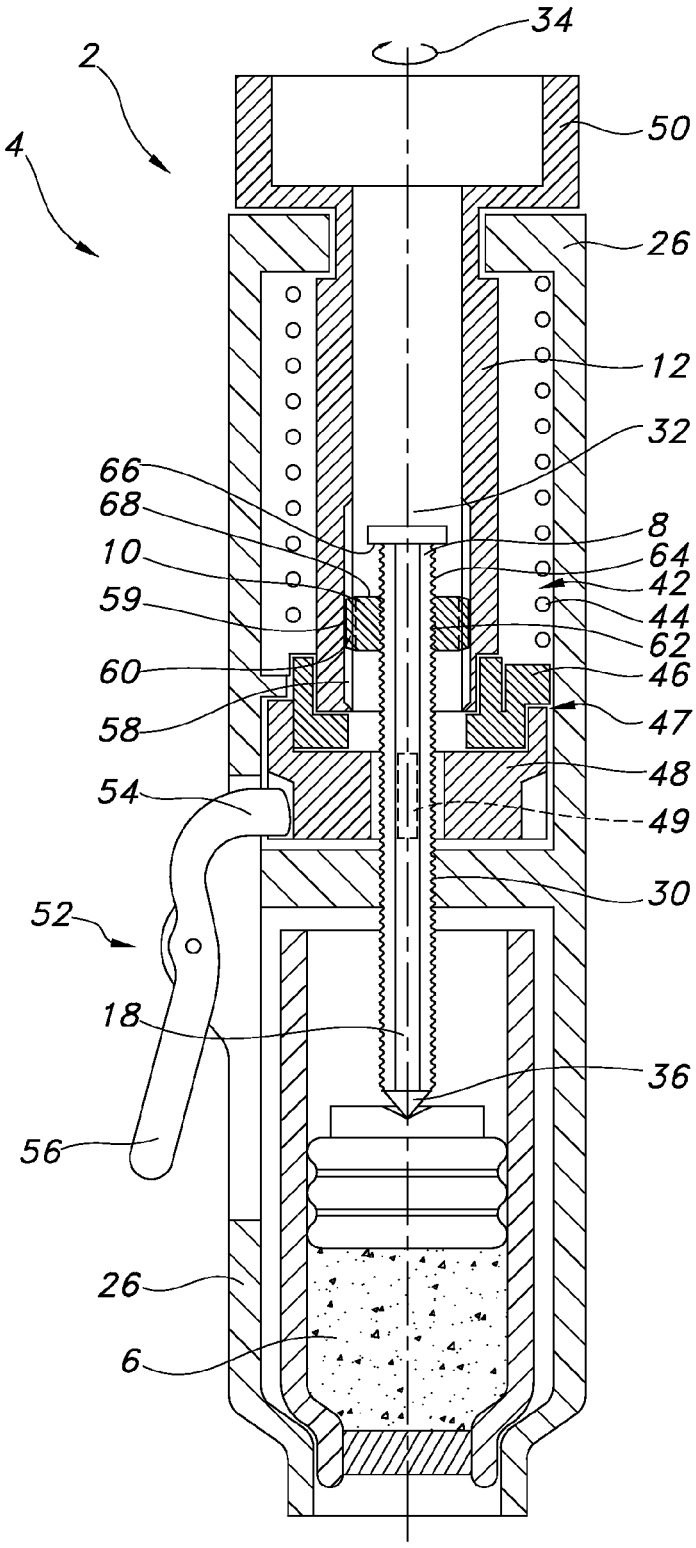
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FIG. 7

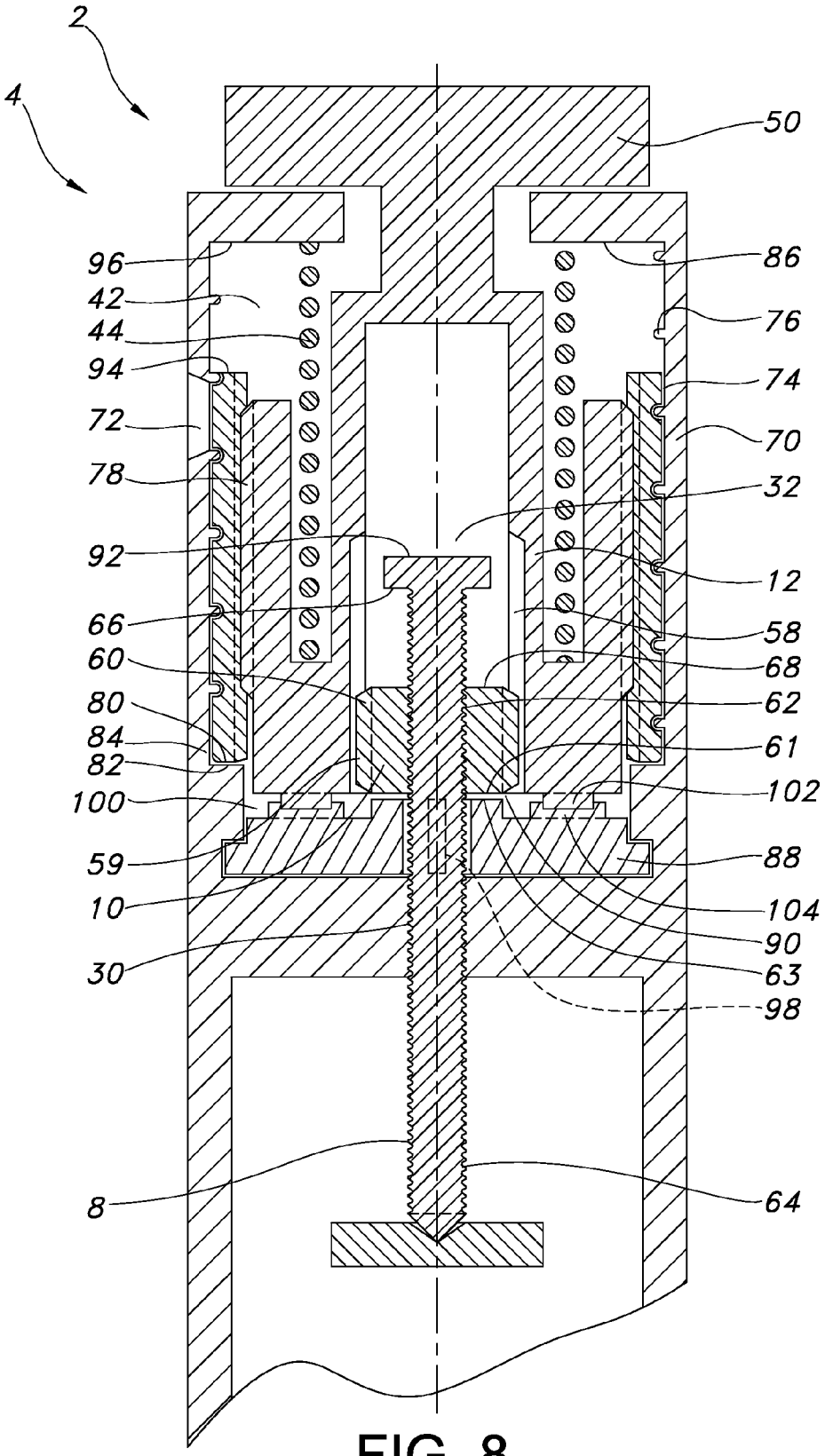
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FIG. 8

DOSE MECHANISM FOR AN INJECTION DEVICE FOR LIMITING A DOSE SETTING CORRESPONDING TO THE AMOUNT OF MEDICAMENT LEFT

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. application Ser. No. 11/996,409 filed Jan. 22, 2008, which is a 35 U.S.C. §371 national stage application of International Patent Application PCT/EP2006/007004 (published as WO 2007/017052), filed Jul. 17, 2006, which claimed priority of European Patent Application 05016291.6, filed Jul. 27, 2005; this application further claims priority under 35 U.S.C. §119 of U.S. Provisional Application 60/708,618, filed Aug. 16, 2005, the contents of which are incorporated herein by reference.

FIELD OF THE INVENTION

The present invention relates to a mechanism for preventing setting of a dose which exceeds the amount of a medicament in a reservoir in an injection device. In particular, the present invention relates to a mechanism wherein the piston rod forms part of said mechanism, whereby a compact structure may be provided.

BACKGROUND OF THE INVENTION

When drugs are to be injected into the human body, it is essential that the dose set by the user is the actual dose injected. If this is not the case, the medicating of the patient is not correct, which in some cases can have serious or even fatal consequences. In order to ensure that the dose selected by a dose setting member does not exceed the remaining amount of medication in a reservoir in a syringe device, an end-of-content mechanism may be provided.

End-of-content mechanisms are known in the art. One such example may be seen in WO 01/19434 A1 which discloses a limiting mechanism for an injection device. A dose is injected by rotating a dose setting member which during this rotation carries a driver with it to rotate this driver which moves a piston forward. The driver is provided with a track having a length which is engaged by a track follower coupled to the dose setting mechanism.

Another example may be seen in WO 2004/007003 A1.

U.S. Pat. No. 5,938,642 disclose an injection device comprising a driver, a nut and a threaded piston rod. During dose setting the nut is rotational screwed up the threaded piston rod and during dosing the nut and the piston rod is brought axial forward the same distance. Once the nut reaches the end of the thread of the threaded piston rod no further dose can be set.

It is an object of a preferred embodiment of the present invention to provide an alternative to the above solution. Especially, it is an object of the present invention to provide a solution which allows an outer surface of a driver to be directly coupled to the inner surface of a drum scale, and thus it is an object of the present invention to provide an end-of-content mechanism which may be positioned in the space defined by the inner walls of a driver.

SUMMARY OF THE INVENTION

The present invention provides a non-accumulative solution to the above problems.

In an accumulative solution which is described below under a first example, the limiter is moved stepwise closer to a stopping position wherein the limiter acts together with other elements of the preventing mechanism to ensure that it is not possible to set a dose exceeding the amount of medicament left in a reservoir.

In the non-accumulative solution which is described under the second example, the limiter is positioned in the same position prior to dose setting and after dose ejection.

The present invention relates to a mechanism for preventing setting of a dose which exceeds the amount of a medicament in a reservoir in an injection device, wherein a dose is set by rotating a dose setting member of a dose setting mechanism, the mechanism comprising:

a piston rod having a threaded outer surface;

a housing defining a passage for the piston rod, the passage having a threaded inner surface for engagement with the threaded outer surface of the piston rod, the housing being arranged with respect to the piston rod such that rotation of the piston rod in relation to the housing causes the piston rod to be displaced relative to the housing in a longitudinal direction:

a limiter defining a passage for the piston rod;

a driver defining a passage for the limiter, the driver being coupled to the dose setting member such that rotation of the dose setting member during dose setting causes the driver to rotate; and

wherein the limiter is coupled to the driver and the piston rod such that relative rotation between the driver and the piston rod during dose setting causes the limiter to move towards a stopping position wherein the limiter prevents setting of a dose which exceeds the amount of a medicament in a reservoir in the injection device.

The housing may form part of the housing of a syringe device into which the mechanism is integrated.

The mechanism may comprise a locking means for locking the piston rod against rotation in at least one direction, relative to the housing. Such a locking means may be a screw which may engage or disengage the piston rod. Advantageously, the screw may be arranged such that it engages a root part of the piston rod, whereby the walls of the thread and especially not the crest are not damaged. Alternatively, the locking means may be provided as a pivotable arm, which is operable from an outer surface of the device. The pivotable arm may be movable between an engaging and a non-engaging position, by means of an arm or button accessible from the outer surface of the syringe device.

The mechanism may comprise a ratchet mechanism interconnecting the driver and the housing. The ratchet mechanism may comprise a first and a second part. The first part may be coupled to the driver while the second part may be coupled to the housing e.g. via the locking means. The ratchet mechanism may be adapted to move in one or two rotational directions.

In order to assist patients with poor dexterity an ejection assisting system for providing an ejection force for assisting an operator during ejection may be provided. Such a system may comprise a spring which is strained when the dose setting member is rotated during dose setting. The spring may interconnect the housing and the first part of the ratchet e.g. in such a way that it co-extend the piston rod. Accordingly, when the driver is rotated by means of the dose setting member, whereby the first part of the ratchet is rotated, the spring is rotationally strained. The potential energy stored in the strained spring is released by disengaging the locking means whereby the ratchet mechanism is free to move,

whereby the strained spring forces the ratchet mechanism to rotate. As the second part of the ratchet mechanism may be locked for rotation in relation to the piston rod, the rotating ratchet mechanism carries the piston rod with it.

In one example the spring is pre-strained, such as one revolution, such as two revolutions, such as three revolutions, such as four revolutions, such as five revolutions.

In the context of the present invention the term "stopping thread" shall be understood as engaging threads of two elements, at least one of which threads prevents a first of the two elements from being rotated beyond a predetermined position relative to a second of the two elements. Normally, said prevention of rotation is caused by engagement of surfaces of each of the two elements.

In the following a first general example is described.

The FIRST general example relates to a mechanism for preventing setting of a dose which exceeds the amount of a medicament in a reservoir in an injection device, wherein a dose is set by rotating a dose setting member of a dose setting mechanism, the mechanism comprising:

a piston rod having a threaded outer surface;

a limiter defining a passage for the piston rod and being rotationally retained in relation to the piston rod, the limiter having a threaded outer surface;

a driver defining a passage for the limiter, the passage having a threaded inner surface for engagement with the threaded outer surface of the limiter, the driver being coupled to the dose setting member such that rotation of the dose setting member during dose setting causes the driver to rotate; and

wherein relative rotation between the driver and the piston rod during dose setting causes the limiter to move towards a stopping position wherein the limiter prevents setting of a dose which exceeds the amount of a medicament in a reservoir in the injection device.

Rotation of the dose setting member during dose setting causes the driver to rotate. If the direction of rotation of the dose setting member and the driver is the same, the driver and the dose setting member may be made as one single unit. Alternatively, the two elements may be made be two separate elements attached or coupled to each other.

The direction of the thread of the piston rod and the driver may be opposite i.e. if the piston rod has a right-handed thread, the driver has a left-handed thread and vice versa. This ensures that the dose setting member is rotated back to the same position such that the user may set a dose starting from an initial dose of 0 IU.

The limiter may comprise a first engaging surface adapted to engage a corresponding second engaging surface of the driver. In one example the limiter comprises a plurality of first engaging surfaces which are adapted to engage corresponding second engaging surfaces of the driver. In some examples, the number of first and second engaging surfaces is not identical. As an example there may be provided two first engaging surfaces while there is provided ten second engaging surfaces. Accordingly, the limiter may be locked in relation to each other in ten different positions, but at each position only two first and two second engaging surfaces engage each other.

The threaded outer surface of the piston rod may comprise the first surface and the threaded inner surface of the driver comprises the second surface. The piston rod and the driver may be arranged such that relative rotational movement may cause the first and the second surface to be brought into engagement, whereby further relative rotational movement is not possible.

Alternatively, the limiter may comprise a plurality of teeth adapted to engage corresponding teeth of the housing and/or the driver when the limiter is in the stopping position. Accordingly, the teeth of the limiter comprise first engaging surfaces, while the teeth of the housing and/or driver may comprise the second stopping surfaces.

In one example there is provided both teeth and a stopping thread. An advantage of this is that a larger torque may be transferred from the driver to the limiter, whereby it may be ensured that even when applying a large torque to the dose setting mechanism, a dose which exceeding the actual amount left in the reservoir cannot be set. Such a larger torque may be between 100 and 1000 Nmm, such as 250 Nmm, such as 500 Nmm, such as 750 Nmm.

In the following a second general example is described.

The SECOND general example relates to a mechanism for preventing setting of a dose which exceeds the amount of a medicament in a reservoir in an injection device, wherein a dose is set by rotating a dose setting member of a dose setting mechanism, the mechanism comprising:

a piston rod having a threaded outer surface;

a limiter defining a passage for the piston rod, the passage having a threaded inner surface for engagement with the threaded outer surface of the piston rod;

a driver defining a passage for the limiter, the driver being rotationally retained in relation to the limiter, the driver being coupled to the dose setting mechanism such that rotation of the dose setting member during dose setting causes the driver to rotate; and

wherein relative rotation between the driver and the piston rod during dose setting causes the limiter to move towards a stopping position wherein the limiter prevents setting of a dose which exceed the amount of a medicament in a reservoir in the injection device

As described above the invention according to the second general example of the invention is a non-accumulative solution, wherein the limiter is positioned in the same position (the reference position) prior to dose setting and after dose ejection.

The limiter may comprise a first engaging surface adapted to engage a corresponding second engaging surface of the piston rod. The engaging surface of the limiter may be an end surface extending in a radial direction of the limiter and facing a corresponding radial surface of a T-shaped piston rod. Accordingly, when the piston rod is rotated relative to the limiter, the two surfaces will abut each other such that the user is prevented from setting a higher dose. In the alternative the threaded outer surface of the piston rod comprises the first surface and the threaded inner surface of the driver comprises the second surface. The two latter surfaces may each define a plane parallel with the axis of the piston rod and the limiter.

DESCRIPTION OF THE DRAWINGS

The invention will now be described in further detail with reference to the drawings, in which:

FIG. **1** illustrates a mechanism according to the first general example of the invention,

FIG. **2** illustrates teeth of the limiter and the housing according to the first general example,

FIG. **3** illustrates a cross-section through of the piston rod, the limiter and the driver of FIG. **1**,

FIG. **4** illustrates a syringe device with injection assisting means and a mechanism according to the first general example of the invention,

FIG. **5** illustrates a mechanism according to the second general example of the invention,

FIG. **6** illustrates a cross-section through the piston rod, the limiter and the driver of FIG. **2**,

FIG. **7** illustrates a syringe device with injection assisting means and a mechanism according to the second general example of the invention, and

FIG. **8** illustrates a syringe device according to the second general example of the invention wherein the limiter is used both as an end-of-content and as a safety mechanism.

FIG. **1** discloses syringe device **2** comprising a mechanism **4** for preventing setting of a dose which exceeds the amount of a medicament in a reservoir **6**. The mechanism **4** comprises a piston rod **8**, a limiter **10** and a driver **12**. The driver is coupled to a dose setting member (not shown) such that rotation of the dose setting member during dose setting, causes the driver to rotate in the same direction—both when dialling up and down. The inner surface **14** of the driver **12** has a threaded surface which is adapted to engage a corresponding thread of the outer surface **16** of the limiter **10**. Moreover, the limiter **10** is locked for rotation in relation to the piston rod **8** by means of groove **18** in the piston rod **8** and a tongue **20** in the limiter **10** (in the figure the tongue is indicated by a dotted line). Due to the grove-tongue arrangement the limiter **10** and the piston rod **8** may move translationally (i.e. up and down in the figure) in relation to each other.

The limiter comprises a first set of teeth **22** adapted to engage a second set of teeth **24** of the housing **26**. The function of the teeth is to ensure that the dose set does not exceed the amount of a medicament left in the reservoir **6**. Furthermore, the threads of the inner surface **14** and the outer surface **16** comprises a stopping thread which are also used to ensure that that the user cannot set a dose which exceed the amount of a medicament in the reservoir. The two systems are redundant and designed to stop dose setting simultaneously.

The syringe device further comprises a locking means **28** in the form of a screw, which is used to lock the piston rod **8** for rotation in relation to the housing **26**. Due the threaded engagement **30** between the housing **26** and the piston rod **8**, rotational locking of said two elements, results in a translational lock. When the locking means is in the form of a screw, it is desirable that the tip of the screw engages the piston rod in a root of the thread, such that the crest of the thread is not damaged.

In the initial state i.e. when the pen is delivered to the user, the limiter **10** is located in proximal end **32** of the piston rod (i.e. the end opposite the needle of the syringe device).

In order to set a dose the user locks the piston rod for rotation by means of the locking means **28**. The dose is then set by rotating the driver as indicated by the arrow **34**. Due to the relative rotational movement between the piston rod **8** and the driver **12** the limiter **10** moves towards in a distal end **36** of the piston rod.

When the desired dose has been set, the driver, the limiter and the piston rod are locked rotationally in relation to each other such that when a dose is ejected, they all rotate together. Due to the threaded engagement **30** between the housing and the piston rod **8**, the rotation of the piston rod causes the piston rod to move in the distal direction. However, due to the grove-tongue between the piston rod and the limiter, the translational movement of the piston rod is not transmitted to the limiter and the driver. Accordingly, the limiter (and the driver) remains in the same longitudinal position.

It will be appreciated, that during each dose setting the limiter moves closer to the stopping position in which the first and second set of teeth engage and wherein the stopping thread engage. In this position the driver cannot be rotated further, and any torque applied to the dose setting member by the user is transferred from the dose setting member to the driver and via two torque paths. When the torque is transferred through the first torque path **38**, it is transferred from the driver to the limiter, further through the grove-tongue connection to the piston rod and finally from the piston rod to the housing, due to the rotational locking means **28**. When the torque is transferred through the second torque path **40** it is transferred from the driver to the limiter, further from the first set of teeth **22** to the second set of teeth **24** of the housing. By providing a first torque path and a second torque path it is possible to apply a larger torque without breaking the parts of the device e.g. the teeth, and, thus, the risk of user causing damage to the device is reduced.

FIG. **2** shows the housing **26** comprising the second set of teeth **24** which are adapted to engage the first set of teeth **22** of the housing. Each tooth may have a one surface **21** which is substantially parallel with the axial direction of the limiter and another surface **23** which is transverse to said axial direction.

FIG. **3** discloses an alternative to the grove-tongue described in connection with FIG. **1**. In the alternative the piston rod **8** has two flat surfaces **39** and due to corresponding flat surfaces **41** of the limiter **10**, the limiter and the piston rod are locked for relative rotational movement.

FIG. **4** discloses a syringe device **2** comprising the mechanism **4** described in relation to FIG. **1**.

However, the syringe device of FIG. **4** further comprises an injection assisting mechanism **42** comprising a spring **44** interconnecting the housing **26** and a first part **46** of a ratchet mechanism **47**, which further comprises a second part **48**. When the dose setting member **50** is rotated, the rotation is transferred to the driver **12** and the first part **46** of the ratchet mechanism. During the rotation of the dose setting member, the spring **44** is strained whereby potential energy is stored.

The stored energy may be released by disengaging the pawl **52** which during dose setting engages the second part **48** of the ratchet mechanism. The pawl **52** is pivotally connected to the housing and comprises an engaging part **54** and a button part **56**. When the pawl is disengaged the strained spring **44** causes the first part **46** to rotate. Due to the engagement between the first part **46** and the second part **48**, and due to the grove-tongue connection **49** between the second part **48** and the piston rod **8**, the rotation of the first part **46** causes the piston rod to rotate. As described under FIG. **1** the rotation of the piston rod causes the piston rod to move forward.

FIG. **5** discloses the mechanism according to the second general example of the invention. Identical reference numbers refer to identical elements. In FIG. **5** the driver **12** is coupled to a dose setting member (not shown) such that rotation of the dose setting member during dose setting, causes the driver to rotate in the same direction—both when dialling up and down. The inner surface of the driver **12** comprises a groove **58** which is adapted to engage a corresponding radially extending spline **60** of the limiter **10**. Accordingly, the driver **12** and the limiter **10** are locked for relative rotational movement, while relative translational movement is possible. Furthermore, the limiter **10** has a threaded inner surface **62** which engages a corresponding threaded outer surface **64** of the piston rod **8**. Accordingly, relative rotation between the piston rod and the driver results

in relative translational movement between the limiter and each of the piston rod and the driver.

Unlike FIG. **1** the device of FIG. **5** does not comprise first and second sets of teeth. However, it will be appreciated that such sets of teeth could have been provided in the same manner as in FIG. **1**. The only difference is that such sets of teeth should have been provided on the surface **66** and on the other, upper side of the limiter as the limiter moves in the direction of the proximal end **32** when a dose is set, as will be described in the following.

In the initial state i.e. when the pen is delivered to the user, the limiter is located in a reference position wherein a surface **61** of the limiter engages a surface **63** of the housing **26**. In some examples the surfaces **61**,**63** are spaced apart when the limiter is positioned in the reference position.

In order to set a dose the user locks the piston rod for rotation by means of the locking means **28**. The dose is then set by rotating the driver as indicated by arrow **34**. Due to the relative rotational movement between the piston rod **8** and the driver **12** the limiter moves towards a proximal end **32** of the piston rod.

When the desired dose has been set, the driver, the limiter and the piston rod are locked rotationally in relation to each other such that, when a dose is ejected, they all rotate together. Due to the threaded engagement **30** between the housing and the piston rod **8**, the rotation of the piston rod causes the piston rod to move in the distal direction. Due to the grove-spline connection **59** between the driver and the limiter, the translational movement of the piston rod is not transmitted to the driver. However, due to the threaded connection between the piston rod and the limiter, the limiter will move with the piston rod and arrive at the reference position, i.e. the position it had prior to setting the dose. Accordingly, as described in the aforementioned, the invention according to the second general example does not have the accumulative effect which is seen in connection with the invention according to first general example (FIG. **1**-**4**). On the contrary the limiter returns to the reference position during ejecting of the set dose. This may be used to provide a safety mechanism adapted to prevent ejection of a dose exceeding the set dose, this is described in further detail in connection with FIG. **8**.

At a point the piston rod arrives in the stopping position wherein a first stopping thread **66** of the thread **64** of the piston rod engages a second stopping thread **68** of the limiter. The result is that a set dose may not be increased and any torque applied to the driver is transferred to the limiter due to the grove-spline-connection and further to the piston rod due to the stopping thread and finally from the piston rod to the housing—this is indicated by arrow **38**. As the piston rod is locked in relation to the housing by means of the locking means **28**, further rotation of the driver is not possible.

FIG. **6** discloses a cross-section through the piston rod **8**, the limiter **10** and the driver **12**. The limiter **10** is locked for rotational movement relative to the driver **12** due to engagement between the groove **58** and the radially extending spline **60** of the limiter **10**.

FIG. **7** discloses a syringe device **2** comprising the mechanism **4** described in relation to FIG. **5**. However, the syringe device of FIG. **6** further comprises an injection assisting mechanism **42** comprising a spring **44** interconnecting the housing **26** and a first part **46** of a ratchet mechanism **47**, which further comprises a second part **48**. When the dose setting member **50** is rotated, the rotation is transferred to the driver **12** and the first part **46** of the ratchet mechanism. During the rotation of the dose setting member **50**, the pre-strained spring **44** is strained even more whereby further potential energy is stored. The stored energy may be released by disengaging the pawl **52** which during dose setting engages the second part **48** of the ratchet mechanism. The pawl **52** is pivotally connected to the housing and comprises an engaging part **54** and a button part **56**. When the pawl is disengaged the strained spring **44** causes the first part **46** to rotate. Due to the engagement between the first part **46** and the second part **48**, and due to the grove-tongue connection **49** between the first part **46** and the piston rod **8**, the rotation of the first part **46** causes the piston rod to rotate. As described under FIG. **1** the rotation of the piston rod causes the piston rod to move forward.

In the example disclosed in FIG. **8** the syringe device comprises means for preventing ejection of a dose exceeding the set dose. Said means comprises a dose limiting mechanism and a safety mechanism as will be described in detail below. An advantage of the two redundant mechanisms is that if one fails the other may still prevent ejection of a dose exceeding the set dose. The example of FIG. **8** further comprises an end-of-content mechanism.

FIG. **8** discloses a syringe device **2** comprising a housing **4** and a piston rod **8**. The syringe device **2** further comprises a dose setting member **50** and a driver **12**, which in the figure are combined into one single unit. The syringe device further comprises a scale drum **70** for indicating a set dose through a window **72**. The scale drum **70** has a threaded outer surface **74** adapted to engage a corresponding threaded inner surface **76** of the housing. The scale drum **70** is rotationally retained relative to the driver **12** through a grove-tongue engagement **78**. The drum scale **70** comprises a first stopping surface **80** adapted to engage a second stopping surface **82** of the housing. The first stopping surface **80** and the second stopping surface **82** constitutes the dose limiting mechanism **84**. The first stopping surface **80** is moved away from the second stopping surface **82** during dose setting and towards each other during dose ejecting. When the two surfaces abut each other, the device is prevented from ejecting the medicament. Thus, a dose larger than the set dose cannot be expelled as the first and second stopping surfaces abut when the set dose has been expelled

The syringe device comprises an ejection assisting system **42** in the form of a pre-strained torsional spring **44** extending between a proximal part **86** of the housing and the driver **12**. Accordingly, when the dose setting member **50** is rotated to set a dose, the spring **44** is strained even further.

The piston rod **8** comprises a threaded outer surface **64** adapted to engage a corresponding threaded inner surface **30** of the housing and accordingly rotation of the piston rod relative to the housing causes the piston rod to move translationally in relation to the housing. The threaded outer surface **64** of the piston rod also engages a threaded inner surface **62** of a limiter **10**, which in FIG. **8** is positioned in a stopping position wherein a bottom surface **61** of the limiter engages an upper surface **63** of a piston rod guide **88**. The bottom surface **61** and the upper surface **63** constitute the safety mechanism **90**. An air gap may be provided between the bottom surface **61** and the upper surface **63** when the limiter is in said stopping position, which allows the limiter and the piston rod to rotate and angel corresponding to a non-lethal dose e.g. 3 IU of insulin, if the dose limiting mechanism **84** fails.

Moreover, an upper end-of-contend surface **68** of the limiter **10** is adapted to engage a lower end-of-contend surface **66** of a T-shaped end part **92** of the piston rod. The end-of-contend surfaces are adapted to engage when the set dose correspond to the amount of a medicament remaining

in a reservoir (not shown) of the device. Accordingly, the engagement of the end-of-contend surfaces prevents setting of a dose exceeding the amount of a medicament remaining in the reservoir. It will be appreciated that the distance between the end-of-contend surfaces thus corresponds to the amount of the medicament remaining in the reservoir.

Moreover, an upper surface **94** of the drum **70** may be adapted to engage a lower surface **96** of the housing, when the maximum dose is set. The maximum dose is the largest dose which may be set for each ejection (provided that the syringe device comprises the required amount of medicament). The maximum dose does not correspond to the end-of-content dose which relates the remaining amount of a medicament in the device. Accordingly, as long as the remaining amount of medicament in the device is larger than the maximum dose, the end-of-content surfaces will not abut each other during dose setting, whereas when the remaining amount of medicament in the device is lower than the maximum dose, the maximum dose surfaces may abut each other during dose setting, as the end-of-content surfaces prevents further rotation.

The limiter **10** and the driver **12** are locked for relative rotation by means of grove-tongue engagement **59**. Thus, when the piston rod is locked for rotation relative to the housing, a relative rotation between the driver **12** and the piston rod **8** causes the limiter to move away from the stopping position and towards the t-shaped end part **92** (i.e. upwards in the figure). The piston rod is locked for rotation relative to the housing when the piston rod guide **88** is locked for rotation relative to the housing (not shown), as the piston rod guide **88** and the piston rod are locked for relative rotation due to the grove-tongue engagement **98**.

The driver **12** and the piston rod guide **88** are interconnected by a two-way ratchet mechanism **100** comprising at least one first retaining member **102** defined by the driver **12** and at least one second retaining member **104** defined by the piston rod guide **88**. The two-way ratchet mechanism is adapted to allow relative rotational movement between the driver **12** and the piston rod guide **88** during dose setting and to ensure that rotational movement of the driver during dose ejection is transferred to the piston rod guide **88**.

The use of the device is as follows. Initially the piston rod guide is locked for rotation relative to the housing. Then the dose setting member is rotated which causes the driver and the drum scale to rotate and the pre-strained spring to be strained even further. At the same time, the limiter moves towards the T-shaped end part. If the user tries to set a dose exceeding the amount of medicament in the device, the limiter abuts the T-shaped end part whereby an even larger dose cannot be set. The dose is ejected by removing the rotational lock between the piston rod guide and the housing, whereby the strained spring forces the driver to rotate. The rotating driver forces the piston rod guide to rotate which again forces the piston rod to rotate. Due to the grove-tongue engagement **44** and the threaded interconnection between the piston rod and the housing, the rotating piston rod is forced to move forward and thus the medicament is expelled from the device.

The invention claimed is:

1. A mechanism for preventing setting of a dose which exceeds the amount of a medicament in a reservoir in an injection device, wherein a dose is set by rotating a dose setting member of a dose setting mechanism, the mechanism comprising:

a piston rod having a threaded outer surface;

a housing defining a passage for the piston rod, the passage having a threaded inner surface for engagement with the threaded outer surface of the piston rod, the housing being arranged with respect to the piston rod such that rotation of the piston rod in relation to the housing causes the piston rod to be displaced relative to the housing in a longitudinal direction;

a limiter defining a passage for the piston rod;

a driver defining a passage for the limiter, the driver being coupled to the dose setting member such that rotation of the dose setting member during dose setting causes the driver to rotate; and

wherein the limiter is coupled to the driver and the piston rod such that relative rotation between the driver and the piston rod during dose setting causes the limiter to move towards a stopping position wherein the limiter prevents setting of a dose which exceeds the amount of a medicament in a reservoir in the injection device.

2. A mechanism according to claim **1**, further comprising a locking structure for locking the piston rod against rotation in at least one direction relative to the housing.

3. A mechanism according to claim **1** or **2**, wherein:

the limiter has a threaded outer surface and is rotationally retained in relation to the piston rod; and

the passage of the driver has a threaded inner surface for engagement with the threaded outer surface of the limiter.

4. A mechanism according to claim **1** or **2**, wherein the limiter comprises a first engaging surface adapted to engage a corresponding second engaging surface of the driver.

5. A mechanism according to claim **1**, wherein the limiter comprises a plurality of teeth adapted to engage corresponding teeth of the housing and/or the driver when the limiter is in the stopping position.

6. A mechanism according to claim **1**, wherein:

the passage of the limiter has a threaded inner surface for engagement with the threaded outer surface of the piston rod; and

the driver is rotationally retained in relation to the limiter.

7. A mechanism according to claim **1**, wherein the limiter comprises a first engaging surface adapted to engage a corresponding second engaging surface of the piston rod.

8. A mechanism according to claim **1**, further comprising a ratchet mechanism interconnecting the driver and the housing.

9. A mechanism according to claim **8**, wherein the ratchet mechanism comprises a first and a second part, the first part being coupled to the driver and the second part being adapted to be locked for rotation relative to the housing by structure of a locking structure .

10. A mechanism according to claim **8**, further comprising an ejection assisting system for providing an ejection force for assisting an operator during ejection.

11. A syringe device according to claim **10**, wherein the ejection assisting system comprises a spring which is strained when the dose setting member is rotated during dose setting.

12. A mechanism according to claim **3**, wherein the limiter comprises a first engaging surface adapted to engage a corresponding second engaging surface of the driver.

13. A mechanism according to claim **2**, wherein the limiter comprises a plurality of teeth adapted to engage corresponding teeth of the housing and/or the driver when the limiter is in the stopping position.

14. A mechanism according to claim **3**, wherein the limiter comprises a plurality of teeth adapted to engage corresponding teeth of the housing and/or the driver when the limiter is in the stopping position.

15. A mechanism according to claim **4**, wherein the limiter comprises a plurality of teeth adapted to engage corresponding teeth of the housing and/or the driver when the limiter is in the stopping position.

16. A mechanism according to claim **2**, wherein:

the passage of the limiter has a threaded inner surface for engagement with the threaded outer surface of the piston rod; and

the driver is rotationally retained in relation to the limiter.

17. A mechanism according to claim **2**, wherein the limiter comprises a first engaging surface adapted to engage a corresponding second engaging surface of the piston rod.

18. A mechanism according to claim **6**, wherein the limiter comprises a first engaging surface adapted to engage a corresponding second engaging surface of the piston rod.

19. A mechanism according to claim **2**, further comprising a ratchet mechanism interconnecting the driver and the housing.

20. A mechanism according to claim **3**, further comprising a ratchet mechanism interconnecting the driver and the housing.

21. A mechanism according to claim **4**, further comprising a ratchet mechanism interconnecting the driver and the housing.

22. A mechanism according to claim **5**, further comprising a ratchet mechanism interconnecting the driver and the housing.

23. A mechanism according to claim **6**, further comprising a ratchet mechanism interconnecting the driver and the housing.

24. A mechanism according to claim **7**, further comprising a ratchet mechanism interconnecting the driver and the housing.

25. A mechanism according to claim **9**, further comprising an ejection assisting system for providing an ejection force for assisting an operator during ejection.

* * * * *

EXHIBIT J

US009861757B2

(12) **United States Patent**
Moller et al.

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(45) **Date of Patent: Jan. 9, 2018**

(54) **INJECTION DEVICE WITH AN END OF DOSE FEEDBACK MECHANISM**

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(72) Inventors: **Claus Schmidt Moller**, Fredensborg (DK); **Bo Radmer**, Hilleroed (DK); **Lars Ulrik Nielsen**, Virum (DK); **Christian Peter Enggaard**, Vejby (DK)

(73) Assignee: **Novo Nordisk A/S**, Bagsvaerd (DK)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **15/241,566**

(22) Filed: **Aug. 19, 2016**

(65) **Prior Publication Data**

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(Continued)

(30) **Foreign Application Priority Data**

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(51) **Int. Cl.**
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A61M 5/20 (2006.01)
A61M 5/24 (2006.01)

(52) **U.S. Cl.**
CPC ***A61M 5/3157*** (2013.01); ***A61M 5/20*** (2013.01); ***A61M 5/24*** (2013.01); ***A61M 5/3155*** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC A61M 5/3157; A61M 5/20; A61M 5/24; A61M 5/3155; A61M 2205/581;
(Continued)

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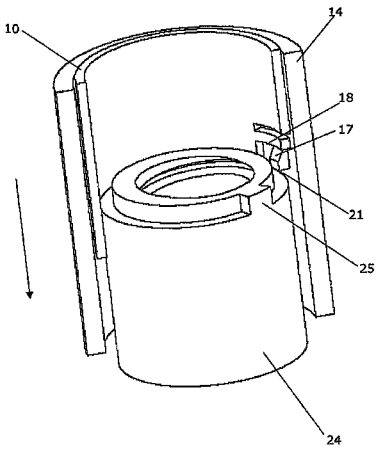
Primary Examiner — Emily Schmidt
Assistant Examiner — Lauren M Peng
(74) *Attorney, Agent, or Firm* — Wesley Nicolas

(57) **ABSTRACT**

An injection device with a dose delivering mechanism being adapted to provide a non-visual, e.g. audible and/or tactile, feedback signal when a set dose has been at least substantially injected. A first and a second part of the injection device are adapted to perform a relative rotational movement with respect to each other. The relative rotational movement causes at least two parts of the injection device to abut or engage, and this abutment or engagement causes the non-visual feedback signal to be generated. A very distinct and precise feedback is provided as compared to prior art axial solutions because the generation of the feedback signal is initiated by the relative rotational movement.
Feedback signal may be generated by a change in a rotational velocity of at least one part, e.g. by changing the pitch of a threaded portion or by engaging a non-rotating part and a rotating part, thereby causing the non-rotating part to start rotating. May alternatively be generated by building up and releasing a tension.
The injection device is suitable for injecting insulin.

12 Claims, 14 Drawing Sheets



Related U.S. Application Data

(60) Provisional application No. 60/647,491, filed on Jan. 27, 2005.

(52) **U.S. Cl.**
CPC *A61M 5/31535* (2013.01); *A61M 5/31551* (2013.01); *A61M 5/31561* (2013.01); *A61M 5/31585* (2013.01); *A61M 2205/581* (2013.01); *A61M 2205/582* (2013.01)

(58) **Field of Classification Search**
CPC A61M 2205/582; A61M 5/31535; A61M 5/31551; A61M 5/31585
See application file for complete search history.

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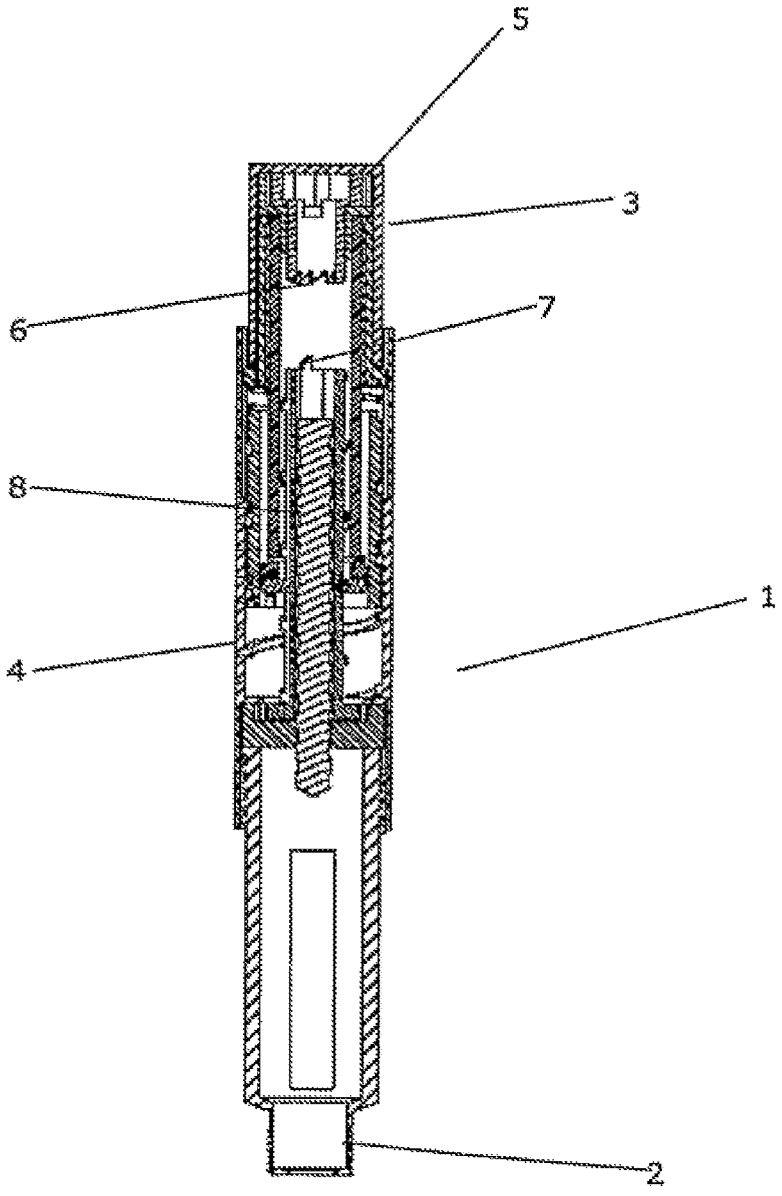

FIG. 1

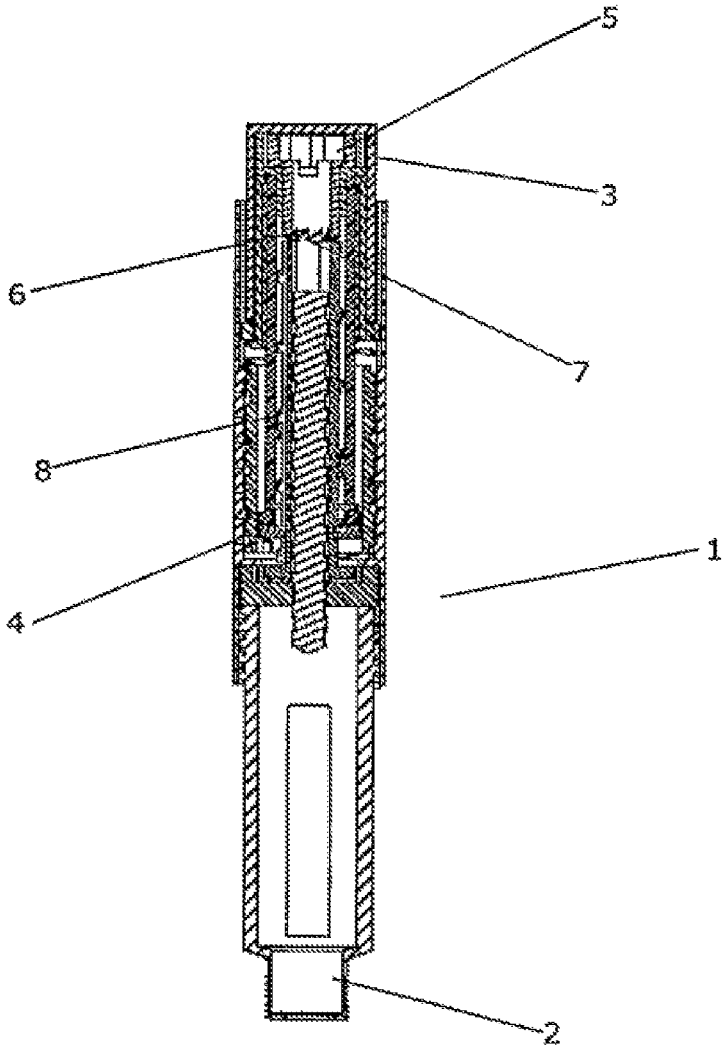

FIG. 2

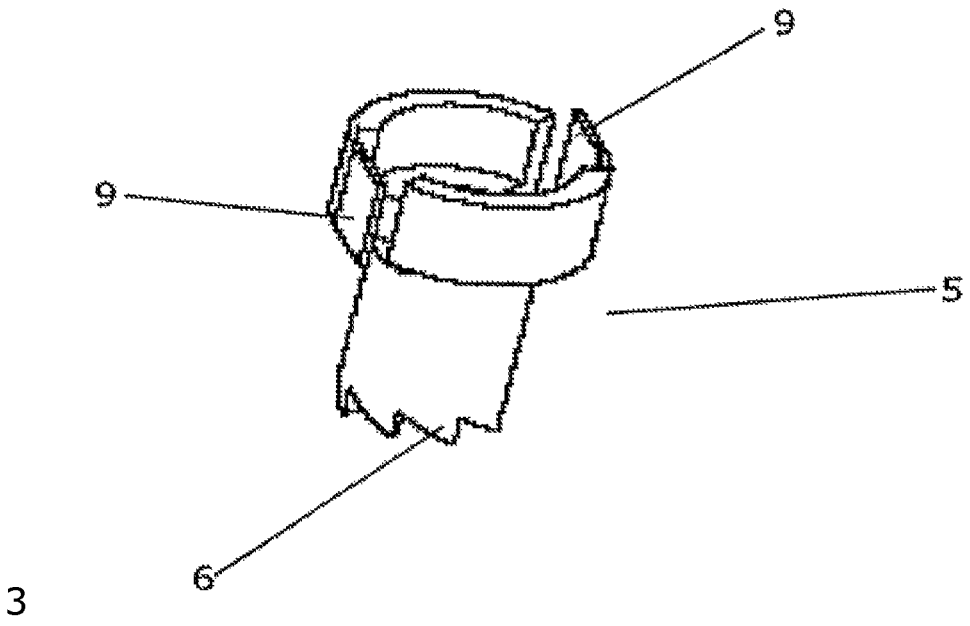

FIG. 3

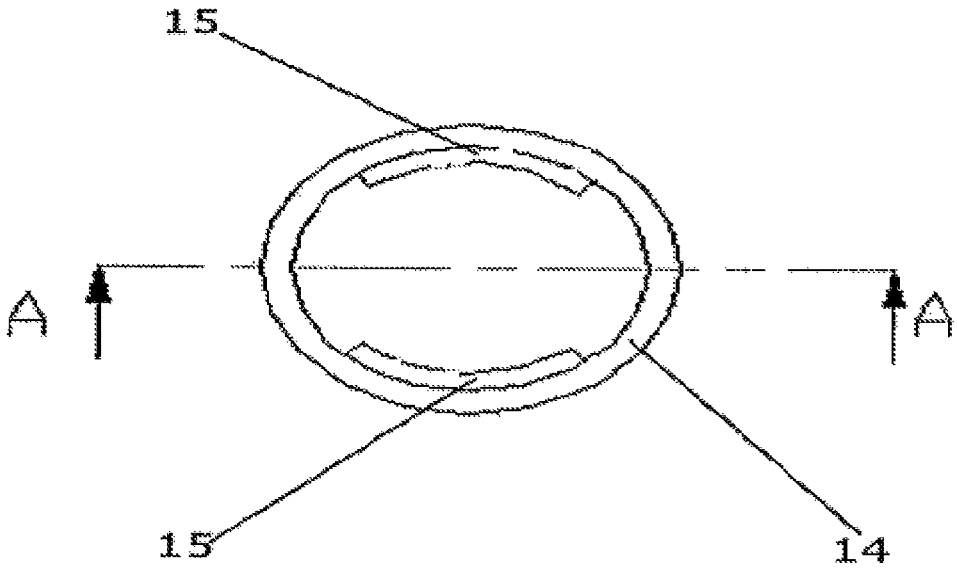

FIG. 5

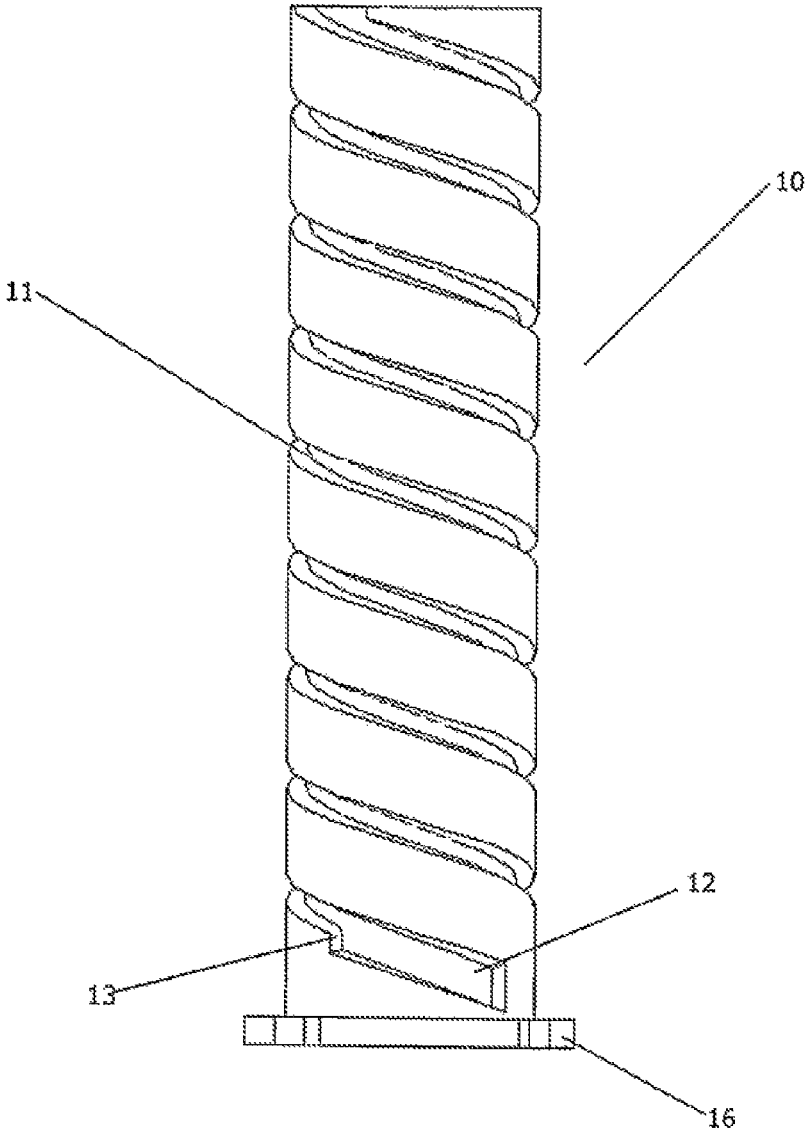

FIG. 4

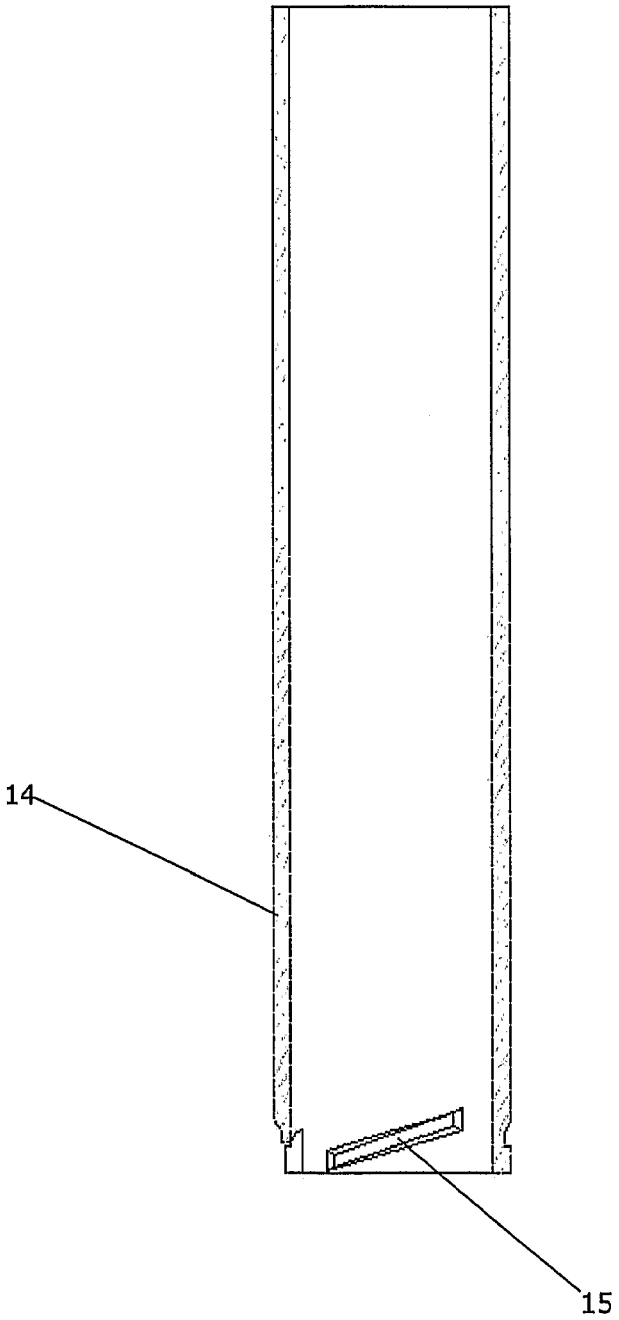

FIG. 6

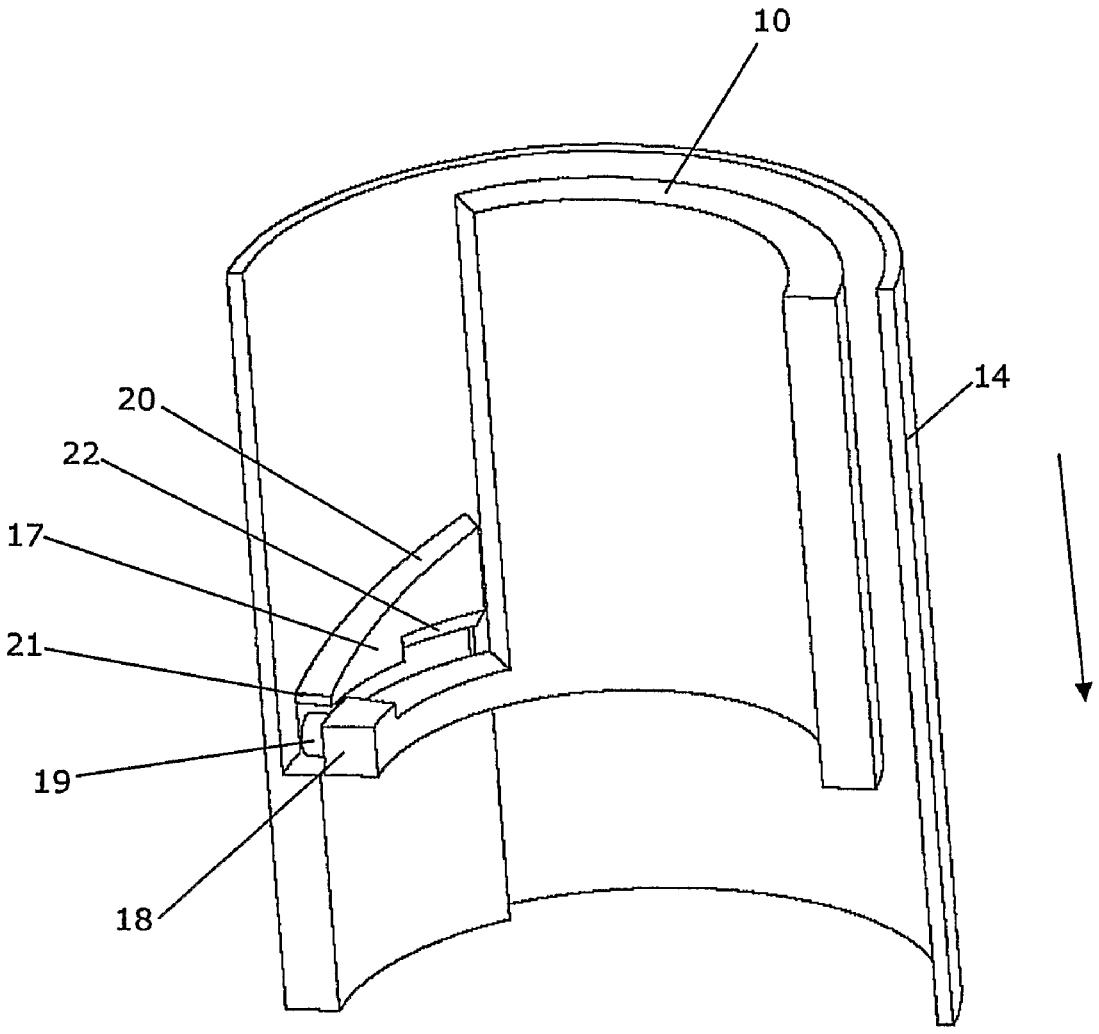

FIG. 7

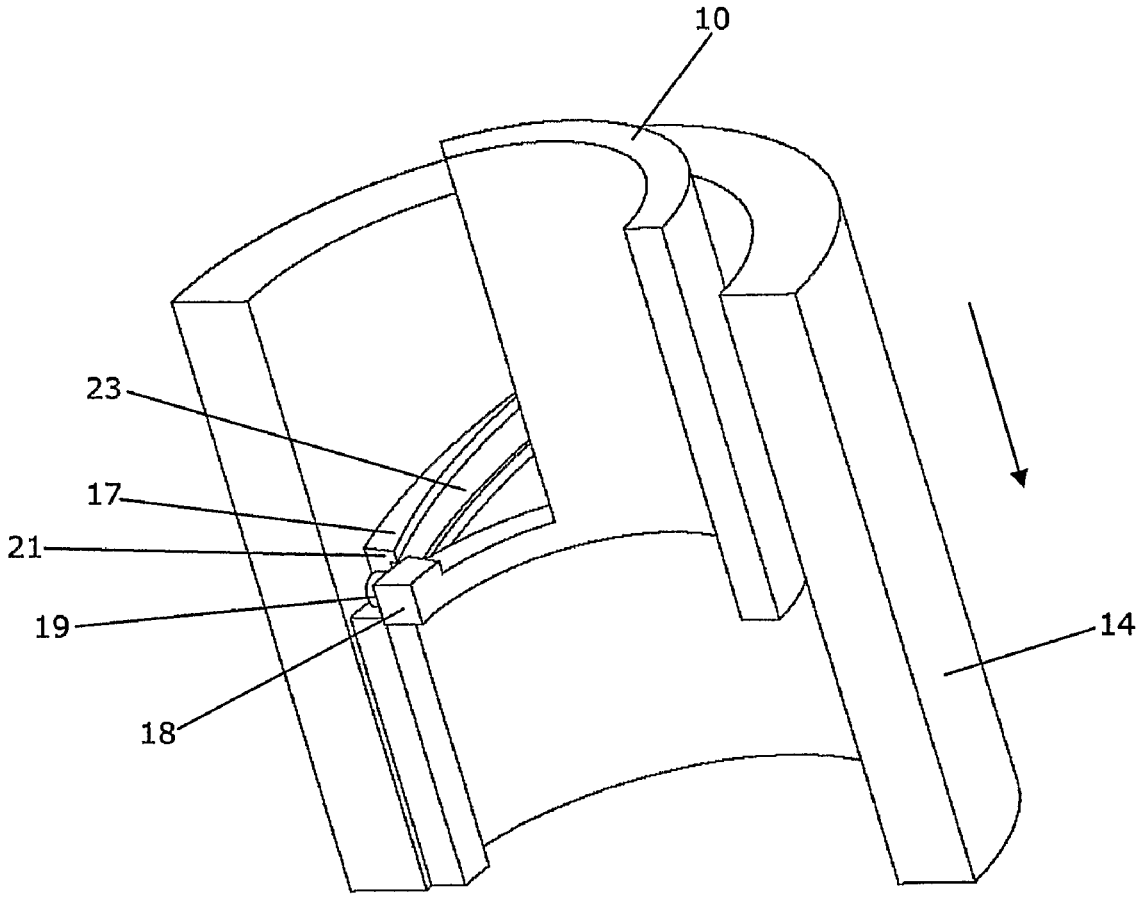

FIG. 8

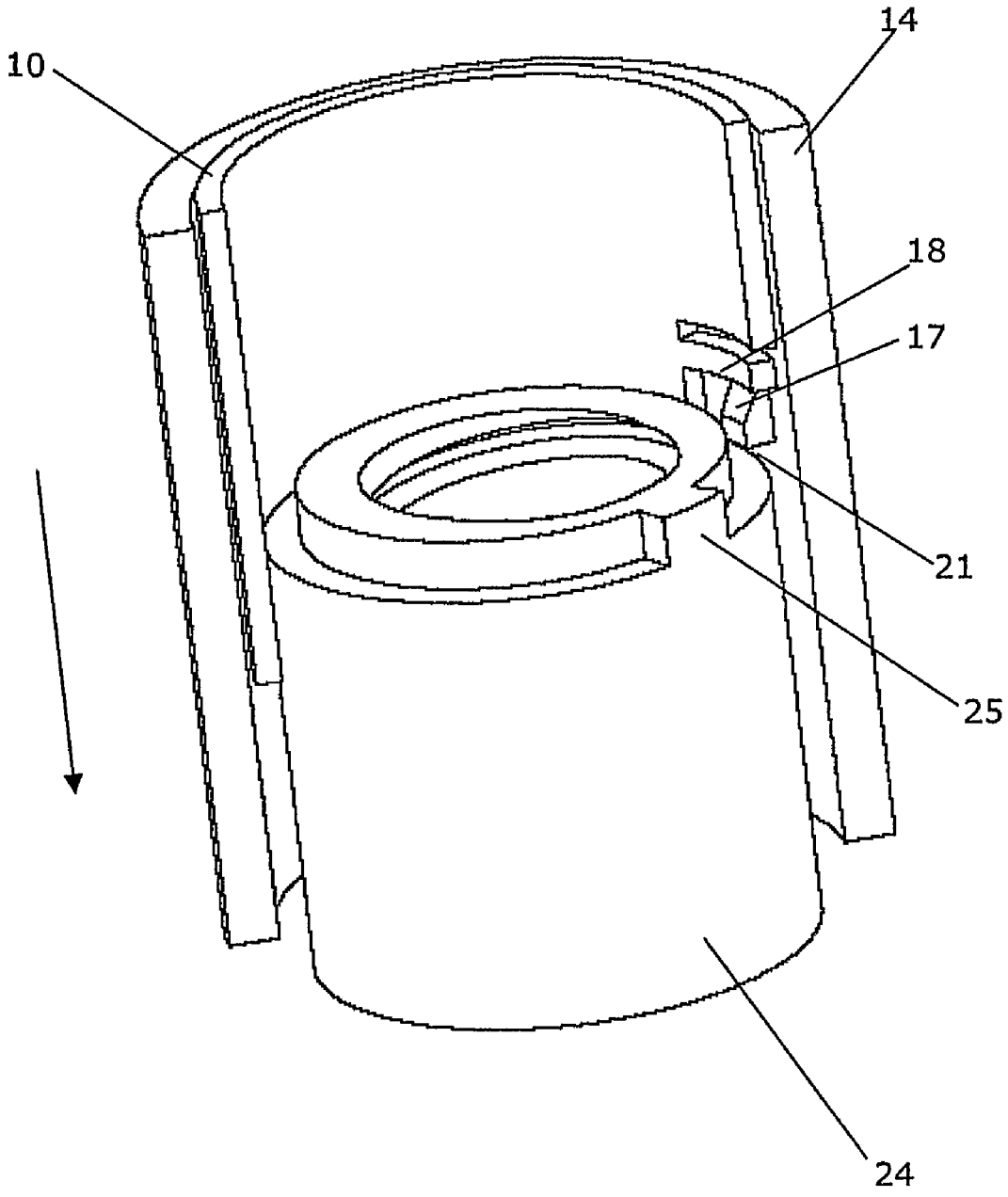

FIG. 9

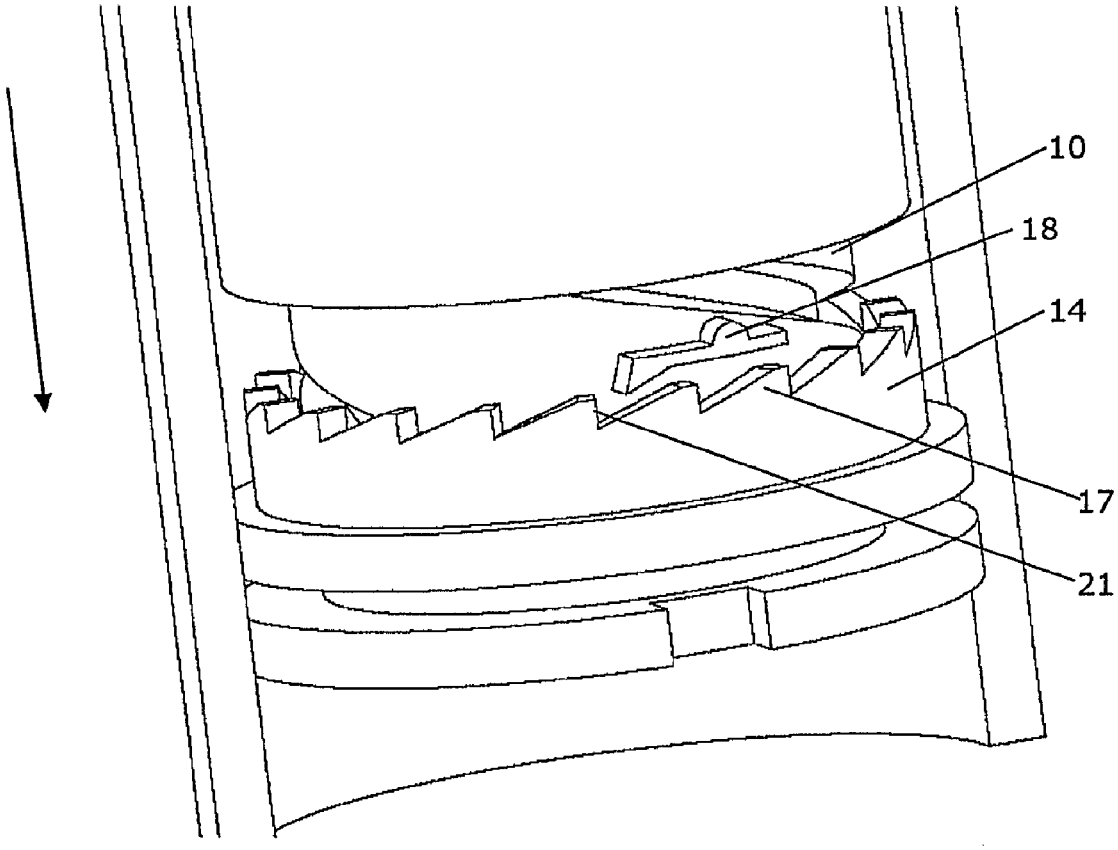

FIG. 10

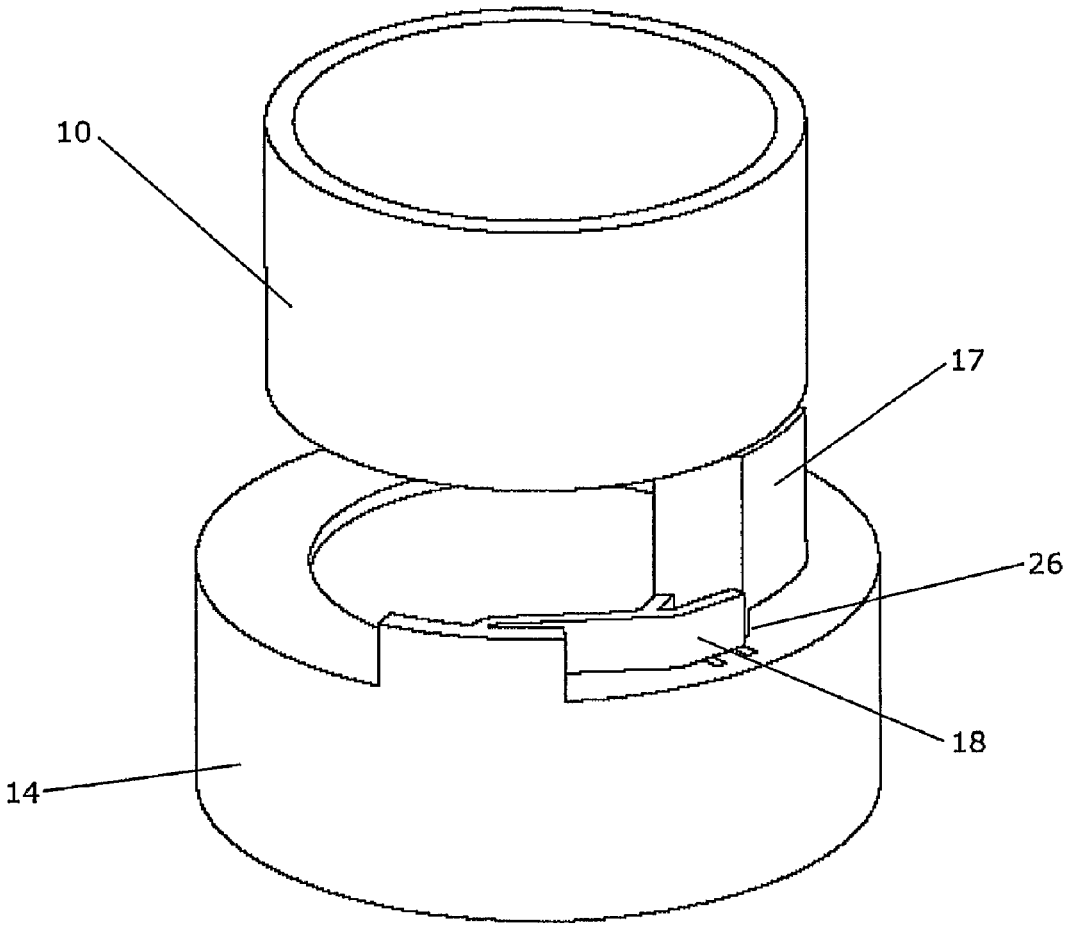

FIG. 11

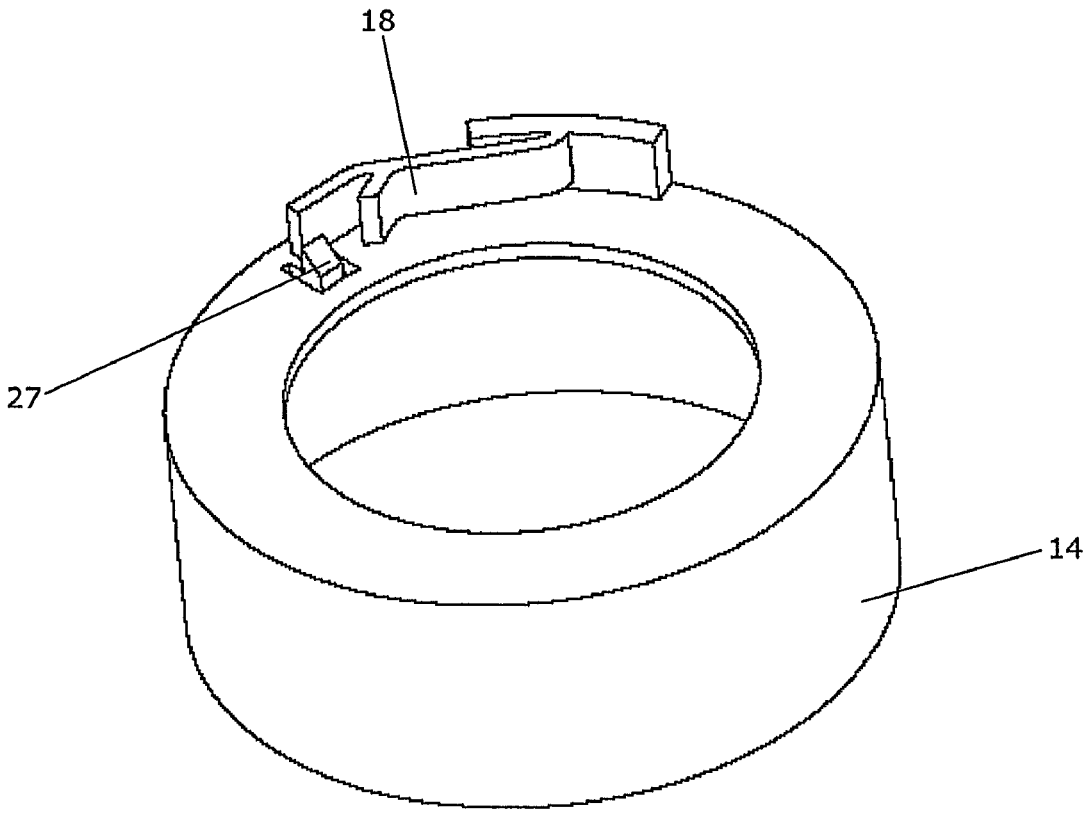

FIG. 12

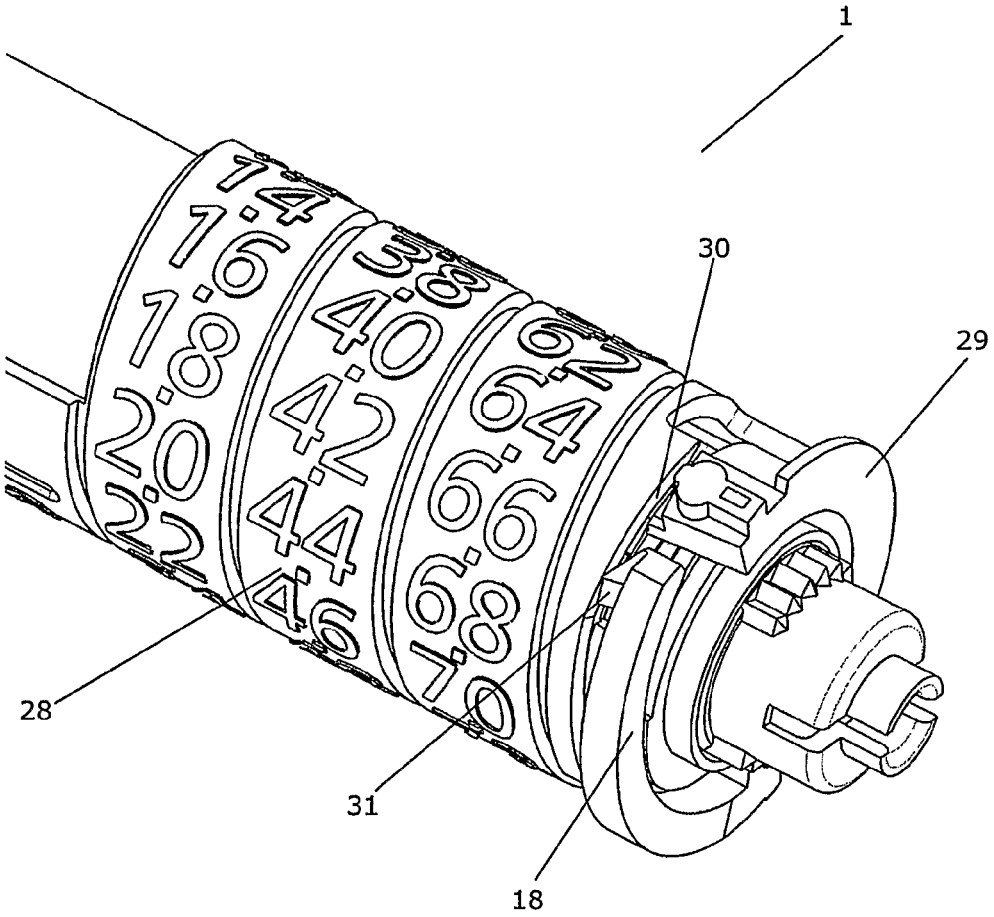

FIG. 13

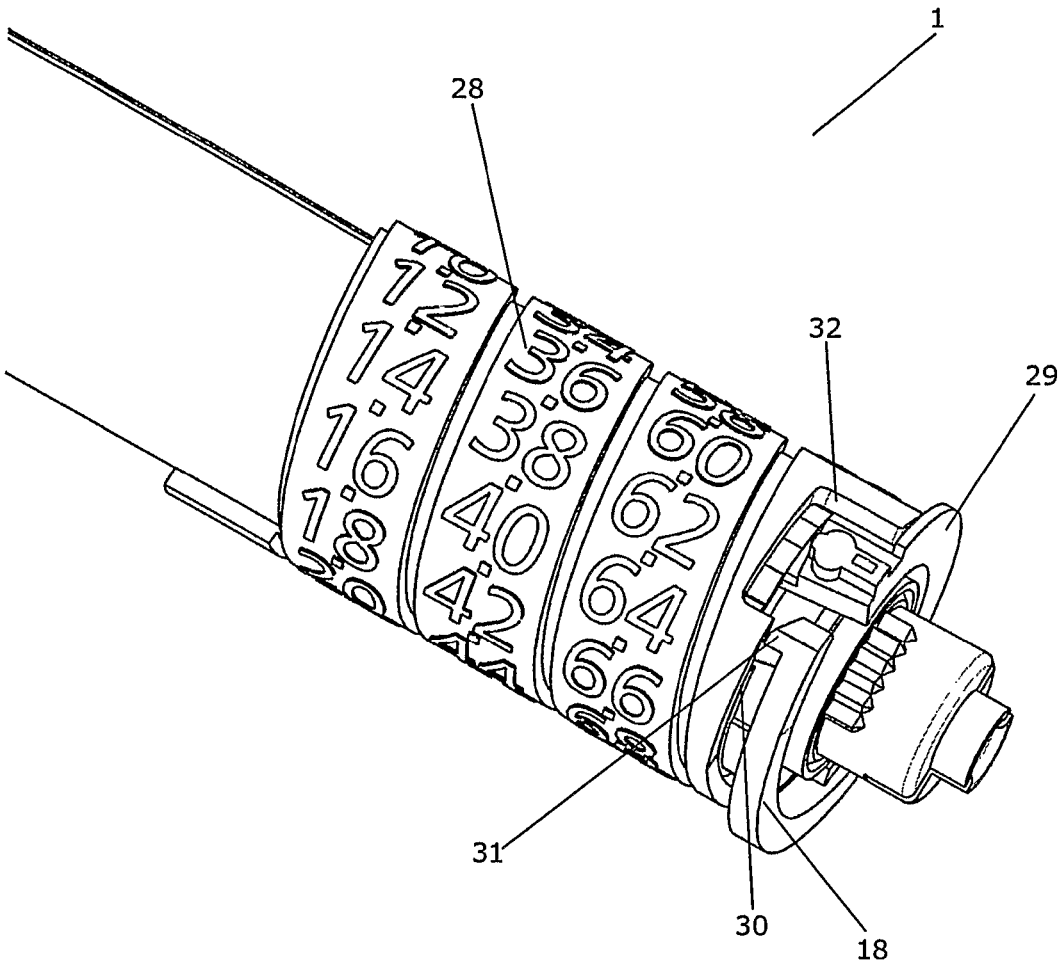

FIG. 14

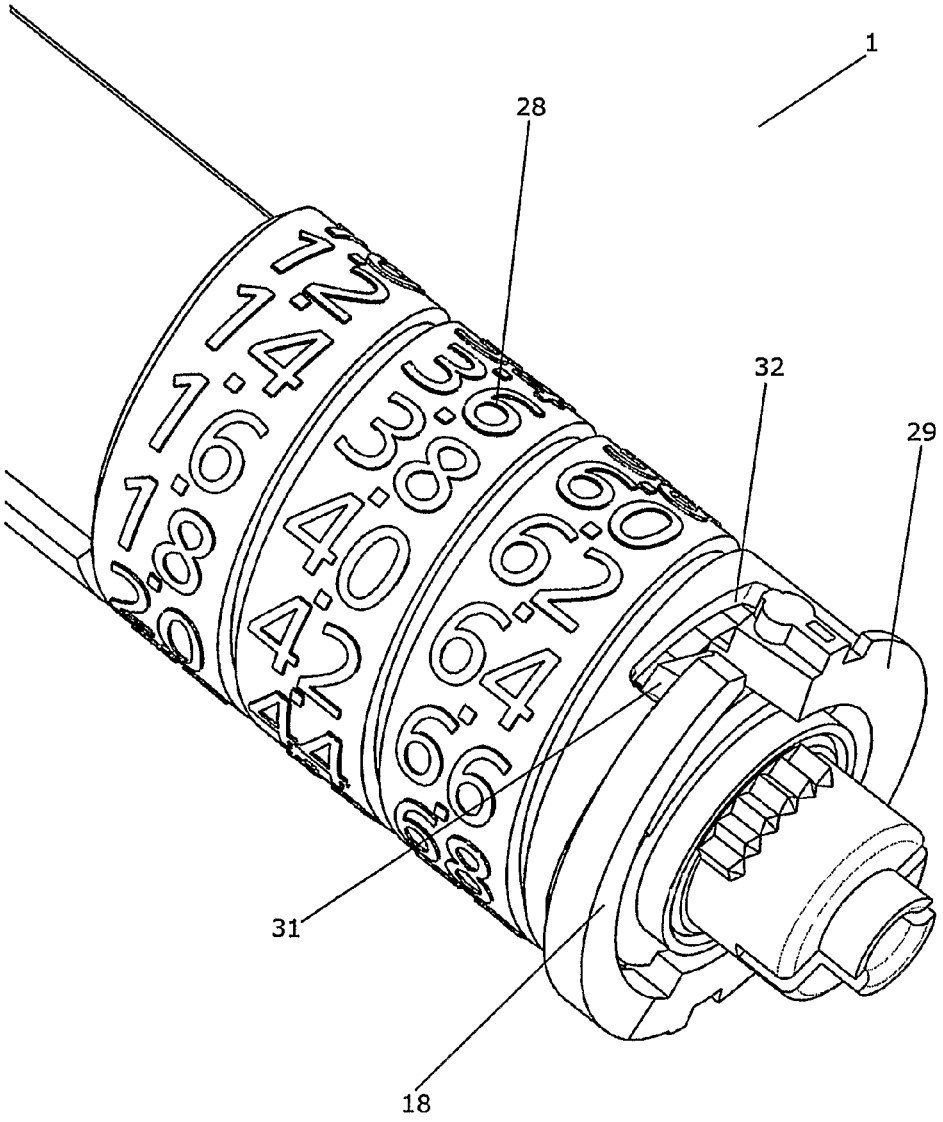

FIG. 15

INJECTION DEVICE WITH AN END OF DOSE FEEDBACK MECHANISM

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of application Ser. No. 11/813,389, filed Jul. 5, 2007 (Notice of Allowance received), which is a 35 U.S.C. §371 national stage application of International Patent Application PCT/EP2006/000486 (published as WO 2006/079481), filed Jan. 20, 2006, which claimed priority of European Patent Application 05075187.4, filed Jan. 25, 2005; this application further claims priority under 35 U.S.C. §119 of U.S. Provisional Application 60/647,491, filed Jan. 27, 2005; the contents of which are incorporated herein by reference.

FIELD OF THE INVENTION

The present invention relates to an apparatus for delivering liquid drugs to a mammal, preferably a human being, preferably in a subcutaneous manner. More particularly, the present invention relates to an injection device which is capable of providing a non-visual feedback signal to a user indicating that a set dose has been injected by the injection device.

BACKGROUND OF THE INVENTION

In the present disclosure reference is mainly made to the treatment of diabetes by injection of insulin. However, this is merely an exemplary use of the present invention. Thus, the present invention may be used for injection of any other suitable kind of drug, e.g. growth hormone.

Injection devices, e.g. in the form of injection pens, are mainly made for users who have to inject themselves frequently, e.g. people having insulin-dependent diabetes or needing treatment by growth hormones. A number of requirements are set to such injection devices. The setting of a dose must be easy and unambiguous and it must be easy to read the set dose. Furthermore, it must be possible, with a minimum of trouble, to cancel or change a wrongly set dose. Finally, when the dose is injected the dose setting mechanism must return to zero. This is very important since it ensures that the set dose is actually injected, thereby allowing the user to keep track of which dose is injected.

Many injection devices work with a threaded piston rod which cooperates with a nut, the nut and the piston being capable of rotating relatively to each other. The dose setting may be obtained by dialling the nut away from a stop to which it is returned during injection by pressing the piston rod forward, either manually or by means of a mechanically biased mechanism, such as a spring, until the nut member abuts the stop. In other injection devices one of the elements, the nut or the piston rod, is kept inrotatable while the other one is allowed to rotate a set angle depending on the set dose, whereby the piston rod is dialled a distance in a forward direction through the nut member.

In such prior art injection devices a dose is normally set by dialling a dose setting member, and the set dose is injected by pushing an injection button. In elongated pen shaped injection devices the dose setting member and the injection button normally form a single member. When the injection button is pushed the set dose is expelled. However, the amount of drug expelled is only equal to the set dose if the injection button has been pushed as far as possible, the dose setting member thereby having been brought back to zero. In order to ensure that the correct dose has actually been injected, the user therefore has to visually inspect the position of the dose setting member during the injection. This is disadvantageous because the injection in some cases will take place in a part of the body where visual inspection during the injection is very difficult or even impossible. Furthermore, in case the user is visually impaired it may be difficult for the user to visually inspect the dose setting member during or after the injection, regardless of where on the body the injection is performed. Since it is not uncommon for people having diabetes to be visually impaired, this is an important aspect.

It is therefore desirable to provide a feedback signal to the user indicating that the set dose has been injected, the feedback signal being of a kind which makes it unnecessary for the user to visually inspect whether or not the set dose is injected.

Some prior art injection devices have a mechanism which informs the user that a dose is being injected by producing an audible 'click' for each dose unit being injected. However, since these clicks appear during the entire injection they do not provide a feedback signal indicating that the set dose has been injected, and the problem indicated above is therefore not solved by these injection devices. Prior art injection devices of this type are, e.g., described in U.S. Pat. No. 4,592,745, EP 0 688 571 and US 2004/0210199.

In WO 98/57688 an injection device is disclosed which addresses the above mentioned problem. Thus, WO 98/57688 discloses an injection device having a dose setting device. A dose is set by dialling a dose setting member. Apart from setting a dose the dialling action causes an injection button to be moved from a position where it abuts a housing of the injection device to a position where it protrudes from the housing. The set dose is subsequently delivered by pushing the injection button back into abutment with the housing.

In one embodiment a lock is activated when the injection button reaches the housing, and the activation of the lock produces an audible click indicating that the injection button is in abutment with the housing and thereby that the set dose has been delivered. During the injection, including the final part when the lock is activated, the injection button is moved linearly. The linear distance travelled by the injection button during the last few doses is relatively short. It may therefore be difficult to determine accurately from the audible click produced by the lock whether or not and when the set dose has been delivered.

EP 0 594 357 discloses another injection device which addresses the above mentioned problem. Thus, EP 0 594 357 discloses an injection device having a top section with resilient legs depending perpendicularly from the top section. The outer surface of the resilient legs has a ridge which rests on a ledge inside of the dose knob. The dose knob may have an elongated section which fits into a cylindrical sleeve such that when the dose knob is pushed into the sleeve, at the end of injection, the top portion of the sleeve touches end of the leg of the resilient legs displacing the ridge from the ledge and causing a snapping noise. As it is the case with the injection device described in WO 98/57688, the dose knob is moved linearly during injection, also during the final part of the injection when the resilient legs are displaced from the ridge causing the snapping noise. Therefore the shortcomings described above are also applicable here.

SUMMARY OF THE INVENTION

It is, thus, an object of the present invention to provide an injection device being capable of precisely and in a non-visual manner indicating to a user when a set dose has been injected.

It is a further object of the present invention to provide an injection device being capable of non-visually indicating to a user when a set dose has been injected, the indication being delivered to the user in a very distinct manner.

It is an even further object of the present invention to provide a dose delivering mechanism for an injection device, the dose delivering mechanism being capable of precisely and in a non-visual manner indicating to a user when a set dose has been injected.

According to the present invention the above and other objects are fulfilled by providing an injection device comprising:

a housing,

a dose setting member being operable to set a desired dose to be injected,

a piston rod being adapted to cooperate with a piston so as to cause a set dose to be injected from an ampoule, and

a dose delivering mechanism being adapted to operate the piston rod in such a way that a set dose is injected, the dose delivering mechanism further being adapted to provide a non-visual feedback signal to a user only at the end of injection of a set dose, wherein first and second parts of the injection device are adapted to perform a relative rotational movement with respect to each other during injection of a dose, and wherein said relative rotational movement causes at least two parts of the injection device to abut or engage, said abutment or engagement causing the non-visual feedback signal to be generated.

The injection device of the present invention is very suitable for use by persons which have to frequently inject themselves, e.g. persons having insulin-dependent diabetes or needing treatment by growth hormones. The desired dose being set by means of the dose setting member is, thus, a dose of a specific drug which the person in question needs to inject at that specific point in time. The desired dose may be a fixed dose which the person needs to inject each time an injection is performed, or it may be a varying amount, e.g. varying according to the time of day and/or one or more parameters which may be measured or chosen prior to setting the dose (e.g. blood glucose (BG) level, contents of a meal, etc.).

The piston rod is preferably adapted to push a piston into an ampoule, thereby causing the set dose to be injected. This may be obtained in various ways and is well known and well described in the art.

The dose delivering mechanism is adapted to provide a non-visual feedback signal to a user only at the end of injection of a set dose. Thus, the feedback signal may be generated when the set dose has been injected, e.g. exactly when or immediately after the last unit has been injected. Alternatively, the feedback signal may be generated before the complete dose has been delivered, e.g. when a few units remain to be injected, the remaining units being injected while the feedback signal is sensed by the user. Thus, when the user perceives the feedback signal the set dose will have been delivered, and the user will therefore not be able to tell the difference between a feedback signal being generated after the dose has been completely injected and a feedback signal being generated immediately before the dose has been completely injected. In any event the user can regard the perception of the feedback signal as an indication that the set dose has been delivered, and the user may therefore react correspondingly, e.g. by removing a pressure applied manually to an injection button.

Since the non-visual feedback signal is provided only at the end of injection of a set dose the user will know distinctly that when the feedback signal is received the set dose has been fully injected. This is an advantage compared to prior art injection devices where a click for each injected dose unit is produced. In this case the user would have to count the number of clicks produced and compare this to the number of set dose units in order to tell exactly when the set dose has been fully injected.

A first part and a second part of the injection device are adapted to perform a relative rotational movement with respect to each other during injection of a dose. This may, e.g., be the housing and the piston rod, or it may be a separate member and any other part of the injection device, e.g. the housing and/or the piston rod, the sole purpose of the separate member being to generate the non-visual feedback signal. Three or more parts of the injection device may perform mutual rotational movements during injection of a dose.

Furthermore, the relative rotational movement may be performed all through the injection of a dose or it may be performed during only part of the injection. Thus, the relative rotational movement may be started or stopped at the end of injection of a set dose as defined above, in which case this starting or stopping may advantageously cause the non-visual feedback signal to be generated.

The relative rotational movement causes at least two parts of the injection device to abut or engage, and this abutment or engagement causes the non-visual feedback signal to be generated. One or both of the parts which abut or engage may be the first and/or second parts, i.e. the parts performing the relative rotational movement. Alternatively, one or both of the parts which abut or engage may be other parts of the injection device. This will be described in further details below.

Due to the fact that the relative rotational movement initiates the generation of the non-visual feedback signal it is ensured that the movement generating the non-visual feedback signal is much longer than a corresponding movement in an injection device where the feedback signal is generated by a linear movement of one or more parts. Thereby the generated signal will be much more precise and distinct, and a far more accurate feedback signal has thereby been provided. This is very advantageous because it makes it much easier for the person to ascertain that the expected and desired dose has actually been injected.

The non-visual feedback signal may comprise an audible and/or a tactile signal. In this case the person using the injection device will be able to hear and/or feel that the set dose has been injected. Alternatively or additionally, the non-visual feedback signal may comprise any other suitable kind of signal which can be perceived by other senses than sight. Furthermore, the non-visual feedback signal may be followed by a visual signal, e.g. a scale drum showing a 'zero', a lamp or a diode which is turned on or off or starts flashing simultaneously with the generation of the non-visual feedback signal. Thereby the user may, in addition to the non-visual feedback signal, use this visual feedback signal to further ensure that the set dose has actually been injected.

In one embodiment of the present invention the abutment or engagement is caused by a change in a rotational velocity of at least one part of the dose delivering mechanism. This may, e.g., be accomplished by allowing a separate member to start rotating at the end of injection of a set dose, typically in such a way that this member rotates during injection of the last few units of the set dose. The rotation of this separate

member will in turn generate a non-visual feedback signal to the user. Thus, in this case the rotational velocity of this member relatively to, e.g., the housing, changes from zero to a certain velocity, and this change causes the non-visual feedback signal to be generated, e.g. in the form of a clicking sound generated by protruding parts present on the separate member moving against an inner part of the housing or an outer part of the piston rod.

Alternatively or additionally, the change in rotational velocity may cause a tactile feedback signal to be generated. It may, e.g., be possible to feel the rotational movement itself, and thereby it may be possible for the user to detect a substantial change (decrease or increase) in the rotational velocity.

In one embodiment the injection device may further comprise a ratchet operating the piston rod and having a threaded portion being adapted to engage with a part of the dose delivering mechanism, in which case the change in a rotational velocity is generated by a change in the pitch of the threaded portion of the ratchet, said change in the pitch in return causing a change in a translational velocity of said part of the dose delivering mechanism, said change in translational velocity causing at least two parts of the injection device to abut, thereby causing the non-visual feedback signal to be generated.

In this embodiment the non-visual feedback signal preferably comprises a tactile feedback signal. Thus, the part of the dose delivering mechanism which is adapted to engage with the threaded portion of the ratchet is preferably in directly or indirectly contact with the user during injection of a dose. Thus, the part may be, form part of or be operatively connected to an injection button which the user presses during injection. Thereby the user will be able to feel the change in translational velocity.

The pitch may be changed from a certain value used during the main part of the injection to zero, i.e. the threaded portion simply stops at a position corresponding to the end of injection of a set dose. In this case the user will feel a kind of 'axial resistance' during the injection until the ratchet/dose delivery part reaches the position where the threaded portion stops. Then the part will stop rotating and instead increase the velocity of a translational (axial) movement which is also performed while the ratchet/dose delivery part travels the threaded portion, due to the pitch of the threaded portion. The user will be able to feel this increase in translational velocity. Furthermore, the translational movement is preferably eventually stopped, e.g. due to part of the dose delivery mechanism abutting a stop member. This stop will also be very distinctly felt by the user, thereby producing a non-visual feedback signal, and it may further produce a sound, in which case the non-visual feedback signal comprises a tactile as well as an audible signal. In this embodiment the two parts of the injection device which are caused to abut may advantageously be a scale drum and a part of the housing, the scale drum performing a rotational and axial movement defined by the threaded portion.

Alternatively, the two parts may be a dose knob and a proximal part of the housing, the dose knob performing an axial movement which follows the axial part of the movement of the scale drum as described above.

Alternatively, the pitch may either increase or decrease from one non-zero value to another. This has the advantage that the engaging part is readily moved back into engagement with the threaded portion when a new dose is to be set.

In another embodiment the dose delivering mechanism may comprise a first dose part and a second dose part, the first dose part being adapted to rotate relatively to the housing during injection of a dose and the first dose part comprising means for engaging the second dose part at the end of injection of a set dose, thereby causing the second dose part to rotate along with the first dose part, in which case the non-visual feedback signal is generated by the resulting rotational movement of the second dose part.

In this embodiment the rotational movement of the second dose part increases from zero to a non-zero value at the end of injection of the set dose. The second dose part may be provided with teeth, protrusions, flexible arms or similar means being adapted to be moved against another part of the device during rotation of the second dose part, thereby producing a sound which at least partly constitutes the non-visual feedback signal.

The second dose part may be positioned between the first dose part and the housing. In case the second dose part is provided with teeth, protrusions, flexible arms or the like as described above, these may advantageously be moved against a part of the housing when the second dose part is rotated along with the first dose part.

Alternatively, the non-visual feedback signal may be generated as a result of an abutment between two parts of the dose delivering mechanism performing a relative rotational movement. The feedback signal may, e.g., be obtained by releasing a tension which has previously been introduced in a part of the injection device, the release of the tension being caused by the abutment between the two parts.

The tensed part may comprise a spring means, such as a separate spring member or at least one resilient portion of at least one of the first and second parts performing the relative rotational movement. In case the spring means is in the form of at least one resilient portion of the part(s) the non-visual feedback signal may be generated in the following manner. First the resilient portion(s) is/are bent into a tensed position. At a later time this tension is released, e.g. by rotating the resilient portion(s) away from a part which holds the resilient portion(s) in the tensed position. Thereby the resilient portion(s) will restore its/their relaxed position(s), and this movement will generate a clicking sound, i.e. a non-visual feedback signal. The resilient portion(s) may be in the form of spring arm(s), in which case a sound may be generated due to moving air caused by sudden release of the tensed spring arm(s). Alternatively, abutment between a moving part and a release mechanism may release the tension of the resilient portion(s).

The tension may be introduced during dose setting, e.g. by tightening a spring member or moving a resilient portion into a tensed position as described above. This may be obtained by letting the dose setting mechanism be connected to a spring member, e.g. in such a way that a spring is tightened when a dose setting member is turned, or in such a way that a part being provided with a resilient portion is rotated along with a dose setting member, thereby causing the resilient part to be moved into a tensed position.

Alternatively, the tension may be introduced during injection of a dose. This may be obtained in a manner very similar to what is described above. However, in this case the tensed part should be operatively connected to the dose delivering mechanism.

The dose delivering mechanism may be adapted to be manually operated, e.g. by means of an injection button which the user must press manually during the injection.

Alternatively, the dose delivering mechanism may be adapted to be operated by means of a mechanically biased mechanism, e.g. comprising at least one spring. The mechanically biased mechanism may, in this case, be biased during setting of a dose. When the injection is subsequently

performed this is done by releasing the tension previously built up in the mechanically biased mechanism, and the stored energy will then cause the set dose to be injected. This kind of injection device does not require a force applied by the user in order to inject a set dose.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will now be further described with reference to the accompanying drawings in which:

FIG. **1** shows a cross section through an injection device according to a first embodiment of the invention and being in a position where a dose has been set,

FIG. **2** shows a cross section through the injection device of FIG. **1** in a position where a dose has been injected,

FIG. **3** shows a click item adapted to be positioned in the injection device of FIGS. **1** and **2**,

FIG. **4** shows a threaded inner part being adapted to be positioned in an injection device according to a second embodiment of the invention,

FIG. **5** shows a top view of an outer part being adapted to engage with the inner part of FIG. **4**,

FIG. **6** is a cross section along line A-A in FIG. **5**,

FIGS. **7-10** show parts of injection devices according to a third, fourth, fifth and sixth embodiment of the invention, respectively, all having a spring arm and a wedge structure,

FIG. **11** shows part of an injection device according to a seventh embodiment of the invention having a spring arm and a release mechanism,

FIG. **12** shows an outer part of the injection device of FIG. **11** from a different angle, and

FIGS. **13-15** show part of an injection device according to an eighth embodiment of the invention having a spring arm, at various points in time.

The Figures are schematic and simplified for clarity, and they only show details which are essential to the understanding of the invention while other details are left out. Throughout the description of the drawings the same reference numerals will be used for identical or corresponding parts.

DETAILED DESCRIPTION OF THE DRAWINGS

When in the following terms as 'upper' and 'lower', 'left' and 'right', 'horizontal' and 'vertical', 'clockwise' and 'counter clockwise' or similar relative expressions are used, these only refer to the accompanying drawings and not to the actual situation of use. The shown Figures are schematic representations for which reason the configuration of the different structures as well as their relative dimensions are intended to serve illustrative purposes only. In that context it may be convenient to define that the term 'distal end' in the accompanying drawings is meant to refer to the end of the injection device carrying an injection needle, whereas the term 'proximal end' is meant to refer to the opposite end pointing away from the injection needle.

FIG. **1** shows a cross section through an injection device **1** according to a first embodiment of the invention. At its distal end the injection device **1** is provided with a portion **2** being adapted to carry an injection needle (not shown). At its proximal end the injection device **1** comprises a combined dose setting and injection button **3**. During dose setting the dose setting and injection button **3** is rotated. This causes the dose setting and injection button **3** to be moved away from a housing **4** to the position shown in FIG. **1**. During injection the user presses the dose setting and injection button **3**, thereby moving it back into the housing **4**.

This movement causes the set dose to be injected from the injection device **1**. Inside the dose setting and injection button **3** there is positioned a click item **5** which is provided with a set of teeth **6** being adapted to engage with a corresponding tooth **7** positioned on a ratchet **8**. During injection the ratchet **8** will rotate relatively to the housing **4** while the click item **5** will not rotate.

FIG. **2** shows a cross section of the injection device **1** of FIG. **1**. However, in FIG. **2** a dose has just been injected, i.e. the dose setting and injection button **3** has been pushed to a position inside the housing **4**. Thereby the set of teeth **6** on the click item **5** engage with the tooth **7** on the ratchet **8**. Since the ratchet **8** rotates during the injection, this will cause the click item **5** to be rotated along with the ratchet **8**. This rotational movement will cause the click item **5** to produce a sound in a manner which will be explained further below with reference to FIG. **3**. Since the click item **5** is only rotated during the injection of the last few units of the set dose the produced sound indicates that the set dose has been substantially injected. Thereby a non-visual feedback signal has been generated.

FIG. **3** is a perspective view of a click item **5** adapted to be inserted in the injection device **1** of FIGS. **1** and **2**. The part of the click item **5** positioned opposite the set of teeth **6** is provided with two resilient parts **9**. The resilient parts **9** are resilient due to a reduced thickness of the material making up the parts **9** as compared to the thickness of the material making up the remaining parts of the click item **5**. When the click item **5** is rotated as described above the resilient parts **9** will be moved against the inner part of the housing **4**, and this will cause the resilient parts **9** to be alternatingly tensed and released. Each time the resilient parts **9** are released they will produce a clicking sound, thereby generating the non-visual feedback signal.

FIG. **4** shows a threaded inner part **10** being adapted to be inserted inside a housing of an injection device according to a second embodiment of the invention. The main part of the thread **11** has a constant pitch. However, in the lower part of the thread **12** the pitch is abruptly decreased. This can be seen in the form of an axial edge **13**. Thereby a part engaging with the thread **11**, **12** will be moved abruptly relatively to the inner part **10** along an axial direction when the engaging part reaches the lower part of the thread **12**, i.e. when it reaches the axial edge **13**. This abrupt movement, and not the least the following abrupt stop when this movement stops, can be felt by the user as will be described below. Furthermore, the location of the axial edge **13** towards the end of the threaded portion **12** ensures that the felt abrupt movement indicates the end of injection of a set dose. Thereby a non-visual (tactile) feedback signal has been provided as a result of a change in the pitch of a threaded portion **11**, **12**.

FIG. **5** shows a top view of an outer part **14** being adapted to be positioned around the threaded inner part **10** of FIG. **4**. The outer part **14** is provided with two protruding parts **15** each being adapted to engage with the thread **11**, **12** of the inner part **10**.

FIG. **6** shows a cross section through the outer part **14** shown in FIG. **5** along the line A-A. During injection of a dose the inner part **10** and the outer part **14** will initially be relatively positioned in such a way that the protruding parts **15** engage with the part of the thread **11** being positioned opposite the lower part of the thread **12**. The outer part **14** is then pushed inwards, thereby allowing the protruding parts **15** to travel the threaded portion **11**. Due to the thread **11** the inner part **10** and the outer part **14** perform a relative rotational movement. When the protruding parts **15** reach

the axial edge **13** the axial velocity of the outer part **14** will increase abruptly as described above, and because the user is manually pressing the outer part **14** this abrupt movement, as well as the abrupt stop occurring when the outer part **14** abuts a stop member **16** present on the inner threaded part **10** (see FIG. **4**), will be felt by the user. Thereby a tactile feedback signal is provided. Furthermore, the outer part **14** abruptly abutting the stop member **16** may produce a sound, thereby providing an audible feedback signal in addition to the tactile feedback signal.

FIG. **7** shows part of an injection device according to a third embodiment of the invention. The Figure shows an inner part **10** and an outer part **14**. The inner part **10** and the outer part **14** are adapted to be rotated relatively to each other during injection. The outer part **14** is provided with a wedge structure **17** and the inner part **10** is provided with a spring arm **18**. During injection, in addition to the mutual rotation, the inner part **10** is moved in an axial direction indicated by the arrow. When the spring arm **18** reaches the wedge structure **17** a protruding part **19** of the spring arm **18** will engage an upper part **20** of the wedge structure **17**. This will cause the spring arm **18** to be pressed in a direction opposite to the one indicated by the arrow, thereby introducing a tension in the spring arm **18**. The tension is, thus, built up during injection. The protruding part **19** will subsequently be moved along the upper part **20** of the wedge structure **17** until it reaches the end **21** of the wedge structure **17**. The protruding part **19** will then 'fall over the edge' to the position shown in FIG. **7**, thereby releasing the tension which was previously built up in the spring arm **18**. This sudden release of the tension produces a sound due to air being moved by the spring arm **18** and/or due to the protruding part **19** hitting a stationary part of the outer part **14**. Thereby an audible feedback signal has been produced, and by positioning the wedge structure **17** in an appropriate manner, the feedback signal will indicate to the user that the set dose has been injected.

When a new dose is to be set, the protruding part **19** will pass the wedge structure **17** via a tapered part **22** on the wedge structure **17**.

FIG. **8** shows part of an injection device according to a fourth embodiment of the invention. The fourth embodiment is very similar to the third embodiment shown in FIG. **7**. FIG. **8** also shows an inner part **10** having a spring arm **18** and an outer part **14** having a wedge structure **17**, the inner part **10** and the outer part **14** being adapted to rotate in relation to each other during injection. The spring arm is provided with a protruding part **19**. During injection the inner part **10** moves relatively to the outer part **14** in a direction indicated by the arrow. When the spring arm reaches the wedge structure **17** the protruding part **19** will be caught in a track **23** and moved along this track **23**. Due to the geometry of the wedge structure **17** this movement will result in the spring arm **18** being pressed in a direction away from the outer part **14**, thereby introducing a tension in the spring arm **18**. Thus, the tension is built up during the injection. When the protruding part **19** reaches the end **21** of the wedge structure **17** it will 'fall over the edge', thereby releasing the tension which was previously built up in the spring arm **18**. This will result in an audible feedback signal being generated as described above.

When a new dose is to be set, the protruding part **19** will pass the wedge structure **17** by being lifted in an axial direction along the end **21** of the wedge structure **17**.

FIG. **9** shows part of an injection device according to a fifth embodiment of the invention. FIG. **9** shows an inner part **10** having a spring arm **18** and an outer part **14** having a wedge structure **17**. During injection the inner part **10** will move relatively to the outer part **14** in a direction indicated by the arrow. However, in this embodiment the inner part **10** and the outer part **14** do not rotate relatively to each other. Instead the injection device comprises a rotational part **24** which rotates during injection relatively to the inner part **10** and the outer part **14**. When the spring arm **18** reaches the wedge structure **17** it will be pushed in a direction away from the outer part **14** and towards the rotational part **24**. Thereby it is moved into a path of a protruding part **25** on the rotating part **24**. When the protruding part **25** is rotated to the position of the spring arm **18**, it will therefore push the spring arm **18** out of its path again, thereby introducing a tension in the spring arm **18**. When the protruding part **25** has passed the position of the spring arm **18**, the spring arm **18** will again be free to move into the path of the protruding part **25**, thereby releasing the tension which was previously built up in the spring arm **18**. Thereby an audible feedback signal is generated due to air being moved be the spring arm **18** and/or due to the spring arm **18** hitting a wall of the rotational part **24**, as described above.

FIG. **10** shows part of an injection device according to a sixth embodiment of the invention. The Figure shows an inner part **10** having a spring arm **18** and an outer part **14** having a wedge structure **17**. The inner part **10** and the outer part **14** are adapted to rotate relatively to each other during injection. Furthermore, the inner part **10** moves relatively to the outer part **14** in the direction indicated by the arrow during injection. When the spring arm **18** reaches the wedge structure **17** it will be caught by one of the wedges. Due to the geometry of the wedge structure **17** and to the continued rotational and axial movement (in the direction of the arrow) of the inner part **10**, the spring arm **18** will be pressed in a direction opposite the direction indicated by the arrow, thereby introducing a tension in the spring arm **18**. Subsequently when the spring arm **18** reaches the end **21** of the wedge it will 'fall over the edge', thereby releasing the previously built up tension. This will cause an audible feedback signal to be generated as described above.

FIG. **11** shows part of an injection device according to a seventh embodiment of the invention. The Figure shows an inner part **10** having a wedge structure **17** and an outer part **14** having a spring arm **18** and a locking mechanism (not shown in FIG. **11**). The inner part **10** and the outer part **14** are adapted to rotate in relation to each other during setting of a dose and during injection. The inner part **10** is typically a scale drum or is adapted to rotate along with a scale drum during setting of a dose and during injection. Thus, when a dose is set the inner part **10** is rotated in such a way that the wedge structure **17** presses the spring arm **18** outwards and into engagement with the locking mechanism, thereby introducing a tension in the spring arm **18**. Thus, in this embodiment the tension is introduced during setting of the dose. The locking mechanism will maintain the spring arm **18** in the tensed position during the remaining setting of the dose and during the main part of the injection.

However, when the inner part **10** is returning to the initial position a release mechanism **26** on the wedge structure **17** releases the locking mechanism, thereby releasing the tension which was previously built up in the spring arm **18**. Thereby an audible signal is generated as described above, and because the locking mechanism is released when the inner part **10** is returning to the initial position, this audible signal indicates that the set dose has been injected.

FIG. **12** shows the outer part **14** of the injection device of FIG. **11**. The outer part **14** has a locking mechanism **27** which is in a locking position, i.e. it engages the spring arm

18. Thus, in FIG. 12 the spring arm 18 is tensed. When the inner part (not shown) approaches the outer part 14 as described above, the release mechanism (not shown) will push the locking mechanism 27 downwards, and the tensed spring arm 18 will then restore its relaxed position, i.e. it will move towards the centre of the outer part 14. Thereby the tension built up in the spring arm 18 is suddenly released.

FIG. 13 shows part of an injection device 1 comprising a scale drum 28 and a spring arm member 29 positioned at the proximal end of the injection device 1. The spring arm member 29 is provided with a spring arm 18 which may be deflected in a proximal direction, i.e. away from the scale drum 28.

During injection of a set dose, the scale drum 28 performs a rotational movement as well as an axial movement towards the spring arm member 29. This movement will eventually cause an upper portion 30 of the scale drum to abut a protrusion 31 of the spring arm 18. As the scale drum 28 continues the rotational and axial movement, the spring arm 18 is deflected in a proximal direction, thereby causing a tension to be built up in the spring arm 18.

FIG. 13 shows a situation where the upper portion 30 of the scale drum 29 and the protrusion 31 of the spring arm 18 abut, and a tension has started to build up in the spring arm 18.

FIG. 14 shows the injection device of FIG. 13. In FIG. 14 a tension has been built up in the spring arm 18 as described above. The protrusion 31 of the spring arm 18 is positioned very near a recess 32 formed in the scale drum 28. Thus, further rotation of the scale drum 28 will cause the protrusion 31 to 'fall over the edge' into the recess 32. Thereby the tension which has previously been built up in the spring arm 18 is released, and an audible feedback signal is generated by vibrating air and/or by the protrusion 31 hitting a lower edge of the recess 32.

This situation is illustrated in FIG. 15, showing the injection device 1 of FIGS. 13 and 14 in a situation where the tension previously built up in the spring arm 18 has been released as described above.

When a new dose is to be set, the feedback mechanism needs to be reset in order to be able to provide an audible feedback signal when the subsequent dose has been injected. This is done by leading the protrusion 31 of the spring arm 18 via a path or track (not visible in FIGS. 13-15) positioned behind the upper portion 30 of the scale drum 28 during the next dose setting. When the set dose is sufficiently large, the scale drum 28 and the spring arm member 29 will be sufficiently spaced apart to allow the protrusion 31 to be positioned above the upper part 30 of the scale drum 28. Thereby the feedback mechanism has been reset, i.e. the spring arm 18 is once again ready for being deflected in a proximal direction as described above.

The injection device shown in FIGS. 13-15 is particularly suitable for having a dose delivering mechanism which is adapted to be operated by means of a mechanically biased mechanism, such as a spring.

Some preferred embodiments have been shown in the foregoing, but it should be stressed that the invention is not limited to these, but may be embodied in other ways within the subject matter defined in the following claims.

The invention claimed is:

1. An injection device comprising:

a housing having a longitudinal axis,

a dose setting member being operable to set a desired dose to be injected,

a piston rod being adapted to cooperate with a piston so as to cause a set dose to be injected from an ampoule, and

a dose delivering mechanism being adapted to operate the piston rod in such a way that a set dose is injected by a mechanically biased mechanism comprising at least one spring, the dose delivering mechanism further being adapted to provide a tactile feedback signal to a user only at the end of injection of a set dose,

wherein first and second parts of the injection device are adapted to perform a relative rotational movement around a longitudinal axis with respect to each other during injection of a dose, and wherein said relative rotational movement causes at least two parts of the injection device to abut or engage, said abutment or engagement causing the tactile feedback signal to be generated.

2. An injection device according to claim 1, wherein the tactile feedback signal comprises an audible signal.

3. An injection device according to claim 1, wherein the tactile feedback signal comprises a tactile signal.

4. An injection device according to claim 1, wherein the abutment or engagement is caused by a change in a rotational velocity of at least one part of the dose delivering mechanism.

5. An injection device according to claim 4, further comprising a ratchet operating the piston rod and having a threaded portion being adapted to engage with a part of the dose delivering mechanism, and wherein the change in a rotational velocity is generated by a change in the pitch of the threaded portion of the ratchet, said change in the pitch in return causing a change in a translational velocity of said part of the dose delivering mechanism, said change in translational velocity causing at least two parts of the injection device to abut, thereby causing the tactile feedback signal to be generated.

6. An injection device according to claim 4, wherein the dose delivering mechanism comprises a first dose part and a second dose part, the first dose part being adapted to rotate relatively to the housing during injection of a dose and the first dose part comprising structure for engaging the second dose part at the end of injection of a set dose, thereby causing the second dose part to rotate along with the first dose part, and wherein the tactile feedback signal is generated by the resulting rotational movement of the second dose part.

7. An injection device according to claim 6, wherein the second dose part is positioned between the first dose part and the housing.

8. An injection device according to claim 1, wherein the tactile feedback signal is generated as a result of an abutment between two parts of the dose delivering mechanism performing a relative rotational movement.

9. An injection device according to claim 8, wherein the tactile feedback signal is generated by a tensed part whereby the tactile feedback signal is provided by releasing a tension which has previously been introduced in a part of the injection device, the release of the tension being caused by the abutment between the two parts.

10. An injection device according to claim 9, wherein the tensed part comprises a spring structure.

11. An injection device according to claim 9, wherein the tension is introduced during dose setting.

12. An injection device according to claim 9, wherein the tension is introduced during injection of a dose.

* * * * *

EXHIBIT K

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(54) **SYRINGE DEVICE WITH A DOSE LIMITING MECHANISM AND AN ADDITIONAL SAFETY MECHANISM**

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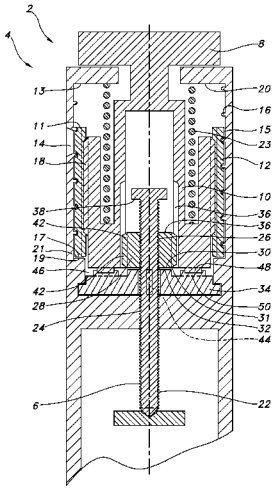
(57) **ABSTRACT**

A syringe device for ejecting a dose of a medicament, the syringe device comprising: a dose limiting mechanism arranged to interact with a dose ejecting mechanism to prevent ejection of a dose exceeding a set dose, and a safety mechanism, which is arranged such with respect to the dose ejecting mechanism that, if the dose limiting mechanism fails, the safety mechanism prevents ejection of a dose exceeding the set dose.

8 Claims, 1 Drawing Sheet



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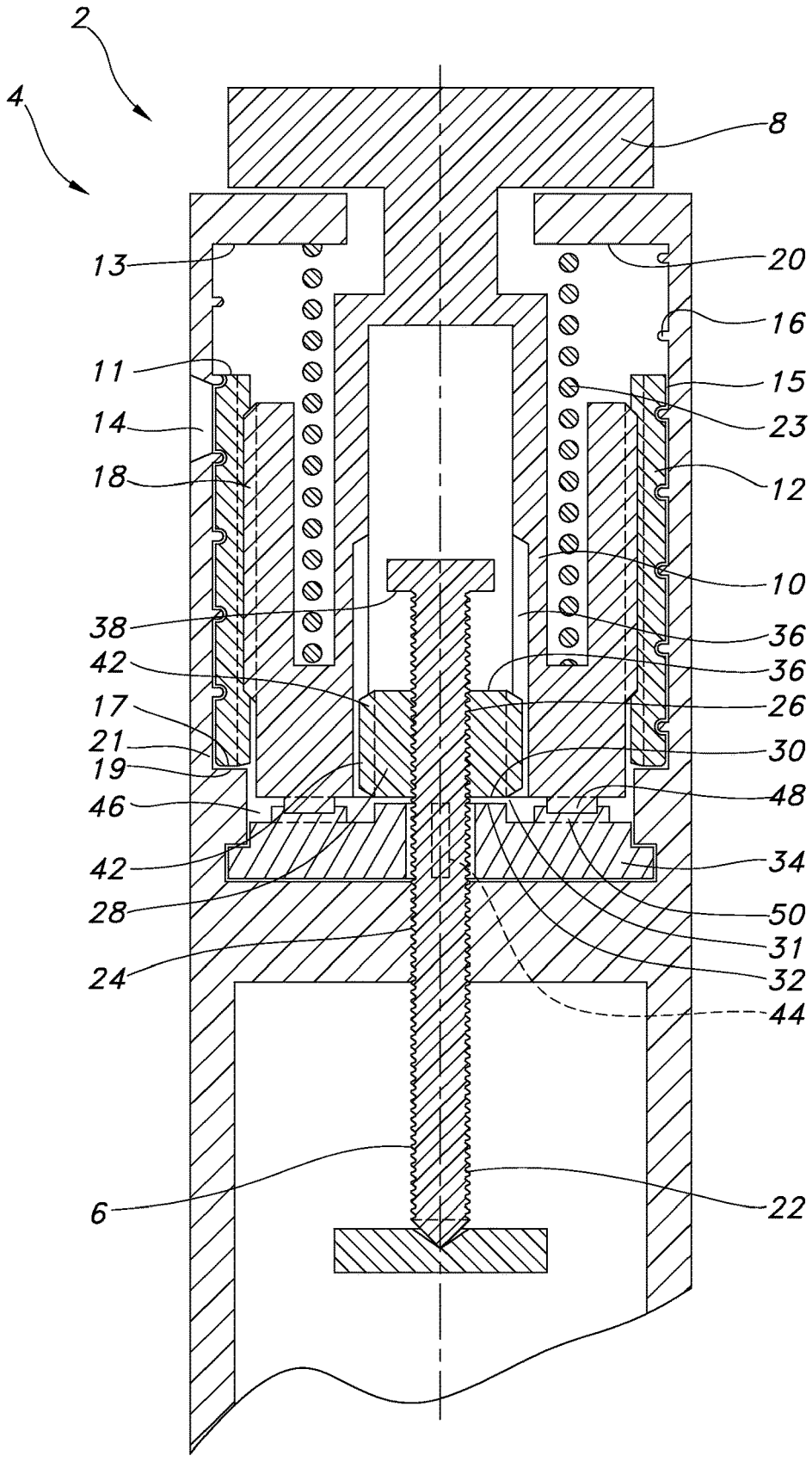
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SYRINGE DEVICE WITH A DOSE LIMITING MECHANISM AND AN ADDITIONAL SAFETY MECHANISM

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a 35 U.S.C. § 371 national stage application of International Patent Application PCT/EP2006/007006 (published as WO 2007/017053), filed Jul. 17, 2006, which claimed priority of European Patent Application 05016286.6, filed Jul. 27, 2005; this application further claims priority under 35 U.S.C. § 119 of U.S. Provisional Application 60/708,211, filed Aug. 15, 2005.

FIELD OF THE INVENTION

The present invention relates to a syringe device comprising a mechanism for preventing ejection of a dose exceeding a set dose. In particular the present invention relates to a syringe device comprising two independent mechanisms for preventing ejection of a dose exceeding a set dose.

BACKGROUND OF THE INVENTION

When drugs are to be injected into the human body, it may have serious or even lethal consequences if the injected dose exceeds the set dose. Accordingly, it is important that the syringe devices comprises means for limiting ejection to the set dose.

It is an object of the present invention to provide a syringe device comprising means for prevention ejection of a dose exceeding the set dose. Furthermore, as such means may fail, it is an object of the present invention to provide a syringe device comprising a safety mechanism adapted to prevent ejection of a dose exceeding the set dose if the means for preventing fails.

SUMMARY OF THE INVENTION

The present invention relates to a syringe device for ejecting a dose of a medicament, the syringe device comprising:

- a housing,
- a dose ejecting mechanism comprising:
  - a dose setting member being rotatable in relation to the housing so as to set a dose to be ejected,
  - a piston rod arranged with respect to the housing such that translational movement of the piston rod in a distal direction causes the dose to be ejected,
  - means for transforming translational movement of the dose setting member into translational movement of the piston rod,
- a dose limiting mechanism arranged to interact with the dose ejecting mechanism to prevent ejection of a dose exceeding the set dose, and
- a safety mechanism, which is arranged such with respect to the dose ejecting mechanism that, if the dose limiting mechanism fails, the safety mechanism prevents ejection of a dose exceeding the set dose.

An advantage of the present invention is that if a dose limiting mechanism fails to limit the ejected dose, the security mechanism is activated, and, thus, provides an extra safety for the patient.

In one embodiment the dose limiting mechanism and the safety mechanism are two independent mechanisms working independently from each other.

In one embodiment the two mechanisms are adapted to simultaneously prevent ejection of a dose exceeding the set dose. In another embodiment the safety mechanism is only activated if the dose limiting mechanism fails to prevent ejection of a dose exceeding the set dose. In one embodiment the two mechanisms are arranged such that even if the dose limiting mechanism fails, the safety mechanism is activated instantaneously such that the ejected dose does not exceed the set dose. In another embodiment the ejected dose is insignificantly larger than the set dose, if the dose limiting mechanism fails and the safety mechanism is activated. By insignificantly larger is meant that the change in dose is too small to have serious or fatal consequences.

The housing may define a passage for the piston rod, the passage may have a threaded inner surface for engagement with a threaded outer surface of the piston rod, the piston rod may be arranged with respect to the housing such that rotation of the piston rod relative to the housing causes the piston rod to be displaced translationally relative to the housing.

In one embodiment at least one of the dose limiting mechanism and the safety mechanism is adapted to limit relative rotational movement between the piston rod and the housing, to a rotation corresponding to ejection of the set dose. This may be the case, when the piston rod comprises a threaded outer surface adapted to engage a threaded inner surface of the housing. Accordingly, rotational locking of the piston rod (relative to the housing) results in a translational locking of the piston rod relative to the housing.

The dose limiting mechanism may comprise at least one first stopping surface adapted to engage at least one corresponding second stopping surface of the housing. Furthermore, rotation of the dose setting member during dose setting may cause the first stopping surface to move away from the second stopping surface and rotation during dose ejection may cause the first and the second surface(s) to move towards each other. Furthermore, ejection of a dose may be prevented when the first stopping surface abut the second stopping surface. The dose setting member may comprise the at least one first stopping surface. Alternatively, or as a supplement, the dose setting member may be coupled to a cylinder comprising a first stopping surface, and said cylinder may be adapted to indicate the set dose. The first and second stopping surfaces may be substantially plane surfaces which may extend in a direction parallel with the axial direction of the syringe device. Alternatively, the stopping surfaces may extend in a plane transverse to the axial direction, such as a plane orthogonal to the axial direction.

In one embodiment the safety mechanism comprises: a limiter defining a passage for the piston rod, the passage of the limiter defining a threaded inner surface for engagement with the threaded outer surface of the piston rod, and a driver defining a passage for the limiter, the driver being rotationally retained in relation to the limiter, the driver being coupled to the dose setting member such that rotation of the dose setting member during dose setting causes the driver to rotate, wherein relative rotation between the drive and the piston rod during dose setting causes the limiter to move away from a stopping position wherein the limiter prevents ejection of a dose.

In one embodiment the syringe device is adapted to prevent setting of a dose which exceeds the amount of a medicament in a reservoir of the syringe device. In such

embodiments, the piston rod may comprise an end-of-dose stopping surface adapted engage a corresponding surface of the limiter, when the set dose corresponds to the amount of the medicament in the reservoir of the device. Accordingly, in such embodiments the limiter serves two functions, a first function being prevention of setting of a dose exceeding the amount of the medicament left in the reservoir and a second function being a security function adapted to prevent ejection of a dose exceeding the set dose.

Moreover, the syringe device may comprise an ejection assisting system for providing an ejection force for assisting an operator of the device in forcing the piston in said distal direction so as to eject the set dose. The ejection assisting system may be adapted to force the piston in the distal direction so as to eject the dose, without the aid of the user, when the user has initiated the ejection.

The ejection assisting system may comprise a spring, such as a torsional spring which is arranged to rotate the driver relative to the housing. The spring may be pre-strained when limiter is in the stopping position. Especially when the spring is pre-strained, the redundant security system of the present invention is advantageous, as accidental un-straining of the pre-strained spring, may cause the piston rod to rotate (and thus move translationally) corresponding to a lethal dose, such as 100 IU of insulin.

DESCRIPTION OF THE DRAWINGS

The invention will now be described in further detail with reference to FIG. **1**, which discloses a syringe device according to the present invention.

FIG. **1** shows a syringe device **2** comprising a housing **4** and a piston rod **6**. The syringe device **2** also comprises a dose setting member **8** and a driver **10**, which in the FIGURE are combined into one single unit. The syringe device further comprises a scale drum **12** for indicating a set dose through a window **14**. The scale drum **12** has a threaded outer surface **15** adapted to engage a corresponding threaded inner surface **16** of the housing. The scale drum **12** is rotationally retained relative to the driver **10** through a grove-tongue engagement **18**. The drum scale **12** comprises a first stopping surface **17** adapted to engage a second stopping surface **19** of the housing. The first stopping surface **17** and the second stopping surface **19** constitutes the dose limiting mechanism **21**. The first stopping surface is moved away from the second stopping surface **19** during dose setting and towards each other during dose ejecting. When the two surfaces abut each other, the device is prevented from ejecting the medicament.

FIG. **1** further shows an example of a dose setting member **8** rotatable and longitudinally fixed in relation to the housing **4** so as to set a dose to be injected.

The syringe device comprises an ejection assisting system in the form of a pre-strained torsional spring **23** extending between the driver **10** and a proximal part **20** of the housing. Accordingly, when the dose setting member **8** is rotated to set a dose, the spring is strained even further.

The piston rod **6** comprises a threaded outer surface **22** adapted to engage a corresponding threaded inner surface of the housing **24** and accordingly rotation of the piston rod relative to the housing causes the piston rod to move translationally in relation to the housing. The threaded outer surface **22** of the piston rod also engages a threaded inner surface **26** of a limiter **28**, which in FIG. **1** is positioned in a stopping position wherein a bottom surface **30** of the limiter engages an upper surface **32** of a piston rod guide **34**. The bottom surface **30** and the upper surface **32** constitute the safety mechanism **31**. An air gap may be provided between the bottom surface **30** and the upper surface **32** which allows the limiter and the piston rod to rotate an angel corresponding an insignificant increase in the injected dose e.g. 3 IU of insulin, if the dose limiting mechanism **21** fails during dose injection.

Moreover, an upper end-of-content surface **36** of the limiter **28** is adapted to engage a lower end-of-content surface **38** of a T-shaped end part **40** of the piston rod. The end-of-content surfaces are adapted to engage, when the set dose corresponds to the amount of a medicament remaining in a reservoir (not shown) of the device. Accordingly, the engagement of the end-of-content surfaces prevents setting of a dose exceeding the amount of a medicament remaining in the reservoir. It will be appreciated that the distance between the end-of-content surfaces thus corresponds to the amount of the medicament remaining in the reservoir.

Moreover, an upper surface **11** of the drum **12** may be adapted to engage a lower surface **13** of the housing, when the maximum dose is set. The maximum dose is the largest dose which may be set for each ejection (provided that the syringe device comprises the required amount of medicament). The maximum dose does not correspond to the end-of-content dose which relates the remaining amount of a medicament in the device. Accordingly, as long as the remaining amount of medicament in the device is larger than the maximum dose, the end-of-content surfaces will not abut each other during dose setting, whereas when the remaining amount of medicament in the device is lower than the maximum dose, the maximum dose surfaces will not abut each other during dose setting, as the end-of-content surfaces prevents further rotation.

The limiter **28** and the driver **10** are locked for relative rotation by means of grove-tongue engagement **42**. Thus, when the piston rod is locked for rotation relative to the housing, a relative rotation between the driver **8** and the piston rod **6** causes the limiter to move away from the stopping position and towards the t-shaped end part **40** (i.e. upwards in the FIGURE). The piston rod is locked for rotation relative to the housing when the piston rod guide **34** is locked for rotation relative to the housing (not shown), as the piston rod guide **34** and the piston rod are locked for relative rotation due to the grove-tongue engagement **44**.

The driver **12** and the piston rod guide **34** are interconnected by a two-way ratchet mechanism **46** comprising at least one first retaining member **48** defined by the driver **12** and at least one second retaining member **50** defined by the piston rod guide **34**. The two-way ratchet mechanism is adapted to allow relative rotational movement between the driver **12** and the piston rod guide **34** during dose setting and to ensure that rotational movement of the driver during dose ejection is transferred to the piston rod guide **34**.

The use of the device is as follows. Initially the piston rod guide is locked for rotation relative to the housing. Then the dose setting member is rotated, which causes the driver and the drum scale to rotate and the pre-strained spring to be strained even further. At the same time the limiter moves towards the T-shaped end part. If the user tries to set a dose exceeding the amount of medicament in the device, the limiter abuts the T-shaped end part whereby an even larger dose cannot be set. The dose is ejected by removing the rotational lock between the piston rod guide **34** and the housing whereby the strained spring forces the driver to rotate. The rotating driver forces the piston rod guide to rotate which again forces the piston rod to rotate. Due to the grove-tongue engagement **44** and the threaded interconnection between the piston rod and the housing, the rotating

piston rod is forced to move forward and thus the medicament is expelled from the device.

The invention claimed is:

1. A syringe device for ejecting a dose of a medicament, the syringe device comprising:

a housing;

a dose setting member rotatable and longitudinally fixed in relation to the housing so as to set a dose to be ejected,

a dose ejecting mechanism comprising:

a piston rod arranged with respect to the housing such that translational movement of the piston rod in a distal direction causes the set dose to be ejected,

structure for transforming rotational movement of the dose setting member into translational movement of the piston rod during ejection of the set dose in the form of an ejection assisting system comprising a pre-strained torsional spring arranged to rotate a driver relative to the housing, the pre-strained torsional spring providing an ejection force forcing the piston rod in the distal direction so as to eject the set dose without the aid of a user, when the user has initiated the ejection of the set dose;

a dose limiting mechanism operably connected with the dose ejecting mechanism to prevent ejection of a dose exceeding the set dose; and

a safety mechanism structure operably connected to the dose ejecting mechanism such that if the dose limiting mechanism fails, the safety mechanism structure prevents ejection of a dose exceeding the set dose.

2. A syringe device according to claim **1**, wherein the housing defines a passage for the piston rod, the passage having a threaded inner surface for engagement with a threaded outer surface of the piston rod, the piston rod being arranged with respect to the housing such that rotation of the piston rod relative to the housing causes the piston rod to be displaced translationally relative to the housing.

3. A syringe device according to claim **1**, wherein at least one of the dose limiting mechanism and the safety mechanism structure is adapted to limit relative rotational movement between the piston rod and the housing, to a rotation corresponding to ejection of the set dose.

4. A syringe device according to claim **1**, wherein the dose limiting mechanism comprises a first stopping surface adapted to engage a corresponding second stopping surface of the housing, and wherein rotation of the dose setting member during dose setting causes the first stopping surface to move away from the second stopping surface and wherein ejection of a dose is prevented when the first stopping surface abuts the second stopping surface.

5. A syringe device according to claim **4**, wherein the dose setting member comprises the first stopping surface.

6. A syringe device according to claim **4**, wherein the dose setting member is coupled to a cylinder comprising the first stopping surface, said cylinder being adapted to indicate the set dose.

7. A syringe device according to claim **1**, wherein the safety mechanism structure comprises:

a limiter defining a passage for the piston rod, the passage of the limiter defining a threaded inner surface for engagement with a threaded outer surface of the piston rod; and

the driver defining a passage for the limiter, the driver being rotationally retained in relation to the limiter, the driver being coupled to the dose setting member such that rotation of the dose setting member during dose setting causes the driver to rotate;

wherein relative rotation between the driver and the piston rod during dose setting causes the limiter to move away from a stopping position wherein the limiter prevents ejection of a dose exceeding the set dose.

8. A syringe device according to claim **1**, wherein the torsional spring is prestrained when the dose limiting mechanism is in a stopping position.

* * * * *

EXHIBIT L

US010357616B2

(12) **United States Patent**
Moller et al.

(10) **Patent No.: US 10,357,616 B2**
(45) **Date of Patent: Jul. 23, 2019**

(54) **INJECTION DEVICE WITH AN END OF DOSE FEEDBACK MECHANISM**

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(73) Assignee: **Novo Nordisk A/S**, Bagsvaerd (DK)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **15/815,976**

(22) Filed: **Nov. 17, 2017**

(65) **Prior Publication Data**

US 2018/0071459 A1 Mar. 15, 2018

Related U.S. Application Data

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(30) **Foreign Application Priority Data**

Jan. 25, 2005 (EP) 05075187

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A61M 5/20 (2006.01)
A61M 5/24 (2006.01)
A61M 5/315 (2006.01)

(52) **U.S. Cl.**
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(Continued)

(58) **Field of Classification Search**
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(Continued)

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Primary Examiner — Lauren P Farrar
(74) *Attorney, Agent, or Firm* — Wesley Nicolas

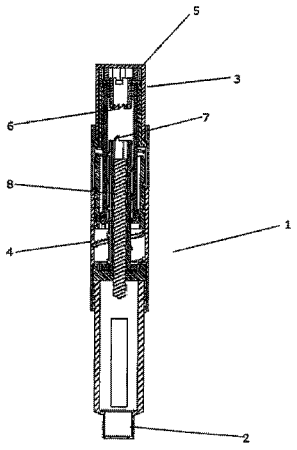
(57) **ABSTRACT**

An injection device with a dose delivering mechanism being adapted to provide a non-visual, e.g. audible and/or tactile, feedback signal when a set dose has been at least substantially injected. A first and a second part of the injection device are adapted to perform a relative rotational movement with respect to each other. The relative rotational movement causes at least two parts of the injection device to abut or engage, and this abutment or engagement causes the non-visual feedback signal to be generated. A very distinct and precise feedback is provided as compared to prior art axial solutions because the generation of the feedback signal is initiated by the relative rotational movement.

Feedback signal may be generated by a change in a rotational velocity of at least one part, e.g. by changing the pitch of a threaded portion or by engaging a non-rotating part and a rotating part, thereby causing the non-rotating part to start rotating. May alternatively be generated by building up and releasing a tension.

The injection device is suitable for injecting insulin.

9 Claims, 14 Drawing Sheets



Related U.S. Application Data

continuation of application No. 11/813,389, filed as application No. PCT/EP2006/000486 on Jan. 20, 2006, now Pat. No. 9,457,154.

(60) Provisional application No. 60/647,491, filed on Jan. 27, 2005.

(52) **U.S. Cl.**
CPC *A61M 5/31535* (2013.01); *A61M 5/31551* (2013.01); *A61M 5/31561* (2013.01); *A61M 5/31585* (2013.01); *A61M 2205/581* (2013.01); *A61M 2205/582* (2013.01)

(58) **Field of Classification Search**
CPC A61M 5/31551; A61M 5/31561; A61M 5/31585; A61M 2205/581; A61M 2205/582
See application file for complete search history.

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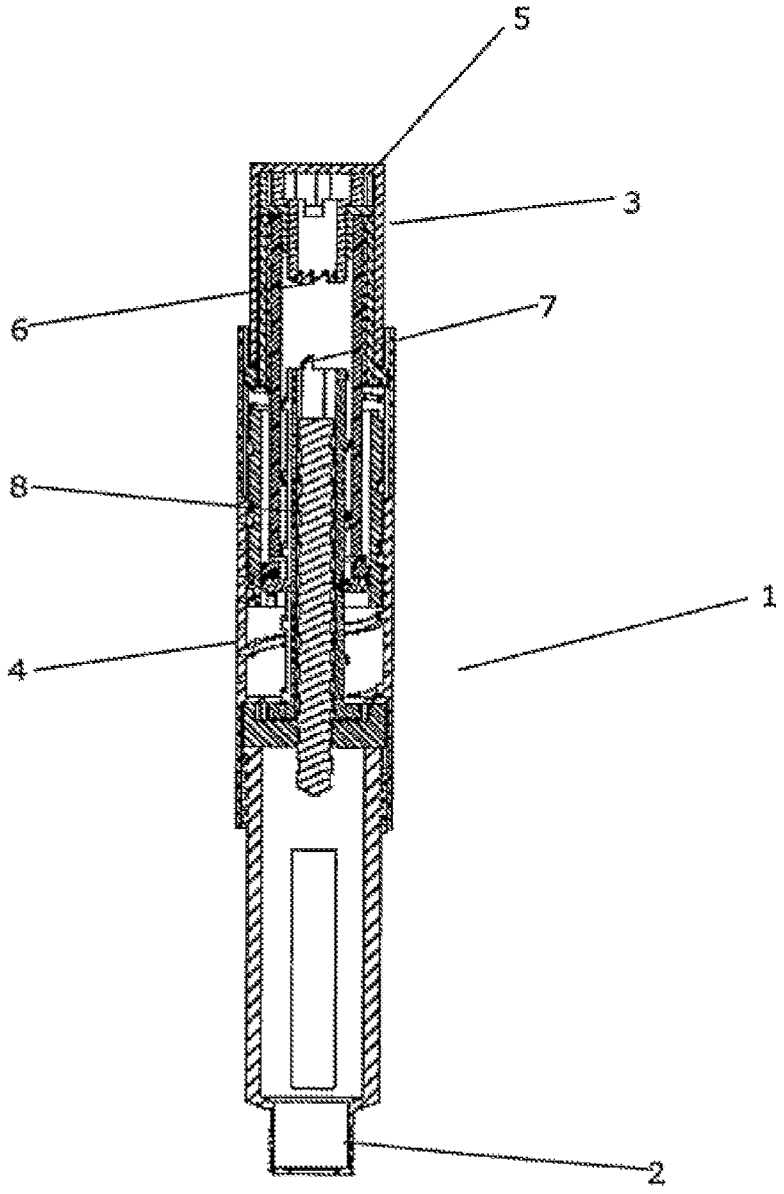

FIG. 1

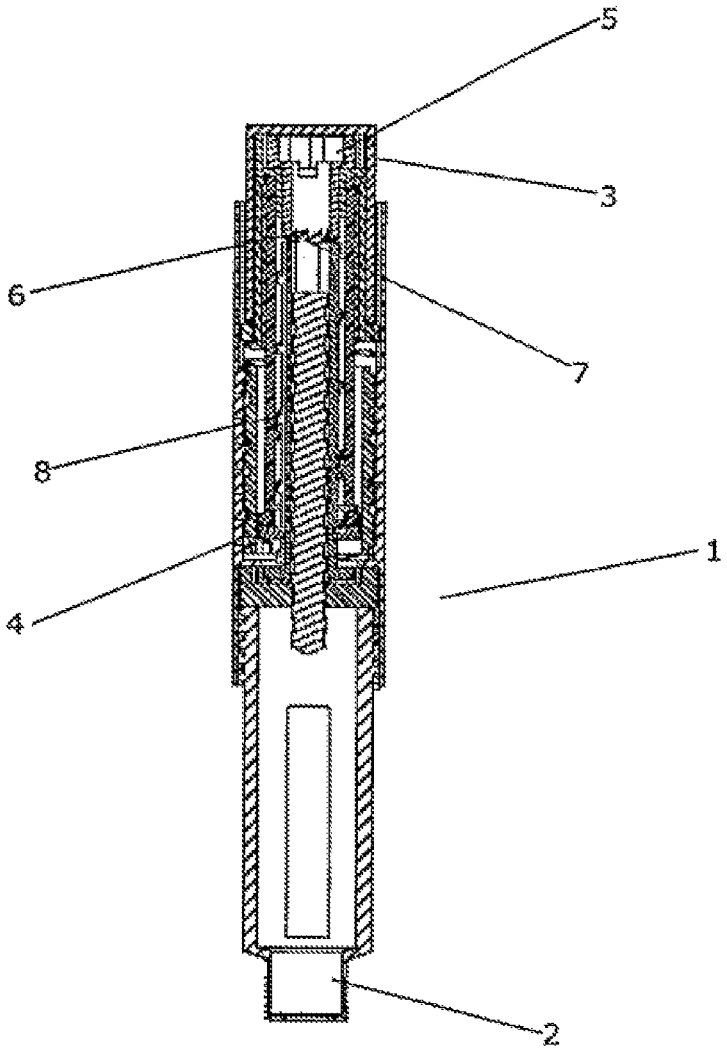

FIG. 2

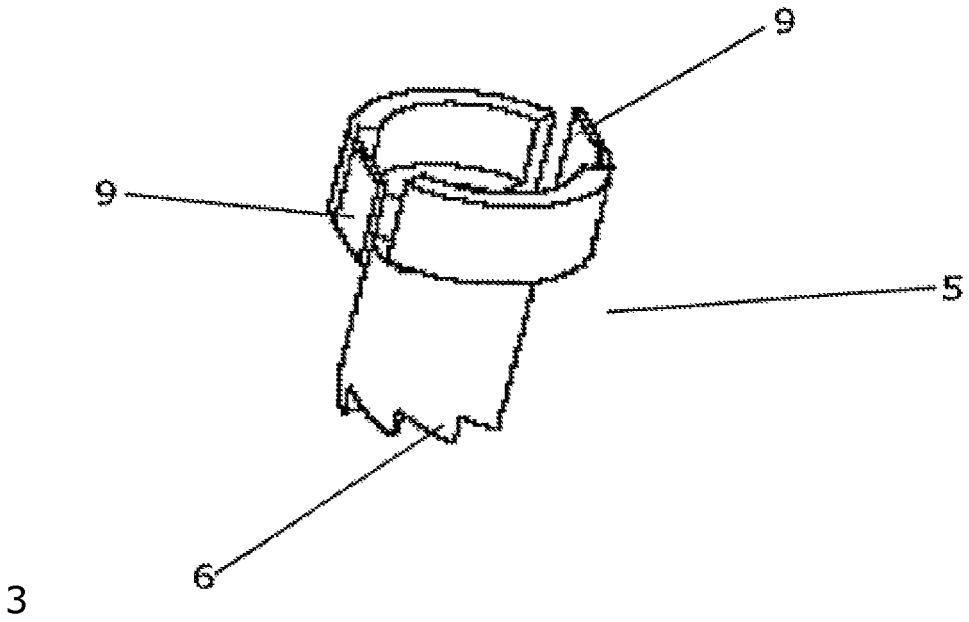

FIG. 3

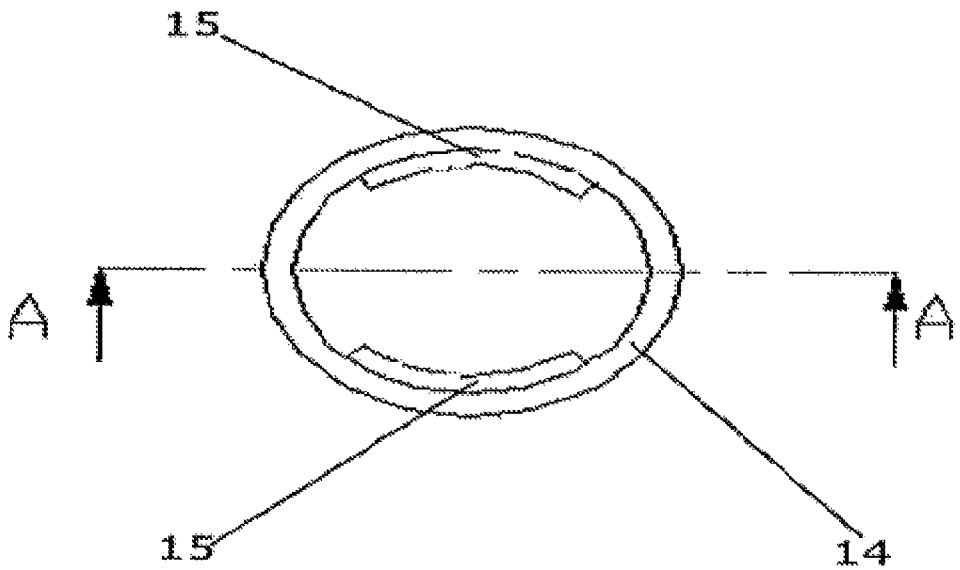

FIG. 5

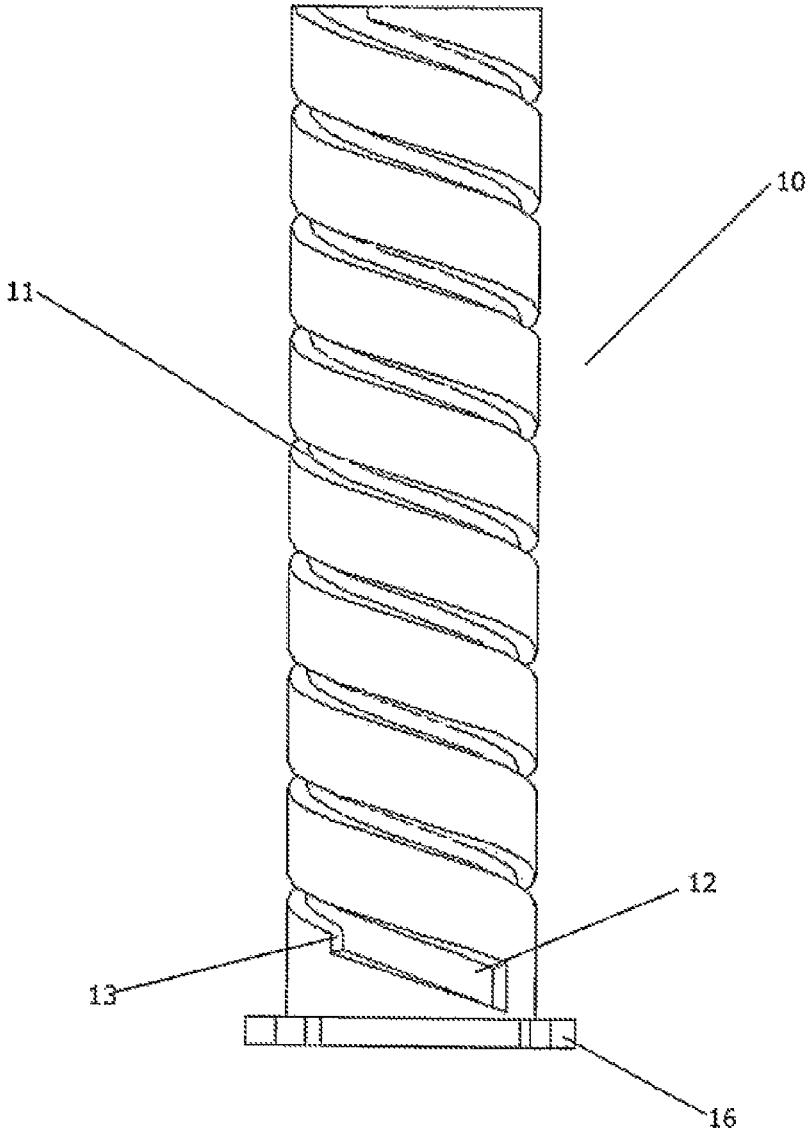

FIG. 4

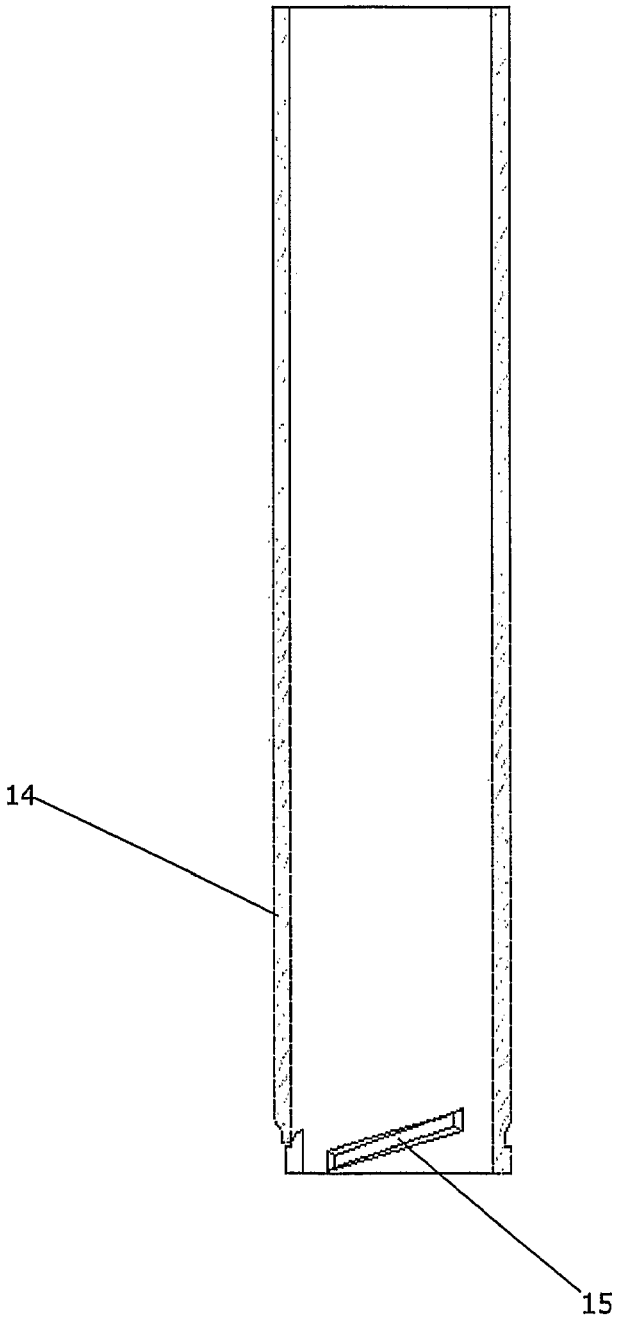

FIG. 6

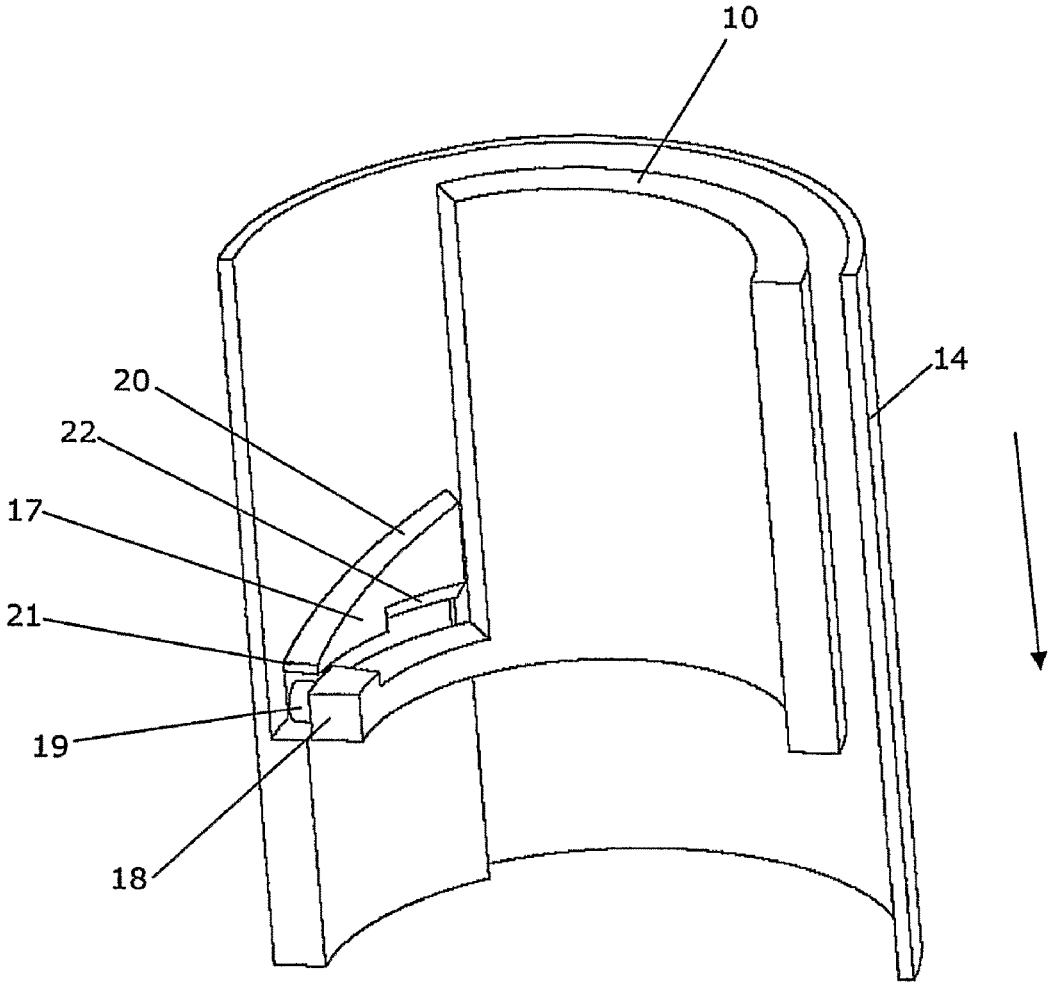

FIG. 7

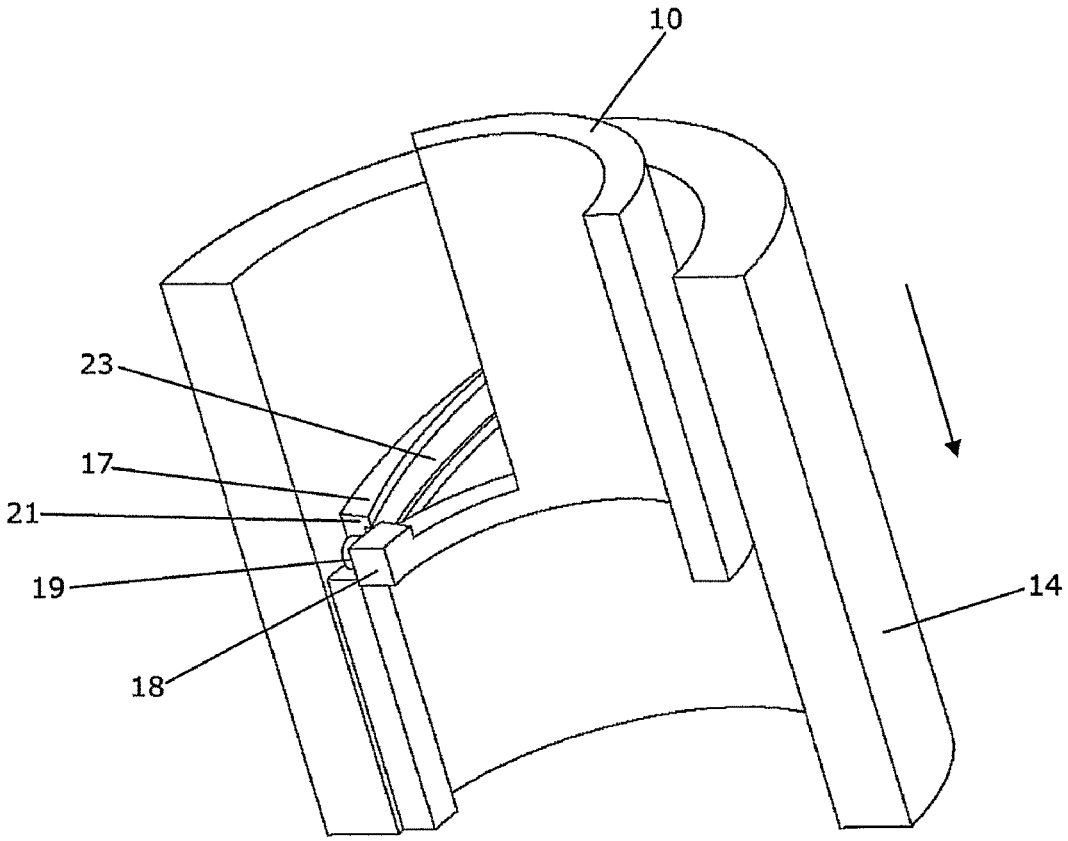

FIG. 8

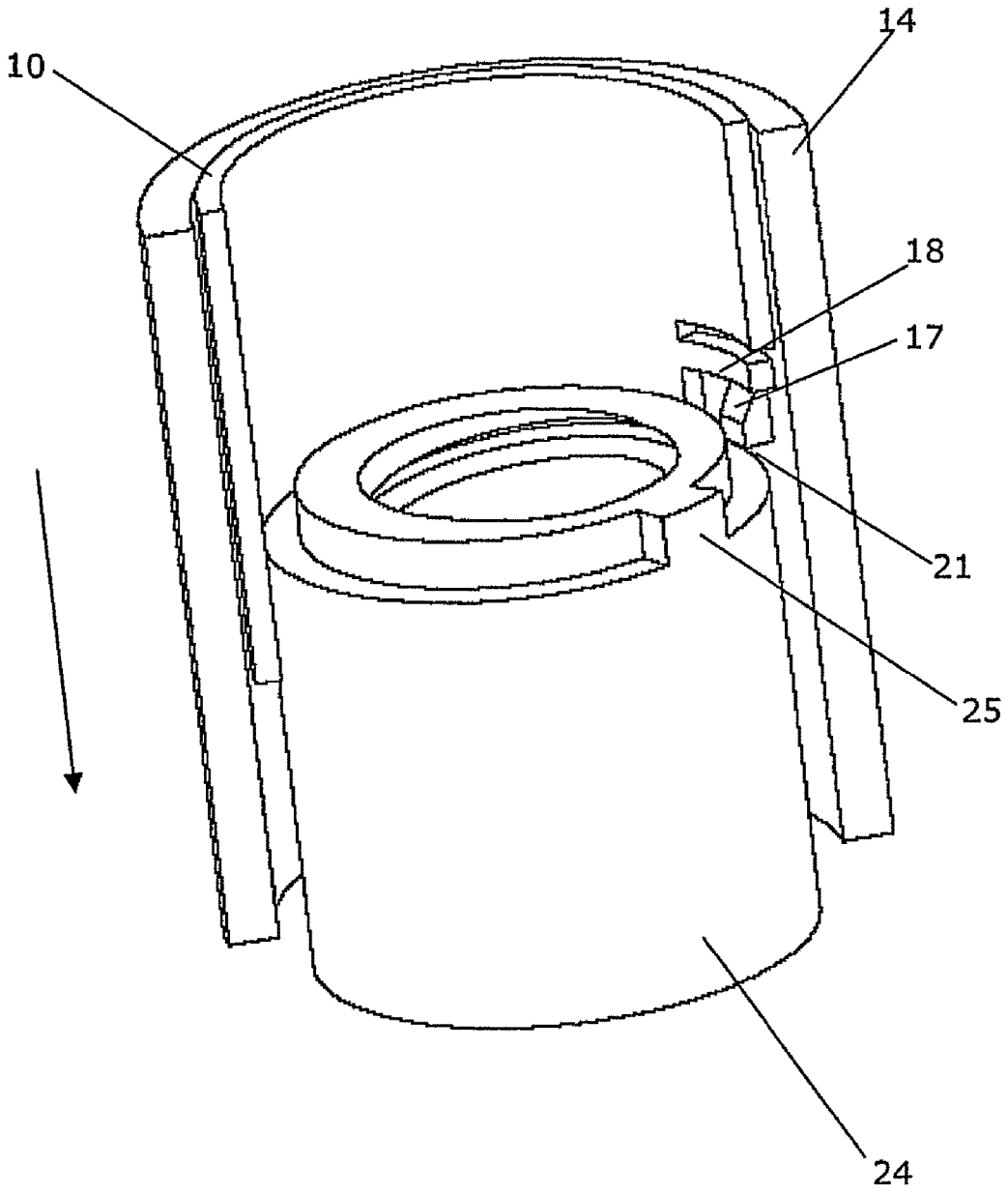

FIG. 9

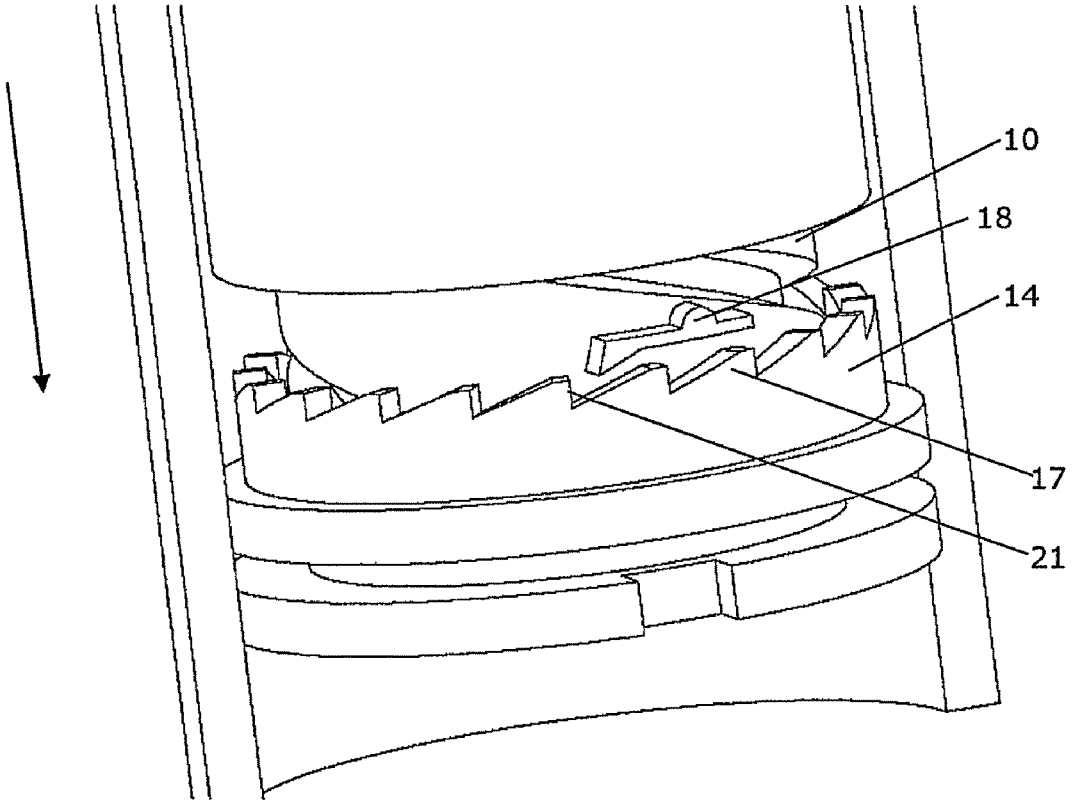

FIG. 10

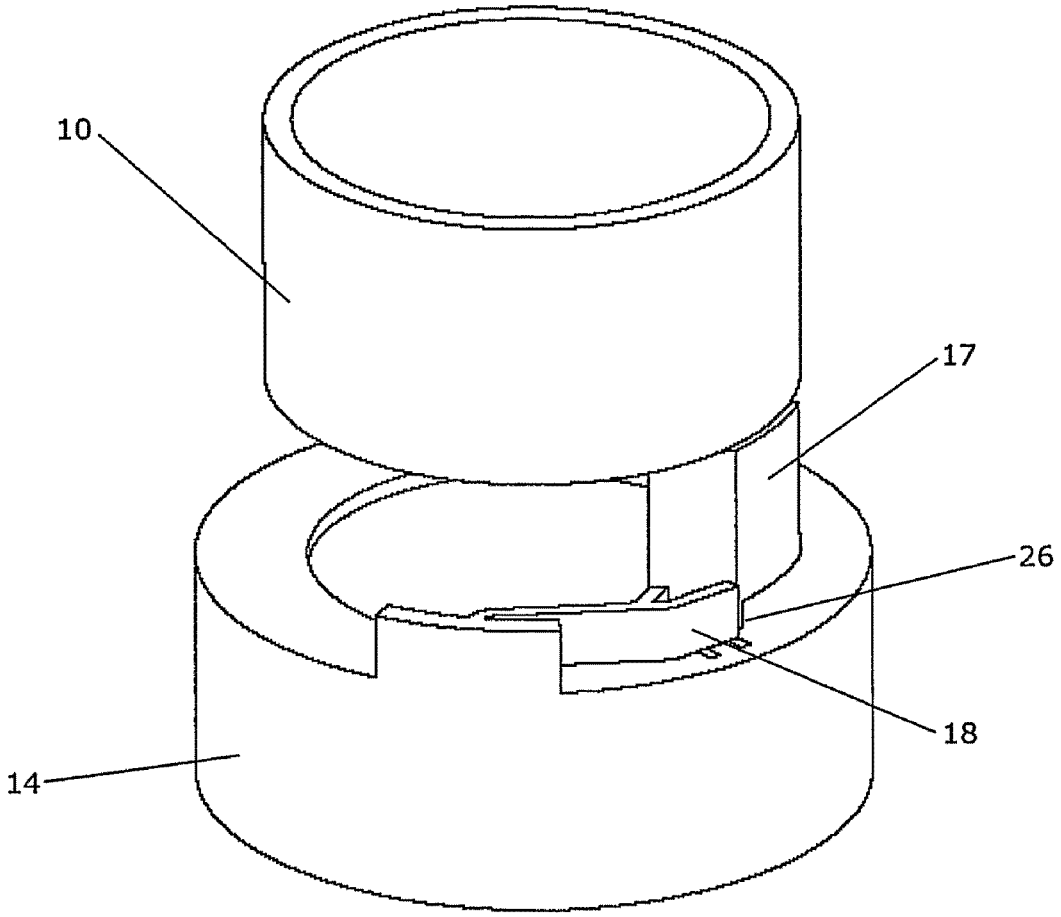

FIG. 11

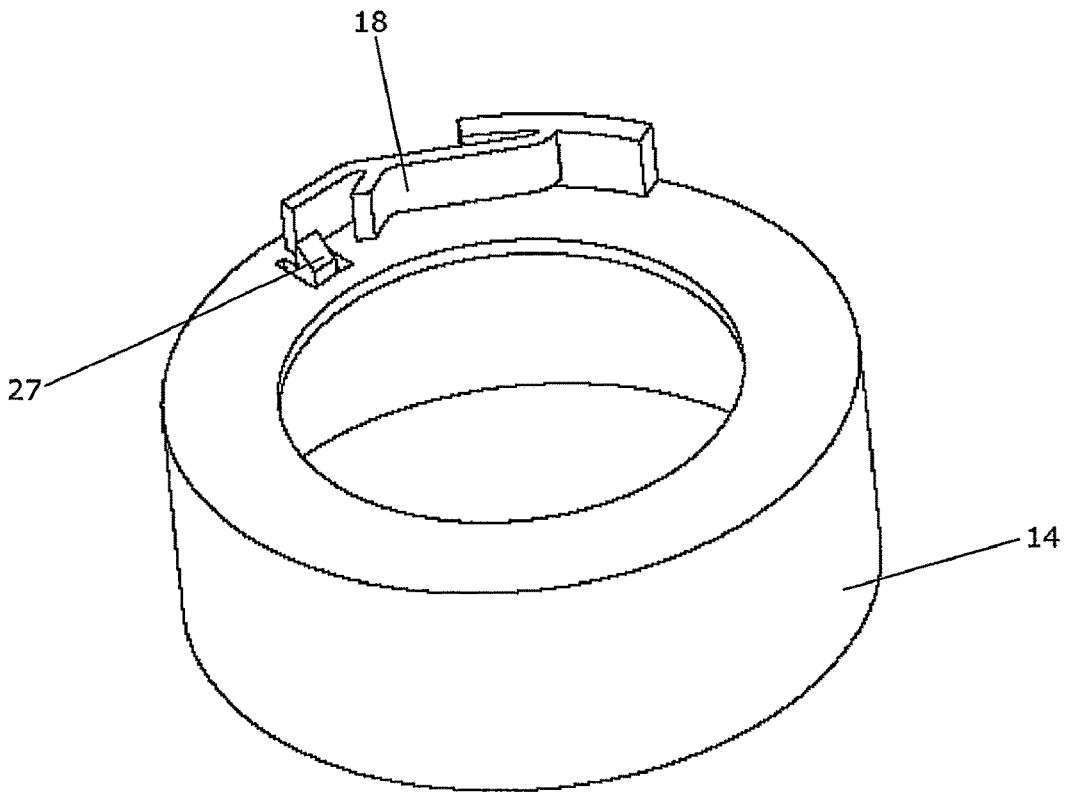

FIG. 12

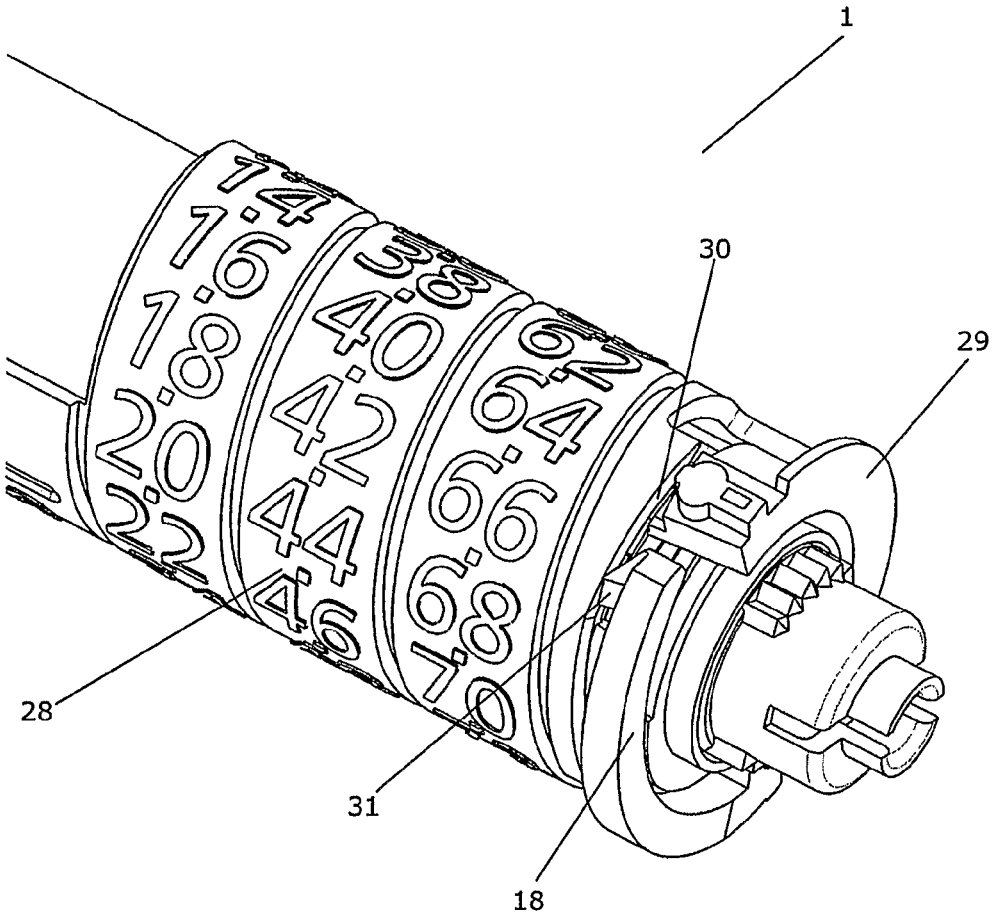

FIG. 13

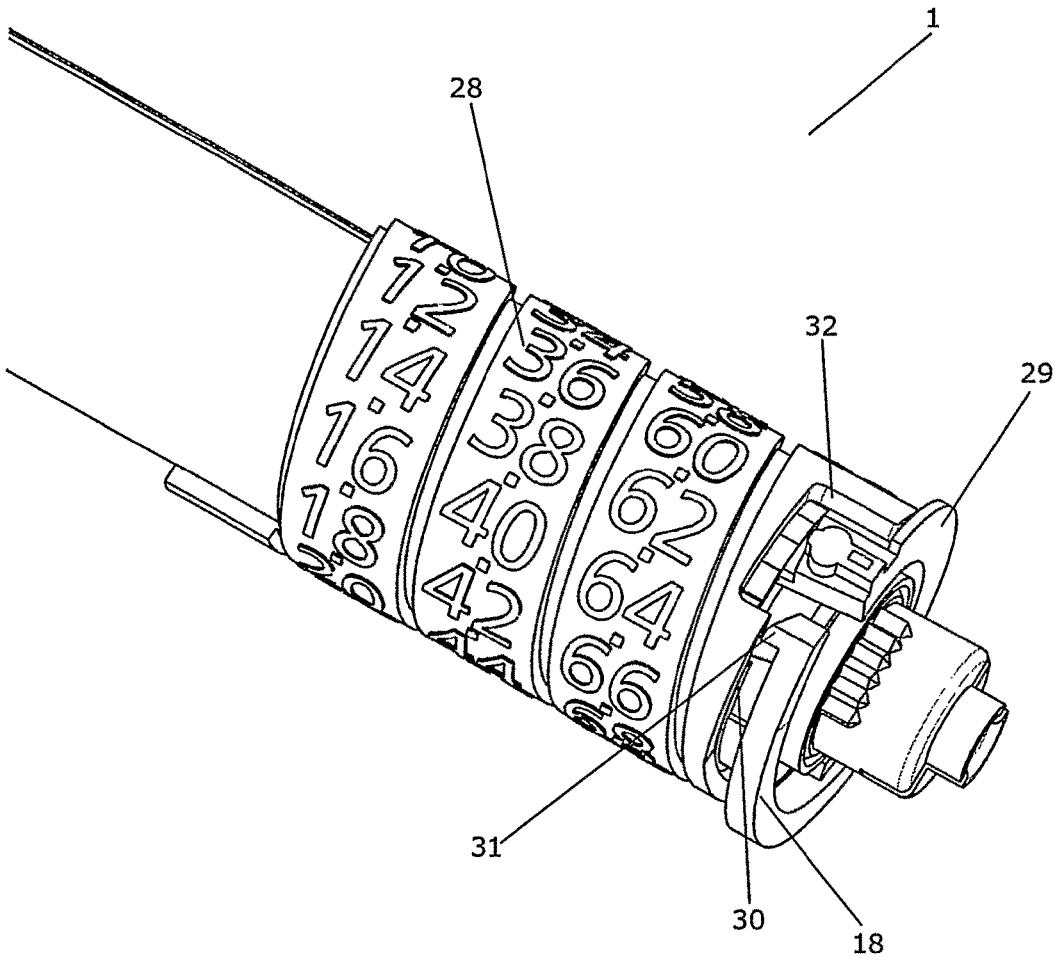

FIG. 14

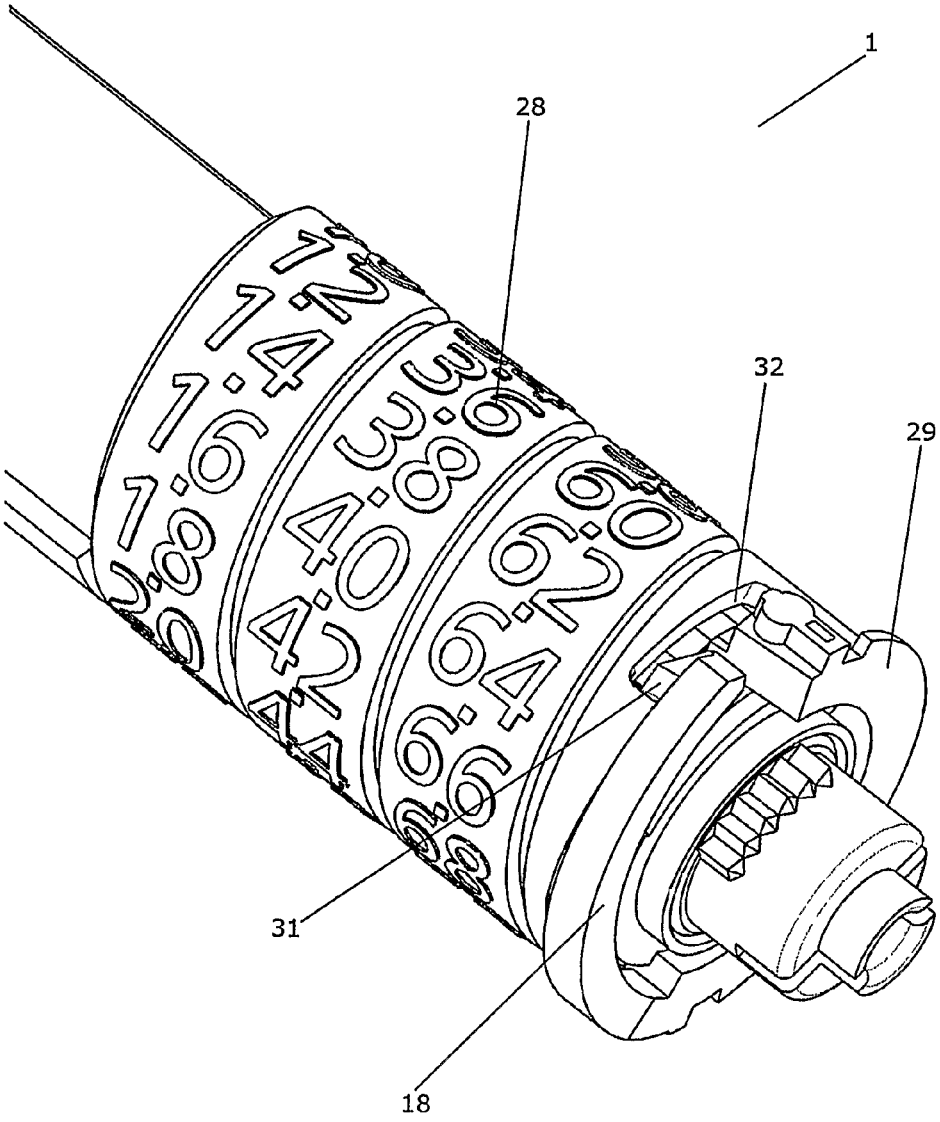

FIG. 15

INJECTION DEVICE WITH AN END OF DOSE FEEDBACK MECHANISM

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of application Ser. No. 15/241,566, filed Aug. 19, 2016, which is a continuation of application Ser. No. 11/813,389, filed Jul. 9, 2008 (issued as U.S. Pat. No. 9,457,154), which is a 35 U.S.C. § 371 national stage application of International Patent Application PCT/EP2006/000486 (published as WO 2006/079481), filed Jan. 20, 2006, which claimed priority of European Patent Application 05075187.4, filed Jan. 25, 2005; this application further claims priority under 35 U.S.C. § 119 of U.S. Provisional Application 60/647,491, filed Jan. 27, 2005; the contents of which are incorporated herein by reference.

FIELD OF THE INVENTION

The present invention relates to an apparatus for delivering liquid drugs to a mammal, preferably a human being, preferably in a subcutaneous manner. More particularly, the present invention relates to an injection device which is capable of providing a non-visual feedback signal to a user indicating that a set dose has been injected by the injection device.

BACKGROUND OF THE INVENTION

In the present disclosure reference is mainly made to the treatment of diabetes by injection of insulin. However, this is merely an exemplary use of the present invention. Thus, the present invention may be used for injection of any other suitable kind of drug, e.g. growth hormone.

Injection devices, e.g. in the form of injection pens, are mainly made for users who have to inject themselves frequently, e.g. people having insulin-dependent diabetes or needing treatment by growth hormones. A number of requirements are set to such injection devices. The setting of a dose must be easy and unambiguous and it must be easy to read the set dose. Furthermore, it must be possible, with a minimum of trouble, to cancel or change a wrongly set dose. Finally, when the dose is injected the dose setting mechanism must return to zero. This is very important since it ensures that the set dose is actually injected, thereby allowing the user to keep track of which dose is injected.

Many injection devices work with a threaded piston rod which cooperates with a nut, the nut and the piston being capable of rotating relatively to each other. The dose setting may be obtained by dialing the nut away from a stop to which it is returned during injection by pressing the piston rod forward, either manually or by means of a mechanically biased mechanism, such as a spring, until the nut member abuts the stop. In other injection devices one of the elements, the nut or the piston rod, is kept inrotatable while the other one is allowed to rotate a set angle depending on the set dose, whereby the piston rod is dialed a distance in a forward direction through the nut member.

In such prior art injection devices a dose is normally set by dialing a dose setting member, and the set dose is injected by pushing an injection button. In elongated pen shaped injection
devices the dose setting member and the injection button normally form a single member. When the injection button is pushed the set dose is expelled. However, the amount of drug expelled is only equal to the set dose if the injection button has been pushed as far as possible, the dose setting member thereby having been brought back to zero. In order to ensure that the correct dose has actually been injected, the user therefore has to visually inspect the position of the dose setting member during the injection. This is disadvantageous because the injection in some cases will take place in a part of the body where visual inspection during the injection is very difficult or even impossible. Furthermore, in case the user is visually impaired it may be difficult for the user to visually inspect the dose setting member during or after the injection, regardless of where on the body the injection is performed. Since it is not uncommon for people having diabetes to be visually impaired, this is an important aspect.

It is therefore desirable to provide a feedback signal to the user indicating that the set dose has been injected, the feedback signal being of a kind which makes it unnecessary for the user to visually inspect whether or not the set dose is injected.

Some prior art injection devices have a mechanism which informs the user that a dose is being injected by producing an audible 'click' for each dose unit being injected. However, since these clicks appear during the entire injection they do not provide a feedback signal indicating that the set dose has been injected, and the problem indicated above is therefore not solved by these injection devices. Prior art injection devices of this type are, e.g., described in U.S. Pat. No. 4,592,745, EP 0 688 571 and US 2004/0210199.

In WO 98/57688 an injection device is disclosed which addresses the above mentioned problem. Thus, WO 98/57688 discloses an injection device having a dose setting device. A dose is set by dialing a dose setting member. Apart from setting a dose the dialing action causes an injection button to be moved from a position where it abuts a housing of the injection device to a position where it protrudes from the housing. The set dose is subsequently delivered by pushing the injection button back into abutment with the housing.

In one embodiment a lock is activated when the injection button reaches the housing, and the activation of the lock produces an audible click indicating that the injection button is in abutment with the housing and thereby that the set dose has been delivered. During the injection, including the final part when the lock is activated, the injection button is moved linearly. The linear distance travelled by the injection button during the last few doses is relatively short. It may therefore be difficult to determine accurately from the audible click produced by the lock whether or not and when the set dose has been delivered.

EP 0 594 357 discloses another injection device which addresses the above mentioned problem. Thus, EP 0 594 357 discloses an injection device having a top section with resilient legs depending perpendicularly from the top section. The outer surface of the resilient legs has a ridge which rests on a ledge inside of the dose knob. The dose knob may have an elongated section which fits into a cylindrical sleeve such that when the dose knob is pushed into the sleeve, at the end of injection, the top portion of the sleeve touches end of the leg of the resilient legs displacing the ridge from the ledge and causing a snapping noise. As it is the case with the injection device described in WO 98/57688, the dose knob is moved linearly during injection, also during the final part of the injection when the resilient legs are displaced from the ridge causing the snapping noise. Therefore the shortcomings described above are also applicable here.

SUMMARY OF THE INVENTION

It is, thus, an object of the present invention to provide an injection device being capable of precisely and in a non-visual manner indicating to a user when a set dose has been injected.

It is a further object of the present invention to provide an injection device being capable of non-visually indicating to a user when a set dose has been injected, the indication being delivered to the user in a very distinct manner.

It is an even further object of the present invention to provide a dose delivering mechanism for an injection device, the dose delivering mechanism being capable of precisely and in a non-visual manner indicating to a user when a set dose has been injected.

According to the present invention the above and other objects are fulfilled by providing an injection device comprising:

- a housing,
- a dose setting member being operable to set a desired dose to be injected,
- a piston rod being adapted to cooperate with a piston so as to cause a set dose to be injected from an ampoule, and
- a dose delivering mechanism being adapted to operate the piston rod in such a way that a set dose is injected, the dose delivering mechanism further being adapted to provide a non-visual feedback signal to a user only at the end of injection of a set dose, wherein first and second parts of the injection device are adapted to perform a relative rotational movement with respect to each other during injection of a dose, and wherein said relative rotational movement causes at least two parts of the injection device to abut or engage, said abutment or engagement causing the non-visual feedback signal to be generated.

The injection device of the present invention is very suitable for use by persons which have to frequently inject themselves, e.g. persons having insulin-dependent diabetes or needing treatment by growth hormones. The desired dose being set by means of the dose setting member is, thus, a dose of a specific drug which the person in question needs to inject at that specific point in time. The desired dose may be a fixed dose which the person needs to inject each time an injection is performed, or it may be a varying amount, e.g. varying according to the time of day and/or one or more parameters which may be measured or chosen prior to setting the dose (e.g. blood glucose (BG) level, contents of a meal, etc.).

The piston rod is preferably adapted to push a piston into an ampoule, thereby causing the set dose to be injected. This may be obtained in various ways and is well known and well described in the art.

The dose delivering mechanism is adapted to provide a non-visual feedback signal to a user only at the end of injection of a set dose. Thus, the feedback signal may be generated when the set dose has been injected, e.g. exactly when or immediately after the last unit has been injected. Alternatively, the feedback signal may be generated before the complete dose has been delivered, e.g. when a few units remain to be injected, the remaining units being injected while the feedback signal is sensed by the user. Thus, when the user perceives the feedback signal the set dose will have been delivered, and the user will therefore not be able to tell the difference between a feedback signal being generated after the dose has been completely injected and a feedback signal being generated immediately before the dose has been completely injected. In any event the user can regard the perception of the feedback signal as an indication that the set dose has been delivered, and the user may therefore react correspondingly, e.g. by removing a pressure applied manually to an injection button.

Since the non-visual feedback signal is provided only at the end of injection of a set dose the user will know distinctly that when the feedback signal is received the set dose has been fully injected. This is an advantage compared to prior art injection devices where a click for each injected dose unit is produced. In this case the user would have to count the number of clicks produced and compare this to the number of set dose units in order to tell exactly when the set dose has been fully injected.

A first part and a second part of the injection device are adapted to perform a relative rotational movement with respect to each other during injection of a dose. This may, e.g., be the housing and the piston rod, or it may be a separate member and any other part of the injection device, e.g. the housing and/or the piston rod, the sole purpose of the separate member being to generate the non-visual feedback signal. Three or more parts of the injection device may perform mutual rotational movements during injection of a dose.

Furthermore, the relative rotational movement may be performed all through the injection of a dose or it may be performed during only part of the injection. Thus, the relative rotational movement may be started or stopped at the end of injection of a set dose as defined above, in which case this starting or stopping may advantageously cause the non-visual feedback signal to be generated.

The relative rotational movement causes at least two parts of the injection device to abut or engage, and this abutment or engagement causes the non-visual feedback signal to be generated. One or both of the parts which abut or engage may be the first and/or second parts, i.e. the parts performing the relative rotational movement. Alternatively, one or both of the parts which abut or engage may be other parts of the injection device. This will be described in further details below.

Due to the fact that the relative rotational movement initiates the generation of the non-visual feedback signal it is ensured that the movement generating the non-visual feedback signal is much longer than a corresponding movement in an injection device where the feedback signal is generated by a linear movement of one or more parts. Thereby the generated signal will be much more precise and distinct, and a far more accurate feedback signal has thereby been provided. This is very advantageous because it makes it much easier for the person to ascertain that the expected and desired dose has actually been injected.

The non-visual feedback signal may comprise an audible and/or a tactile signal. In this case the person using the injection device will be able to hear and/or feel that the set dose has been injected. Alternatively or additionally, the non-visual feedback signal may comprise any other suitable kind of signal which can be perceived by other senses than sight. Furthermore, the non-visual feedback signal may be followed by a visual signal, e.g. a scale drum showing a 'zero', a lamp or a diode which is turned on or off or starts flashing simultaneously with the generation of the non-visual feedback signal. Thereby the user may, in addition to the non-visual feedback signal, use this visual feedback signal to further ensure that the set dose has actually been injected.

In one embodiment of the present invention the abutment or engagement is caused by a change in a rotational velocity

of at least one part of the dose delivering mechanism. This may, e.g., be accomplished by allowing a separate member to start rotating at the end of injection of a set dose, typically in such a way that this member rotates during injection of the last few units of the set dose. The rotation of this separate member will in turn generate a non-visual feedback signal to the user. Thus, in this case the rotational velocity of this member relatively to, e.g., the housing, changes from zero to a certain velocity, and this change causes the non-visual feedback signal to be generated, e.g. in the form of a clicking sound generated by protruding parts present on the separate member moving against an inner part of the housing or an outer part of the piston rod.

Alternatively or additionally, the change in rotational velocity may cause a tactile feedback signal to be generated. It may, e.g., be possible to feel the rotational movement itself, and thereby it may be possible for the user to detect a substantial change (decrease or increase) in the rotational velocity.

In one embodiment the injection device may further comprise a ratchet operating the piston rod and having a threaded portion being adapted to engage with a part of the dose delivering mechanism, in which case the change in a rotational velocity is generated by a change in the pitch of the threaded portion of the ratchet, said change in the pitch in return causing a change in a translational velocity of said part of the dose delivering mechanism, said change in translational velocity causing at least two parts of the injection device to abut, thereby causing the non-visual feedback signal to be generated.

In this embodiment the non-visual feedback signal preferably comprises a tactile feedback signal. Thus, the part of the dose delivering mechanism which is adapted to engage with the threaded portion of the ratchet is preferably in directly or indirectly contact with the user during injection of a dose. Thus, the part may be, form part of or be operatively connected to an injection button which the user presses during injection. Thereby the user will be able to feel the change in translational velocity.

The pitch may be changed from a certain value used during the main part of the injection to zero, i.e. the threaded portion simply stops at a position corresponding to the end of injection of a set dose. In this case the user will feel a kind of 'axial resistance' during the injection until the ratchet/dose delivery part reaches the position where the threaded portion stops. Then the part will stop rotating and instead increase the velocity of a translational (axial) movement which is also performed while the ratchet/dose delivery part travels the threaded portion, due to the pitch of the threaded portion. The user will be able to feel this increase in translational velocity. Furthermore, the translational movement is preferably eventually stopped, e.g. due to part of the dose delivery mechanism abutting a stop member. This stop will also be very distinctly felt by the user, thereby producing a non-visual feedback signal, and it may further produce a sound, in which case the non-visual feedback signal comprises a
tactile as well as an audible signal. In this embodiment the two parts of the injection device which are caused to abut may advantageously be a scale drum and a part of the housing, the scale drum performing a rotational and axial movement defined by the threaded portion.

Alternatively, the two parts may be a dose knob and a proximal part of the housing, the dose knob performing an axial movement which follows the axial part of the movement of the scale drum as described above.

Alternatively, the pitch may either increase or decrease from one non-zero value to another. This has the advantage that the engaging part is readily moved back into engagement with the threaded portion when a new dose is to be set.

In another embodiment the dose delivering mechanism may comprise a first dose part and a second dose part, the first dose part being adapted to rotate relatively to the housing during injection of a dose and the first dose part comprising means for engaging the second dose part at the end of injection of a set dose, thereby causing the second dose part to rotate along with the first dose part, in which case the non-visual feedback signal is generated by the resulting rotational movement of the second dose part.

In this embodiment the rotational movement of the second dose part increases from zero to a non-zero value at the end of injection of the set dose. The second dose part may be provided with teeth, protrusions, flexible arms or similar means being adapted to be moved against another part of the device during rotation of the second dose part, thereby producing a sound which at least partly constitutes the non-visual feedback signal.

The second dose part may be positioned between the first dose part and the housing. In case the second dose part is provided with teeth, protrusions, flexible arms or the like as described above, these may advantageously be moved against a part of the housing when the second dose part is rotated along with the first dose part.

Alternatively, the non-visual feedback signal may be generated as a result of an abutment between two parts of the dose delivering mechanism performing a relative rotational movement. The feedback signal may, e.g., be obtained by releasing a tension which has previously been introduced in a part of the injection device, the release of the tension being caused by the abutment between the two parts.

The tensed part may comprise a spring means, such as a separate spring member or at least one resilient portion of at least one of the first and second parts performing the relative rotational movement. In case the spring means is in the form of at least one resilient portion of the part(s) the non-visual feedback signal may be generated in the following manner. First the resilient portion(s) is/are bent into a tensed position. At a later time this tension is released, e.g. by rotating the resilient portion(s) away from a part which holds the resilient portion(s) in the tensed position. Thereby the resilient portion(s) will restore its/their relaxed position(s), and this movement will generate a clicking sound, i.e. a non-visual feedback signal. The resilient portion(s) may be in the form of spring arm(s), in which case a sound may be generated due to moving air caused by sudden release of the tensed spring arm(s). Alternatively, abutment between a moving part and a release mechanism may release the tension of the resilient portion(s).

The tension may be introduced during dose setting, e.g. by tightening a spring member or moving a resilient portion into a tensed position as described above. This may be obtained by letting the dose setting mechanism be connected to a spring member, e.g. in such a way that a spring is tightened when a dose setting member is turned, or in such a way that a part being provided with a resilient portion is rotated along with a dose setting member, thereby causing the resilient part to be moved into a tensed position.

Alternatively, the tension may be introduced during injection of a dose. This may be obtained in a manner very similar to what is described above. However, in this case the tensed part should be operatively connected to the dose delivering mechanism.

The dose delivering mechanism may be adapted to be manually operated, e.g. by means of an injection button which the user must press manually during the injection.

Alternatively, the dose delivering mechanism may be adapted to be operated by means of a mechanically biased mechanism, e.g. comprising at least one spring. The mechanically biased mechanism may, in this case, be biased during setting of a dose. When the injection is subsequently performed this is done by releasing the tension previously built up in the mechanically biased mechanism, and the stored energy will then cause the set dose to be injected. This kind of injection device does not require a force applied by the user in order to inject a set dose.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will now be further described with reference to the accompanying drawings in which:

FIG. **1** shows a cross section through an injection device according to a first embodiment of the invention and being in a position where a dose has been set,

FIG. **2** shows a cross section through the injection device of FIG. **1** in a position where a dose has been injected,

FIG. **3** shows a click item adapted to be positioned in the injection device of FIGS. **1** and **2**,

FIG. **4** shows a threaded inner part being adapted to be positioned in an injection device according to a second embodiment of the invention,

FIG. **5** shows a top view of an outer part being adapted to engage with the inner part of FIG. **4**,

FIG. **6** is a cross section along line A-A in FIG. **5**,

FIGS. **7-10** show parts of injection devices according to a third, fourth, fifth and sixth embodiment of the invention, respectively, all having a spring arm and a wedge structure,

FIG. **11** shows part of an injection device according to a seventh embodiment of the invention having a spring arm and a release mechanism,

FIG. **12** shows an outer part of the injection device of FIG. **11** from a different angle, and

FIGS. **13-15** show part of an injection device according to an eighth embodiment of the invention having a spring arm, at various points in time.

The Figures are schematic and simplified for clarity, and they only show details which are essential to the understanding of the invention while other details are left out. Throughout the description of the drawings the same reference numerals will be used for identical or corresponding parts.

DETAILED DESCRIPTION OF THE DRAWINGS

When in the following terms as 'upper' and 'lower', 'left' and 'right', 'horizontal' and 'vertical', 'clockwise' and 'counter clockwise' or similar relative expressions are used, these only refer to the accompanying drawings and not to the actual situation of use. The shown Figures are schematic representations for which reason the configuration of the different structures as well as their relative dimensions are intended to serve illustrative purposes only. In that context it may be convenient to define that the term 'distal end' in the accompanying drawings is meant to refer to the end of the injection device carrying an injection needle, whereas the term 'proximal end' is meant to refer to the opposite end pointing away from the injection needle.

FIG. **1** shows a cross section through an injection device **1** according to a first embodiment of the invention. At its distal end the injection device **1** is provided with a portion **2** being adapted to carry an injection needle (not shown). At its proximal end the injection device **1** comprises a combined dose setting and injection button **3**. During dose setting the dose setting and injection button **3** is rotated. This causes the dose setting and injection button **3** to be moved away from a housing **4** to the position shown in FIG. **1**. During injection the user presses the dose setting and injection button **3**, thereby moving it back into the housing **4**.

This movement causes the set dose to be injected from the injection device **1**. Inside the dose setting and injection button **3** there is positioned a click item **5** which is provided with a set of teeth **6** being adapted to engage with a corresponding tooth **7** positioned on a ratchet **8**. During injection the ratchet **8** will rotate relatively to the housing **4** while the click item **5** will not rotate.

FIG. **2** shows a cross section of the injection device **1** of FIG. **1**. However, in FIG. **2** a dose has just been injected, i.e. the dose setting and injection button **3** has been pushed to a position inside the housing **4**. Thereby the set of teeth **6** on the click item **5** engage with the tooth **7** on the ratchet **8**. Since the ratchet **8** rotates during the injection, this will cause the click item **5** to be rotated along with the ratchet **8**. This rotational movement will cause the click item **5** to produce a sound in a manner which will be explained further below with reference to FIG. **3**. Since the click item **5** is only rotated during the injection of the last few units of the set dose the produced sound indicates that the set dose has been substantially injected. Thereby a non-visual feedback signal has been generated.

FIG. **3** is a perspective view of a click item **5** adapted to be inserted in the injection device **1** of FIGS. **1** and **2**. The part of the click item **5** positioned opposite the set of teeth **6** is provided with two resilient parts **9**. The resilient parts **9** are resilient due to a reduced thickness of the material making up the parts **9** as compared to the thickness of the material making up the remaining parts of the click item **5**. When the click item **5** is rotated as described above the resilient parts **9** will be moved against the inner part of the housing **4**, and this will cause the resilient parts **9** to be alternatingly tensed and released. Each time the resilient parts **9** are released they will produce a clicking sound, thereby generating the non-visual feedback signal.

FIG. **4** shows a threaded inner part **10** being adapted to be inserted inside a housing of an injection device according to a second embodiment of the invention. The main part of the thread **11** has a constant pitch. However, in the lower part of the thread **12** the pitch is abruptly decreased. This can be seen in the form of an axial edge **13**. Thereby a part engaging with the thread **11**, **12** will be moved abruptly relatively to the inner part **10** along an axial direction when the engaging part reaches the lower part of the thread **12**, i.e. when it reaches the axial edge **13**. This abrupt movement, and not the least the following abrupt stop when this movement stops, can be felt by the user as will be described below. Furthermore, the location of the axial edge **13** towards the end of the threaded portion **12** ensures that the felt abrupt movement indicates the end of injection of a set dose. Thereby a non-visual (tactile) feedback signal has been provided as a result of a change in the pitch of a threaded portion **11**, **12**.

FIG. **5** shows a top view of an outer part **14** being adapted to be positioned around the threaded inner part **10** of FIG. **4**. The outer part **14** is provided with two protruding parts **15** each being adapted to engage with the thread **11**, **12** of the inner part **10**.

FIG. **6** shows a cross section through the outer part **14** shown in FIG. **5** along the line A-A. During injection of a

dose the inner part **10** and the outer part **14** will initially be relatively positioned in such a way that the protruding parts **15** engage with the part of the thread **11** being positioned opposite the lower part of the thread **12**. The outer part **14** is then pushed inwards, thereby allowing the protruding parts **15** to travel the threaded portion **11**. Due to the thread **11** the inner part **10** and the outer part **14** perform a relative rotational movement. When the protruding parts **15** reach the axial edge **13** the axial velocity of the outer part **14** will increase abruptly as described above, and because the user is manually pressing the outer part **14** this abrupt movement, as well as the abrupt stop occurring when the outer part **14** abuts a stop member **16** present on the inner threaded part **10** (see FIG. **4**), will be felt by the user. Thereby a tactile feedback signal is provided. Furthermore, the outer part **14** abruptly abutting the stop member **16** may produce a sound, thereby providing an audible feedback signal in addition to the tactile feedback signal.

FIG. **7** shows part of an injection device according to a third embodiment of the invention. The Figure shows an inner part **10** and an outer part **14**. The inner part **10** and the outer part **14** are adapted to be rotated relatively to each other during injection. The outer part **14** is provided with a wedge structure **17** and the inner part **10** is provided with a spring arm **18**. During injection, in addition to the mutual rotation, the inner part **10** is moved in an axial direction indicated by the arrow. When the spring arm **18** reaches the wedge structure **17** a protruding part **19** of the spring arm **18** will engage an upper part **20** of the wedge structure **17**. This will cause the spring arm **18** to be pressed in a direction opposite to the one indicated by the arrow, thereby introducing a tension in the spring arm **18**. The tension is, thus, built up during injection. The protruding part **19** will subsequently be moved along the upper part **20** of the wedge structure **17** until it reaches the end **21** of the wedge structure **17**. The protruding part **19** will then 'fall over the edge' to the position shown in FIG. **7**, thereby releasing the tension which was previously built up in the spring arm **18**. This sudden release of the tension produces a sound due to air being moved by the spring arm **18** and/or due to the protruding part **19** hitting a stationary part of the outer part **14**. Thereby an audible feedback signal has been produced, and by positioning the wedge structure **17** in an appropriate manner, the feedback signal will indicate to the user that the set dose has been injected.

When a new dose is to be set, the protruding part **19** will pass the wedge structure **17** via a tapered part **22** on the wedge structure **17**.

FIG. **8** shows part of an injection device according to a fourth embodiment of the invention. The fourth embodiment is very similar to the third embodiment shown in FIG. **7**. FIG. **8** also shows an inner part **10** having a spring arm **18** and an outer part **14** having a wedge structure **17**, the inner part **10** and the outer part **14** being adapted to rotate in relation to each other during injection. The spring arm is provided with a protruding part **19**. During injection the inner part **10** moves relatively to the outer part **14** in a direction indicated by the arrow. When the spring arm reaches the wedge structure **17** the protruding part **19** will be caught in a track **23** and moved along this track **23**. Due to the geometry of the wedge structure **17** this movement will result in the spring arm **18** being pressed in a direction away from the outer part **14**, thereby introducing a tension in the spring arm **18**. Thus, the tension is built up during the injection. When the protruding part **19** reaches the end **21** of the wedge structure **17** it will 'fall over the edge', thereby releasing the tension which was previously built up in the spring arm **18**. This will result in an audible feedback signal being generated as described above.

When a new dose is to be set, the protruding part **19** will pass the wedge structure **17** by being lifted in an axial direction along the end **21** of the wedge structure **17**.

FIG. **9** shows part of an injection device according to a fifth embodiment of the invention. FIG. **9** shows an inner part **10** having a spring arm **18** and an outer part **14** having a wedge structure **17**. During injection the inner part **10** will move relatively to the outer part **14** in a direction indicated by the arrow. However, in this embodiment the inner part **10** and the outer part **14** do not rotate relatively to each other. Instead the injection device comprises a rotational part **24** which rotates during injection relatively to the inner part **10** and the outer part **14**. When the spring arm **18** reaches the wedge structure **17** it will be pushed in a direction away from the outer part **14** and towards the rotational part **24**. Thereby it is moved into a path of a protruding part **25** on the rotating part **24**. When the protruding part **25** is rotated to the position of the spring arm **18**, it will therefore push the spring arm **18** out of its path again, thereby introducing a tension in the spring arm **18**. When the protruding part **25** has passed the position of the spring arm **18**, the spring arm **18** will again be free to move into the path of the protruding part **25**, thereby releasing the tension which was previously built up in the spring arm **18**. Thereby an audible feedback signal is generated due to air being moved be the spring arm **18** and/or due to the spring arm **18** hitting a wall of the rotational part **24**, as described above.

FIG. **10** shows part of an injection device according to a sixth embodiment of the invention. The Figure shows an inner part **10** having a spring arm **18** and an outer part **14** having a wedge structure **17**. The inner part **10** and the outer part **14** are adapted to rotate relatively to each other during injection. Furthermore, the inner part **10** moves relatively to the outer part **14** in the direction indicated by the arrow during injection. When the spring arm **18** reaches the wedge structure **17** it will be caught by one of the wedges. Due to the geometry of the wedge structure **17** and to the continued rotational and axial movement (in the direction of the arrow) of the inner part **10**, the spring arm **18** will be pressed in a direction opposite the direction indicated by the arrow, thereby introducing a tension in the spring arm **18**. Subsequently when the spring arm **18** reaches the end **21** of the wedge it will 'fall over the edge', thereby releasing the previously built up tension. This will cause an audible feedback signal to be generated as described above.

FIG. **11** shows part of an injection device according to a seventh embodiment of the invention. The Figure shows an inner part **10** having a wedge structure **17** and an outer part **14** having a spring arm **18** and a locking mechanism (not shown in FIG. **11**). The inner part **10** and the outer part **14** are adapted to rotate in relation to each other during setting of a dose and during injection. The inner part **10** is typically a scale drum or is adapted to rotate along with a scale drum during setting of a dose and during injection. Thus, when a dose is set the inner part **10** is rotated in such a way that the wedge structure **17** presses the spring arm **18** outwards and into engagement with the locking mechanism, thereby introducing a tension in the spring arm **18**. Thus, in this embodiment the tension is introduced during setting of the dose. The locking mechanism will maintain the spring arm **18** in the tensed position during the remaining setting of the dose and during the main part of the injection.

However, when the inner part **10** is returning to the initial position a release mechanism **26** on the wedge structure **17** releases the locking mechanism, thereby releasing the ten-

sion which was previously built up in the spring arm **18**. Thereby an audible signal is generated as described above, and because the locking mechanism is released when the inner part **10** is returning to the initial position, this audible signal indicates that the set dose has been injected.

FIG. **12** shows the outer part **14** of the injection device of FIG. **11**. The outer part **14** has a locking mechanism **27** which is in a locking position, i.e. it engages the spring arm **18**. Thus, in FIG. **12** the spring arm **18** is tensed. When the inner part (not shown) approaches the outer part **14** as described above, the release mechanism (not shown) will push the locking mechanism **27** downwards, and the tensed spring arm **18** will then restore its relaxed position, i.e. it will move towards the centre of the outer part **14**. Thereby the tension built up in the spring arm **18** is suddenly released.

FIG. **13** shows part of an injection device **1** comprising a scale drum **28** and a spring arm member **29** positioned at the proximal end of the injection device **1**. The spring arm member **29** is provided with a spring arm **18** which may be deflected in a proximal direction, i.e. away from the scale drum **28**.

During injection of a set dose, the scale drum **28** performs a rotational movement as well as an axial movement towards the spring arm member **29**. This movement will eventually cause an upper portion **30** of the scale drum to abut a protrusion **31** of the spring arm **18**. As the scale drum **28** continues the rotational and axial movement, the spring arm **18** is deflected in a proximal direction, thereby causing a tension to be built up in the spring arm **18**.

FIG. **13** shows a situation where the upper portion **30** of the scale drum **29** and the protrusion **31** of the spring arm **18** abut, and a tension has started to build up in the spring arm **18**.

FIG. **14** shows the injection device of FIG. **13**. In FIG. **14** a tension has been built up in the spring arm **18** as described above. The protrusion **31** of the spring arm **18** is positioned very near a recess **32** formed in the scale drum **28**. Thus, further rotation of the scale drum **28** will cause the protrusion **31** to 'fall over the edge' into the recess **32**. Thereby the tension which has previously been built up in the spring arm **18** is released, and an audible feedback signal is generated by vibrating air and/or by the protrusion **31** hitting a lower edge of the recess **32**.

This situation is illustrated in FIG. **15**, showing the injection device **1** of FIGS. **13** and **14** in a situation where the tension previously built up in the spring arm **18** has been released as described above.

When a new dose is to be set, the feedback mechanism needs to be reset in order to be able to provide an audible feedback signal when the subsequent dose has been injected. This is done by leading the protrusion **31** of the spring arm **18** via a path or track (not visible in FIGS. **13-15**) positioned behind the upper portion **30** of the scale drum **28** during the next dose setting. When the set dose is sufficiently large, the scale drum **28** and the spring arm member **29** will be sufficiently spaced apart to allow the protrusion **31** to be positioned above the upper part **30** of the scale drum **28**. Thereby the feedback mechanism has been reset, i.e. the spring arm **18** is once again ready for being deflected in a proximal direction as described above.

The injection device shown in FIGS. **13-15** is particularly suitable for having a dose delivering mechanism which is adapted to be operated by means of a mechanically biased mechanism, such as a spring.

Some preferred embodiments have been shown in the foregoing, but it should be stressed that the invention is not limited to these, but may be embodied in other ways within the subject matter defined in the following claims.

The invention claimed is:

1. An injection device comprising:

a housing having a longitudinal axis,

a dose setting member being operable by a user to set a desired dose of a varying amount to be injected, the desired dose thereby being a set dose,

a piston rod being adapted to cooperate with a piston so as to cause a set dose to be injected from an ampoule, and

a dose delivering mechanism being adapted to operate the piston rod in such a way that the set dose is injected by a mechanically biased mechanism comprising at least one spring and wherein the injection is subsequently performed by releasing the stored energy previously built up in the mechanically biased mechanism and which stored energy will cause the set dose to be injected, the dose delivering mechanism further being adapted to provide an audible feedback signal to a user only at the end of injection of the set dose,

wherein first and second parts of the injection device are adapted to perform a relative rotational movement around a longitudinal axis with respect to each other during injection of the set dose, and wherein said relative rotational movement causes at least the first part and the second part of the injection device to abut or engage, said abutment or engagement causing the audible feedback signal to be generated,

wherein the audible feedback signal is generated as the first part and the second part of the dose delivering mechanism performing said relative rotational movement are moved against each other, and

the audible feedback signal is generated by releasing a tension which has previously been introduced in a part of the injection device comprising at least one resilient portion of at least one of the first part and the second part performing said relative rotational movement.

2. The injection device according to claim **1**, wherein the abutment or engagement is caused by a change in a rotational velocity of at least one part of the dose delivering mechanism.

3. The injection device according to claim **2**, further comprising a ratchet operating the piston rod and having a threaded portion being adapted to engage with a part of the dose delivering mechanism, and wherein the change in a rotational velocity is generated by a change in the pitch of the threaded portion of the ratchet, said change in the pitch in return causing a change in a translational velocity of said part of the dose delivering mechanism, said change in translational velocity causing at least two parts of the injection device to abut, thereby causing the audible feedback signal to be generated.

4. The injection device according to claim **2**, wherein the dose delivering mechanism comprises a first dose part and a second dose part, the first dose part being adapted to rotate relatively to the housing during injection of a dose and the first dose part comprising structure for engaging the second dose part at the end of injection of a set dose, thereby causing the second dose part to rotate along with the first dose part, and wherein the audible feedback signal is generated by the resulting rotational movement of the second dose part.

5. The injection device according to claim **4**, wherein the second dose part is positioned between the first dose part and the housing.

6. The injection device according to claim 1, wherein the at least one resilient portion is a spring arm.

7. The injection device according to claim 6, wherein the tension is introduced during dose setting.

8. The injection device according to claim 1, wherein the tension is introduced during dose setting.

9. The injection device according to claim 1, wherein the tension is introduced during injection of a dose.

* * * * *

EXHIBIT M

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(54) **AUTOMATIC INJECTION DEVICE WITH A TOP RELEASE MECHANISM**

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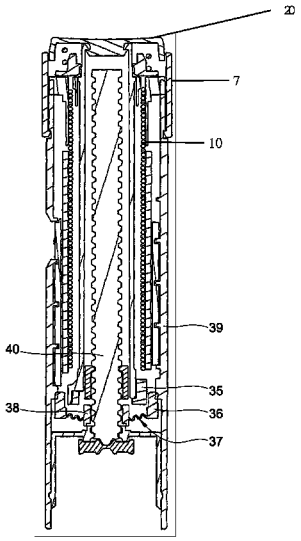
Danish Patent Application No. PA 2004 01576, filed Oct. 14, 2004.

Primary Examiner — Laura A Bouchelle
(74) *Attorney, Agent, or Firm* — Wesley Nicolas

(57) **ABSTRACT**

The present invention relates to a handheld mechanical injection device by which set doses of a liquid medicament can be injected from a medical reservoir. The medicament is expelled through an injection needle by release of a power reservoir in the device, the power reservoir being fully or partially released by actuation of a user operable release member being positioned at or near an upper end of the injection device, the upper end being that end of the injection device which is opposite the injection needle.

15 Claims, 13 Drawing Sheets



Related U.S. Application Data

continuation of application No. 13/326,738, filed on Dec. 15, 2011, now Pat. No. 9,108,002, which is a continuation of application No. 11/813,435, filed as application No. PCT/DK2006/000032 on Jan. 20, 2006, now Pat. No. 8,096,978.

(60) Provisional application No. 60/647,320, filed on Jan. 26, 2005.

(51) **Int. Cl.**
A61M 5/31 (2006.01)
A61M 5/24 (2006.01)

(52) **U.S. Cl.**
CPC ***A61M 5/31525*** (2013.01); ***A61M 5/31528*** (2013.01); ***A61M 5/31553*** (2013.01); ***A61M 5/31585*** (2013.01); *A61M 5/24* (2013.01); *A61M 5/31583* (2013.01); *A61M 5/31593* (2013.01); *A61M 2005/202* (2013.01); *A61M 2005/3126* (2013.01)

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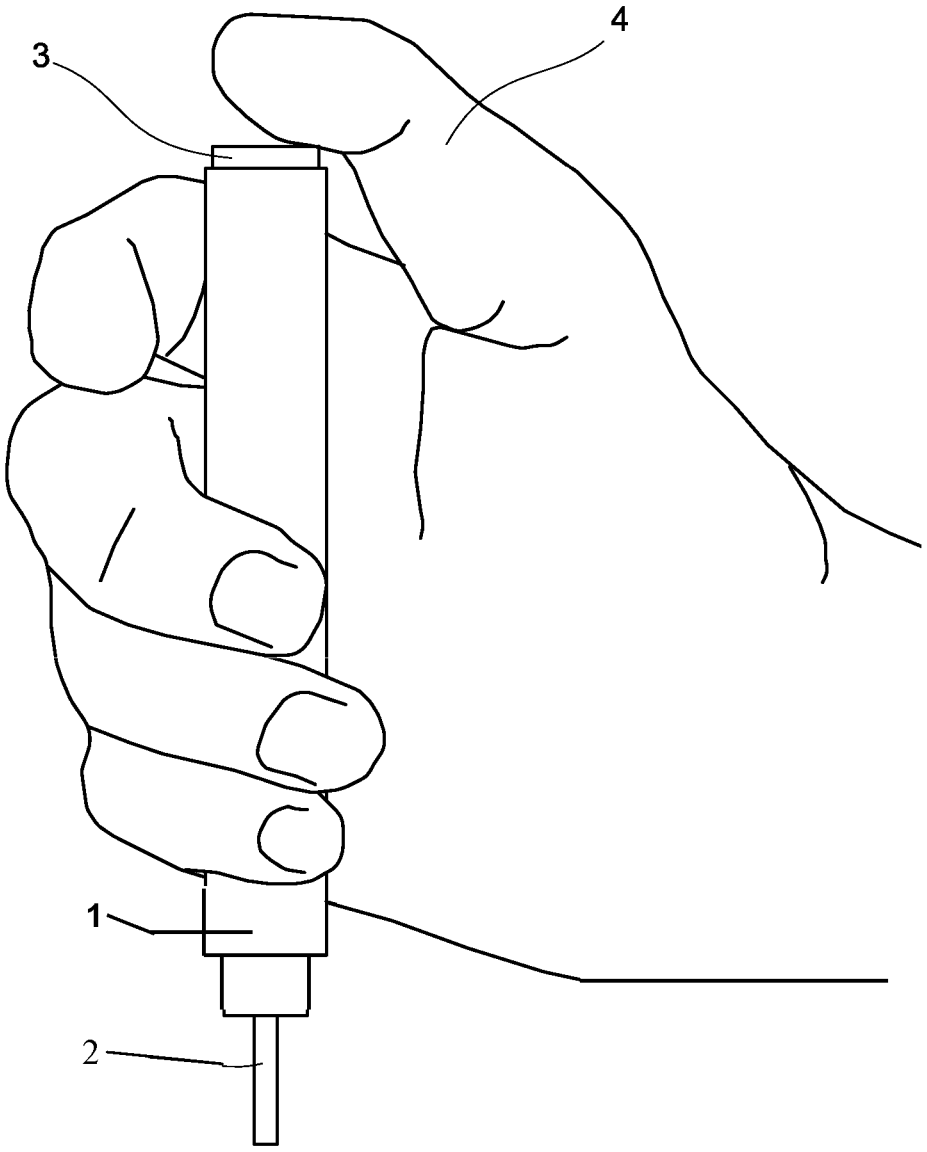

FIG. 1

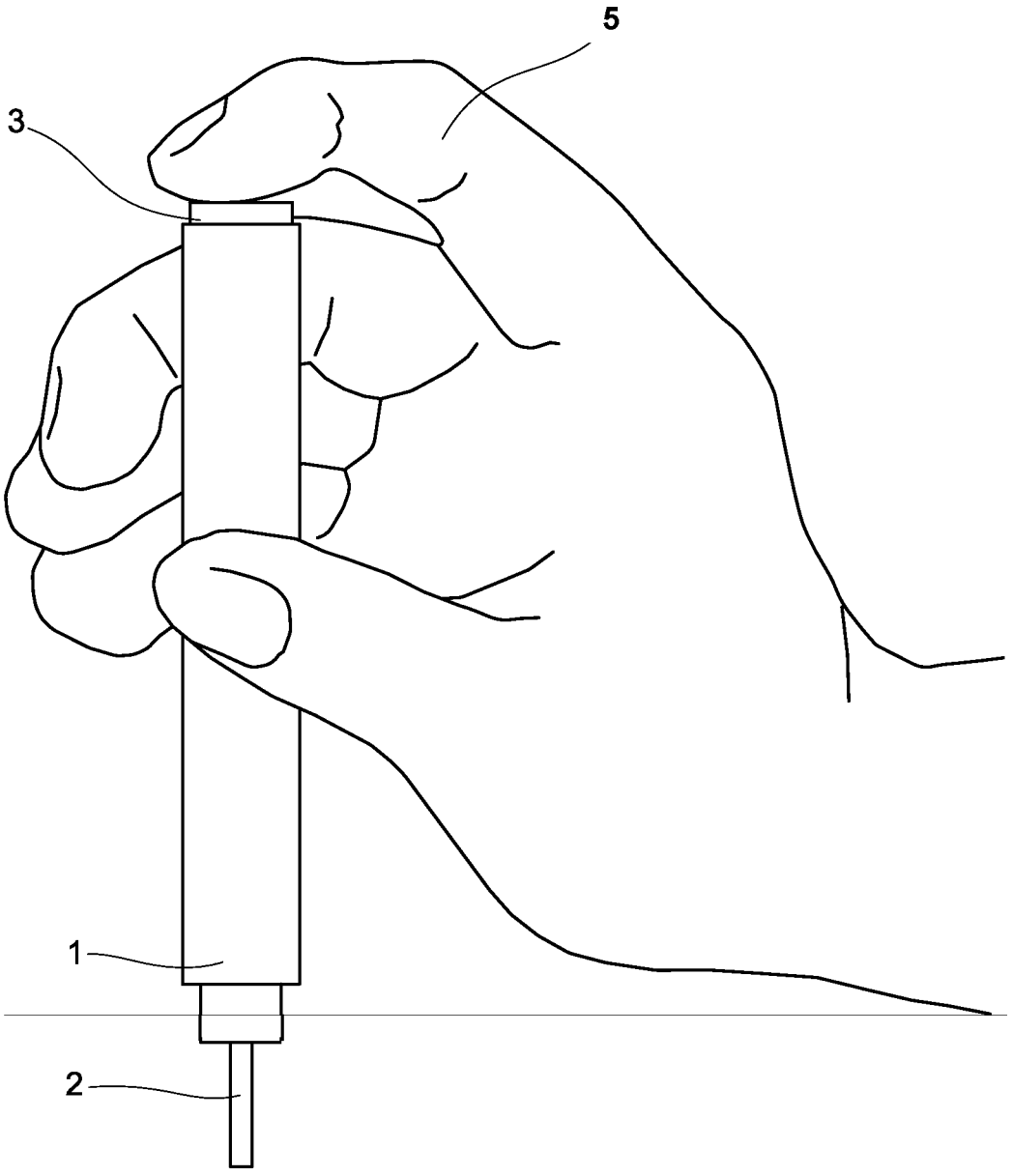

FIG. 2

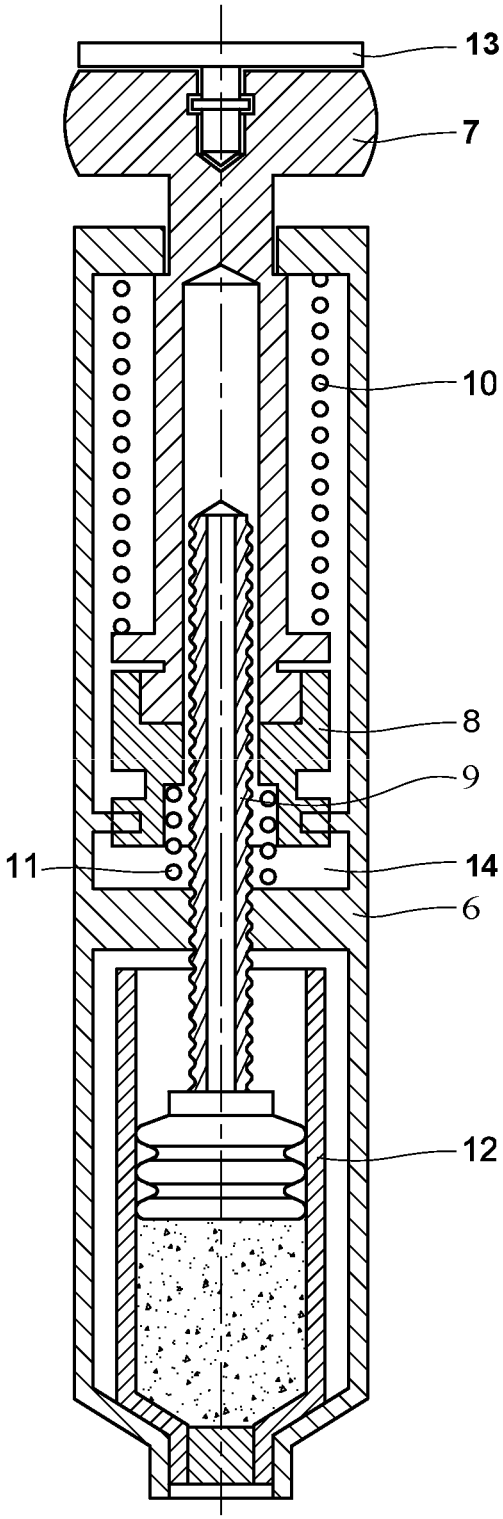

FIG. 3

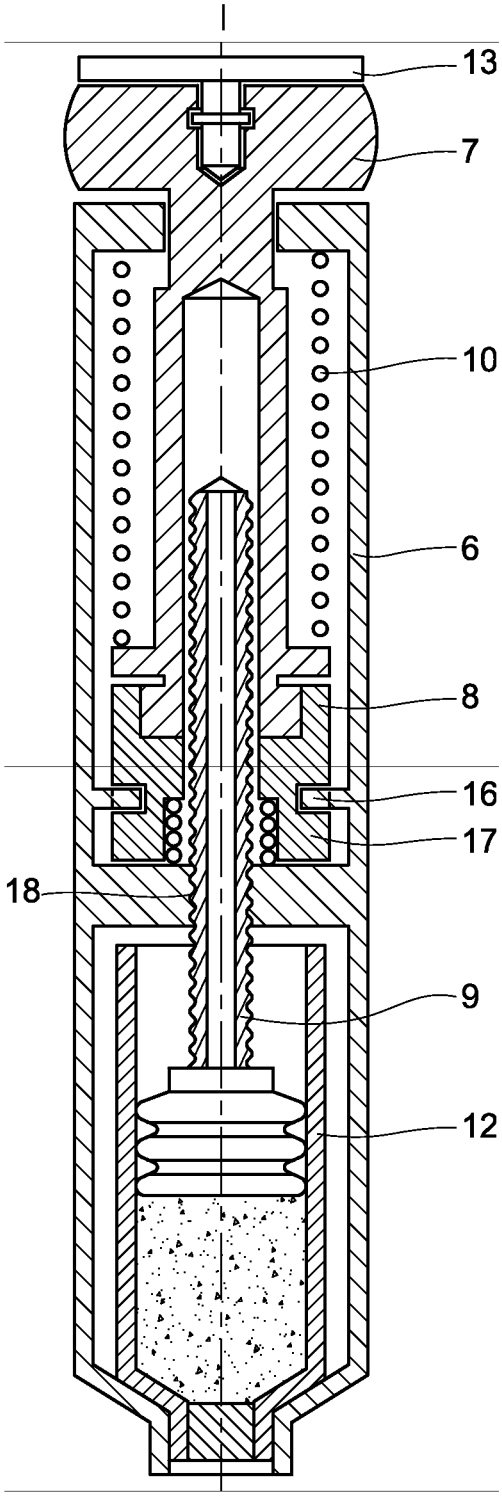

FIG. 4

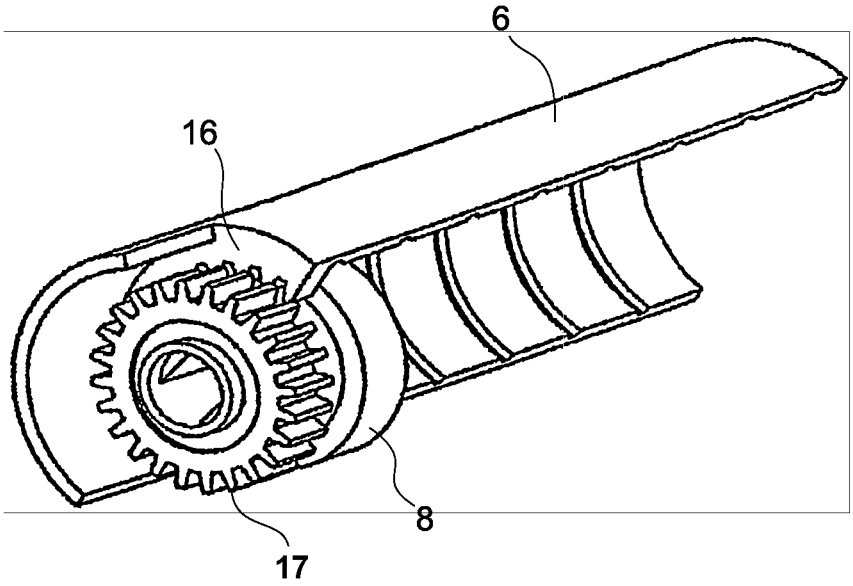

FIG. 5

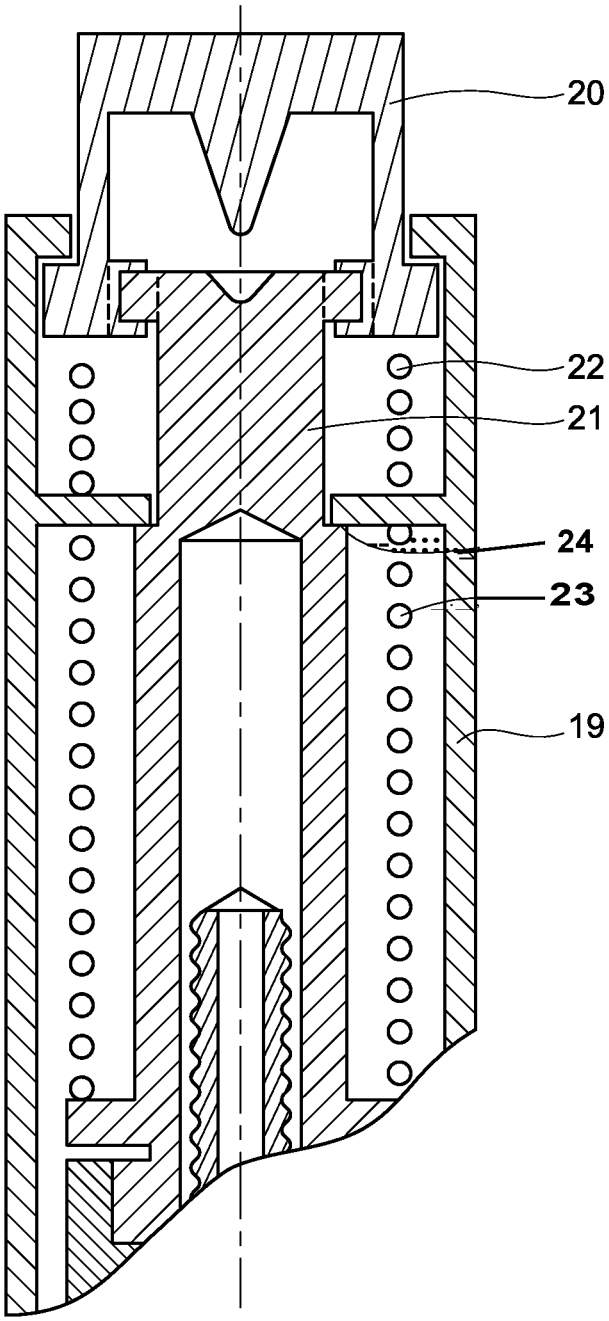

FIG. 6

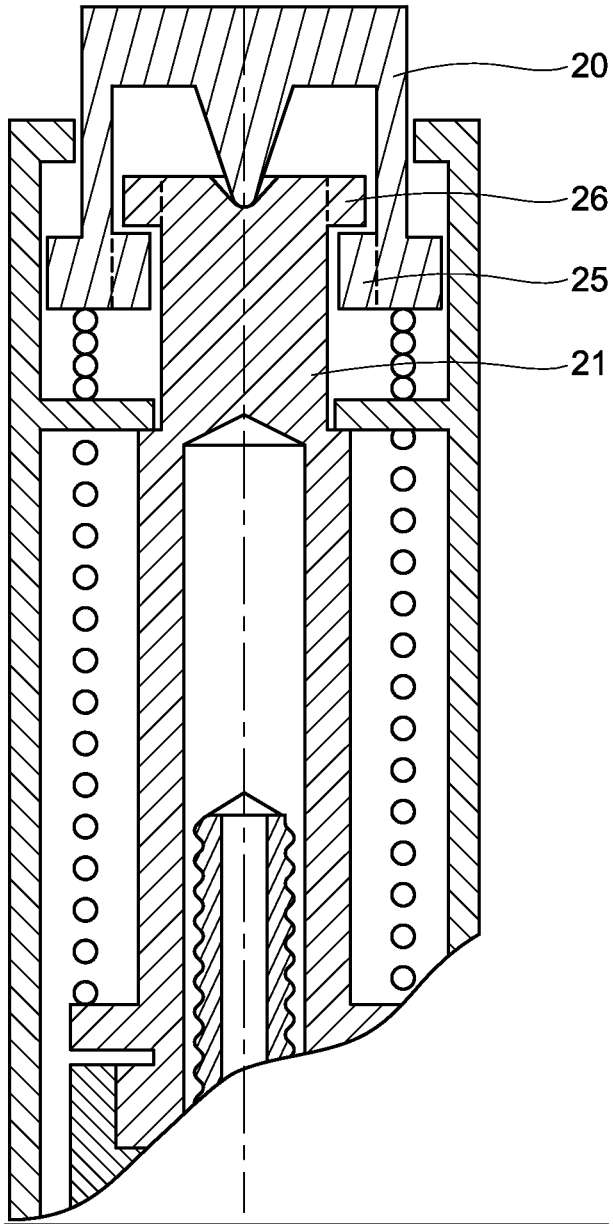

FIG. 7

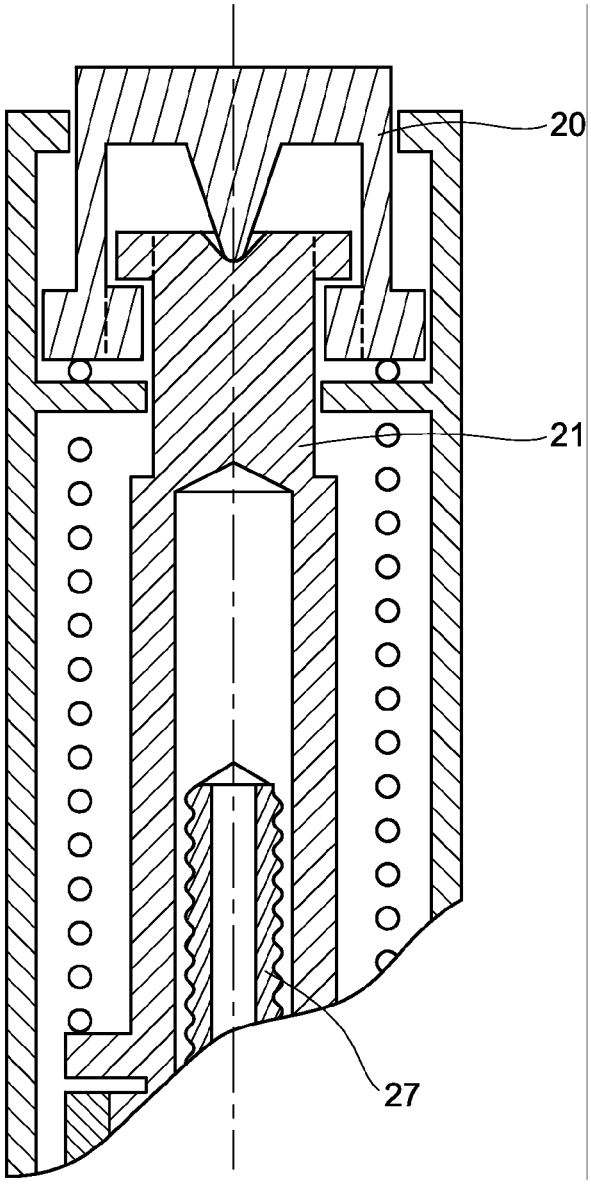

FIG. 8

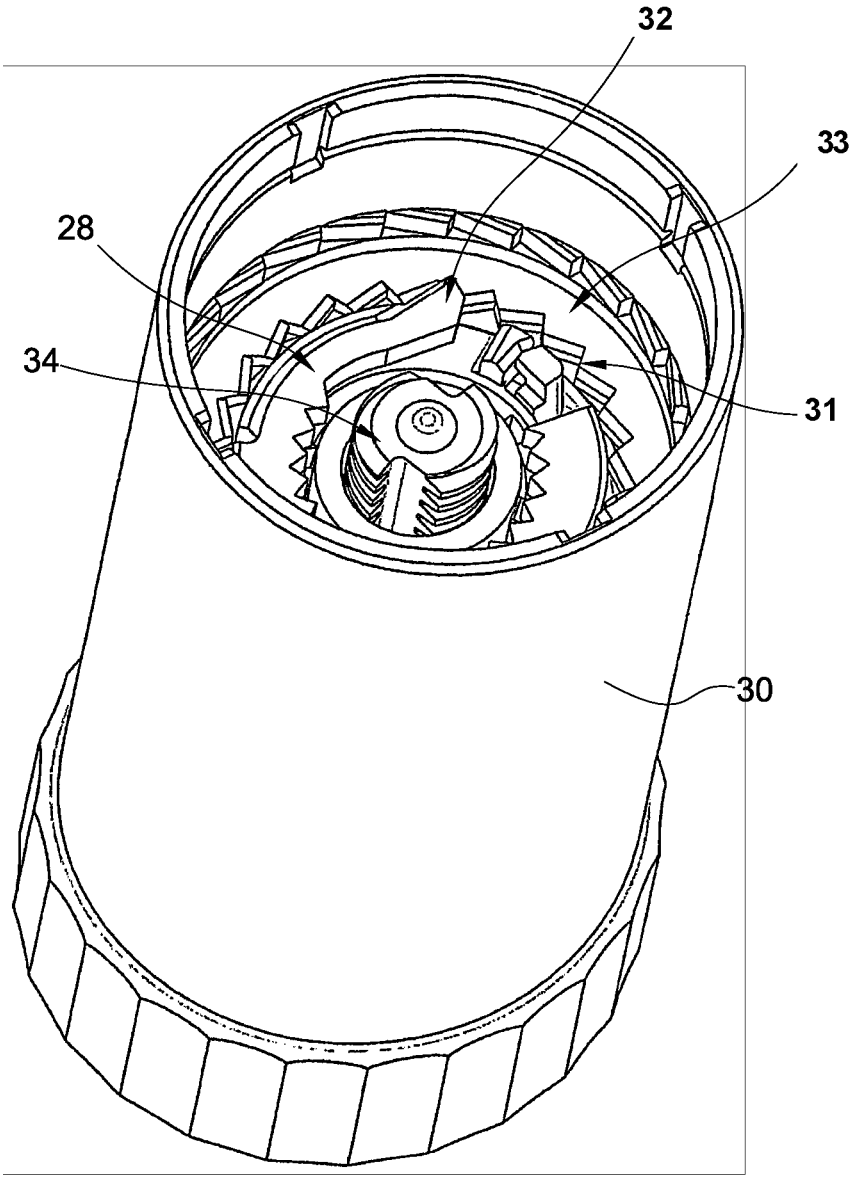

FIG. 9

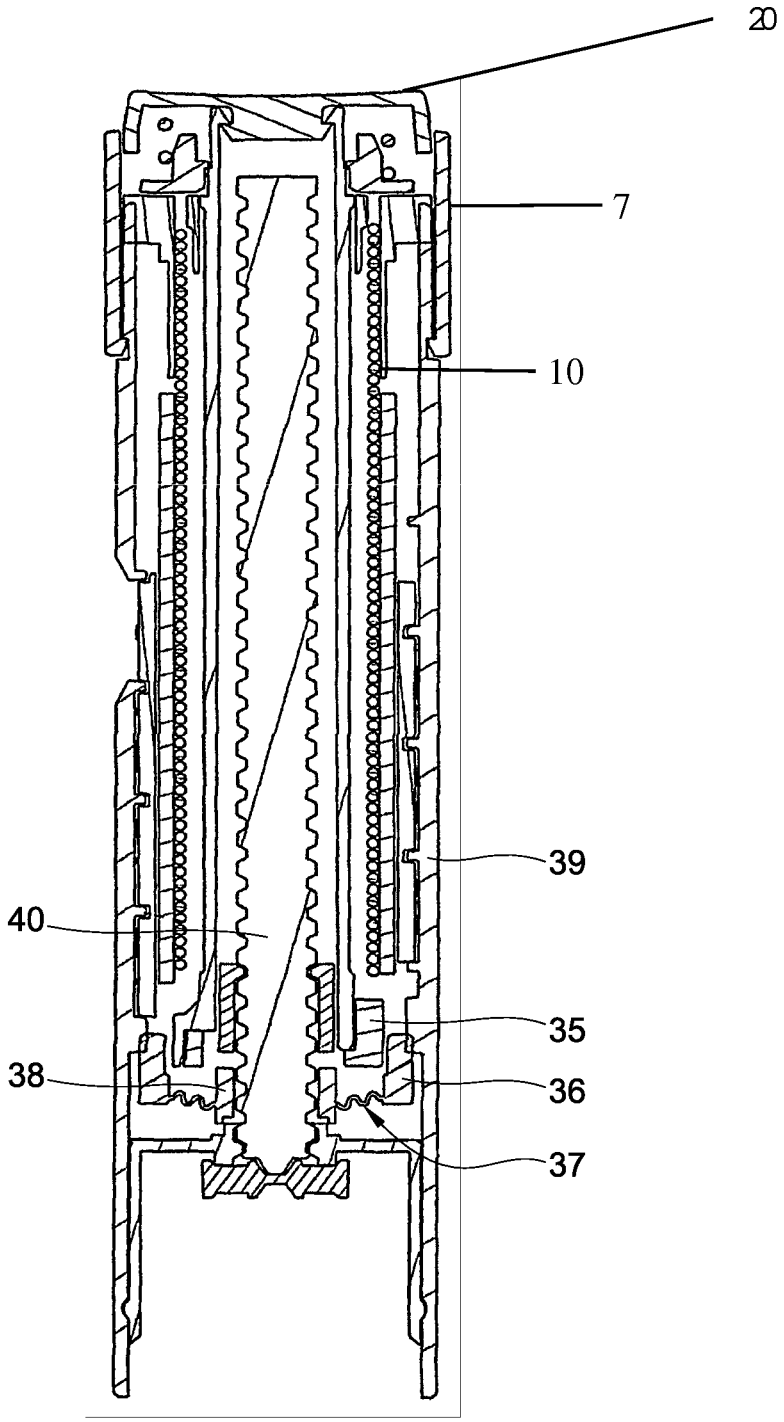

FIG. 10

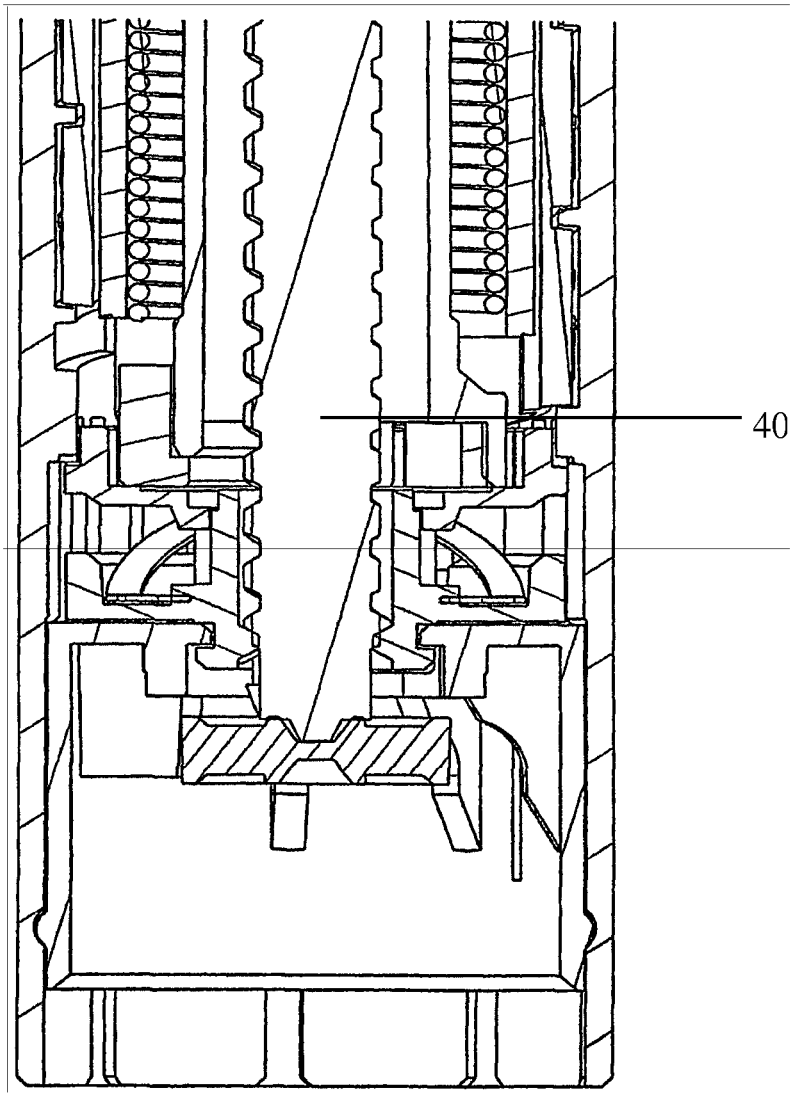

FIG. 11

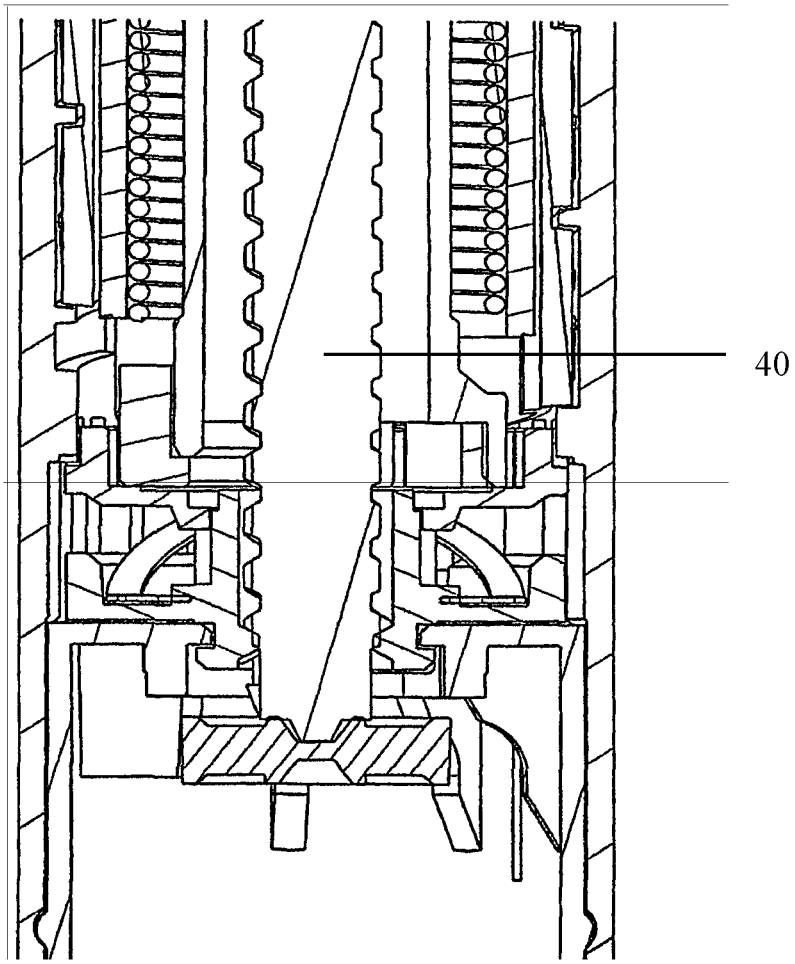

FIG. 12

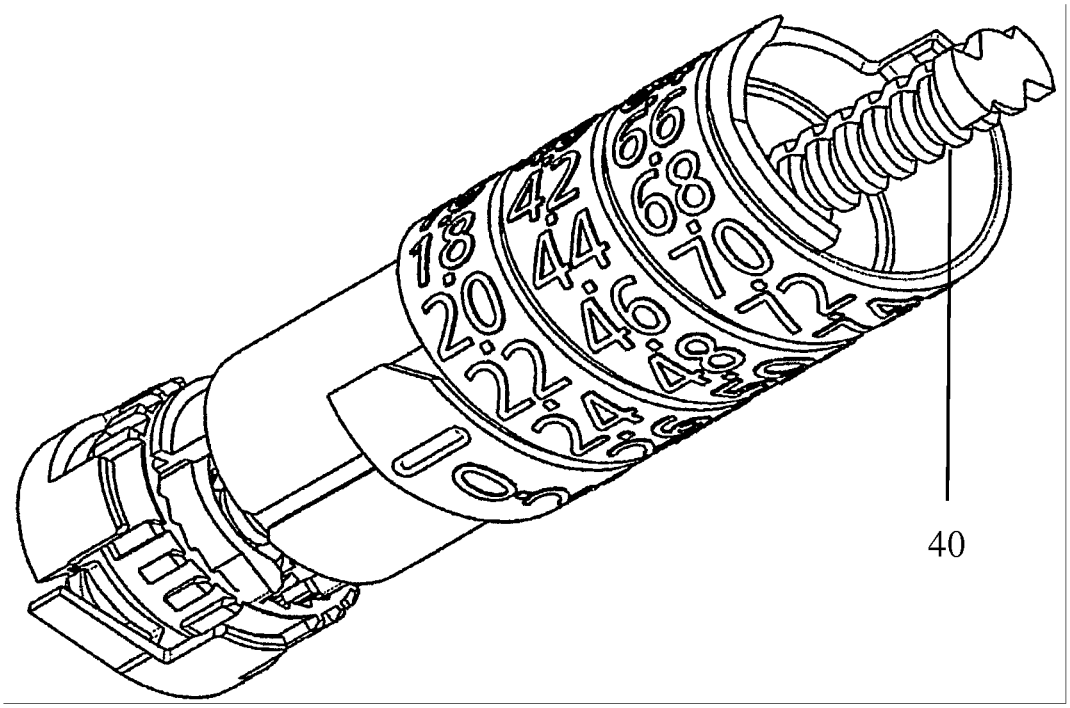
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FIG. 13

AUTOMATIC INJECTION DEVICE WITH A TOP RELEASE MECHANISM

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 14/797,350, filed Jul. 13, 2015 (Issue Fee Paid), which is a continuation of U.S. patent application Ser. No. 13/326,738, filed Dec. 15, 2011 (U.S. Pat. No. 9,108,002) which is a continuation of U.S. patent application Ser. No. 11/813,435 filed Jun. 2, 2008 (U.S. Pat. No. 8,096,978) which is a 35 U.S.C. § 371 national stage application of International Patent Application PCT/DK2006/000032 (published as WO 2006/076921), filed Jan. 20, 2006, which claimed priority of Danish Patent Application PA 2005 00113, filed Jan. 21, 2005; this application further claims priority under 35 U.S.C. § 119 of U.S. Provisional Application 60/647,320, filed Jan. 26, 2005.

The present invention relates to an automatic and handheld mechanical injection device where an injection of a set dose of medicament is initiated by actuating a release member being arranged at or near the top of the injection device.

BACKGROUND OF THE INVENTION

Automatic injection devices have previously been disclosed in the patent literature. Automatic injection devices contain some sort of power reservoir where electrical or mechanical energy can be accumulated. The accumulated energy is easily released by actuating a release mechanism whereby the accumulated energy assists the user in injecting a set dose of medicine and/or assisting needle insertion.

For example, EP 0 516 473 A1 discloses an injection device having a needle which, when the device is operated, is first caused to project, then liquid is forced out through it, and finally the needle is automatically retracted. The needle extends forwardly from a capsule that can slide longitudinally within a barrel-like body, a relatively weak spring normally maintaining the capsule and needle retracted. A more powerful spring acts oppositely on a plunger which, when released, shoots the capsule forward by acting on the liquid therein, and then forces the liquid out through the projecting needle. At the end of the forward stroke the plunger and capsule are decoupled and the weak spring returns the exhausted capsule and its needle to the retracted position. The spring acting on the plunger can be released by a release button positioned on the outer surface of the injection device.

In WO 01/41838 discloses a handheld injection device by which set doses of a liquid medicament can be injected from a medical reservoir, such as cylinder ampoule, by release of a power reservoir in the device. The power reservoir can either be an electric battery by which a motor can be energized to press out a set dose of medicine, or a strained spring maintained in its strained position by a detent which spring when released can press out a set dose of medicine. When the power reservoir is released, the liquid medicine will be pressed out from the cylinder ampoule through an injection needle mounted on the cylinder ampoule or on the injection device carrying the cylinder ampoule. The power reservoir is released fully or partially by activating a release button, such as an electric switch, located on the housing of the injection device and in the distal half of the length of the injection device. By making at least a part of the distal third of the injection device of an ergonomic shaped cross section,

the user can grip the injection device as a pencil is gripped by a thumb, an index finger and a long finger.

In both EP 0 516 473 A1 and WO 01/41838 the release buttons are positioned on an outer surface of the injection devices. In EP 0 516 473 A1 the release button is position on the outer side of the cylindrical body, whereas in WO 01/41838 the release button is positioned close to the injection needle of the injection device. However, it may be advantageous to position the release button or mechanism so that the injection device can be activated by providing a force to the upper region of the injection device—preferably to a release button or mechanism arranged axially with the injection device.

It is an object of the present invention to provide an automatic and handheld mechanical injection device having a combined release member and dose setting member

It is a further object of the present invention to provide an automatic and handheld mechanical injection device where an injection of a set dose can be initiated using the thumb or the index finger of the hand handling the injection device by providing an axial force to an upper region of the injection device.

It is a still further object of the present invention to provide an automatic and handheld mechanical injection device having an exterior design very similar to conventional manual injection devices.

SUMMARY OF THE INVENTION

The above-mentioned objects are complied with by providing, in a first aspect, a handheld injection device by which set doses of a liquid medicament can be injected from a medical reservoir through an injection needle by release of a power reservoir in the device, the power reservoir being adapted to be fully or partially released by actuation of a user operable release member positioned at or near an upper end of the injection device, the upper end being that end of the injection device which is opposite the injection needle, the power reservoir being adapted to be powered by rotation of a rotatably mounted dose setting member.

The amount of power provided to the power reservoir may depend on the angle of rotation of the dose setting member. Thus, a rather limited rotation of the dose setting member provides a relatively small amount energy to the power reservoir, whereas a large rotation of the dose setting member provides a relatively large amount of energy to the power reservoir.

The release member may be positioned less than one fifth or one sixth of the length of the injection device from the upper end. Alternatively, the release member may be axially arranged relative to the injection device so that the release member forms a push button like release member on the top of the injection device.

The release member may be operatively connected to a dose setting member of the injection device in that the release member may engage the dose setting member via a key/keyway connection when the dose setting member is in a dose setting position. The release member may be released from the key/keyway connection with the dose setting member when the dose setting member is in a dose injecting position. With this arrangement, the handheld injection device has no rotating exterior parts or elements.

The power reservoir may be a resilient member, such as a torsion spring or a linear spring, the resilient member being, when released, adapted to press out a set dose of medicine from the medical reservoir through the injection needle. The release member may be operatively connected

to a release mechanism adapted to release the resilient member when said release member is actuated. The release member may have a shape which is ergonomic shaped to be activated by a thumb or an index finger of the user.

The medical reservoir may be a cylindrical ampoule comprising a first and a second end of which the first end is closed by a pierceable membrane which may be pierced by a first end of the injection needle when this needle is mounted on the device. The other end of the injection needle may be sharp so as to be able to pierce the skin at the position where an injection is to be made. The second end of the ampoule may be closed by a piston which may be forced into the ampoule so as to expel medicament through the needle.

The handheld injection device may further comprise a rotatably arranged drive member being adapted to at least partly engage with at least part of a drive track of an associated piston rod, the drive member being adapted to be positioned in a first axial position when the dose setting member is in a dose setting position, the drive member further being adapted to be positioned in a second axial position when the dose setting member is in a dose injection position, the drive member being adapted to release energy accumulated in the power reservoir when the drive member is in its second axial position.

The drive member may be adapted to rotate the associated piston rod upon releasing the accumulated energy in the power reservoir. However, in its first axial position, the drive member is prevented from rotating because the drive member engages at least part of a housing of the injection device. The injection device may further comprise a resilient member, such as a linear spring, for biasing the drive member in a direction towards the dose setting member. The linear spring operatively connects the drive member and the housing.

The dose setting member may be adapted to be moved a distance along an axial direction of the injection device so as to move the drive member between the first and second axial positions. The drive member may be adapted to be moved from the first to the second axial position by applying a force to the dose setting member, the force being applied along the axial direction of the injection device.

The injection device may, as already mentioned, further comprise a push button axially arranged with the dose setting member, the push button being adapted to engage with the dose setting member when the dose setting member is in its dose setting position, and disengage from the dose setting member when the dose setting member is in its dose injection position. By disengage is meant that the push button and the dose setting member are mutually rotatable when this disengaged state is reached. The injection device may further comprise a resilient member, such as a linear spring, for axially biasing the push button in a direction away from the drive member.

The handheld injection device may further comprise a rotatably mounted display member adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member, the rotatably mounted display member being rotatable over an angle corresponding to at least one revolution of the display member. The display member may comprise a dose indicator barrel having numerals arranged along a substantially helical path on an outer surface thereof. Alternatively or in addition, the display member may comprise a counting device having two or more display wheels having numerals arranged on an outer surface thereof.

The handheld injection device may further comprise the associated the piston rod, the piston rod having a threaded outer surface with the drive track arranged in a longitudinal direction of the outer surface of the piston rod. The drive member may be operatively connected to the dose setting member via a ratchet.

The power reservoir may be arranged between the housing and the dose setting member in such a way that when the dose setting member is rotated, energy is accumulated in the power reservoir. The power reservoir may comprise a torsion spring formed as a helical spring extending coaxially with the associated piston rod.

It is to be noted that the interaction between the drive member, the piston rod and the housing may be implemented in various ways. Above, the piston rod has a threaded outer surface and a drive track arranged in the longitudinal direction of the rod. A key arranged on the drive member engages the drive track of the rod and the forward movement of the rod relative to the housing is caused by the threaded outer portion of the rod which meshes with a corresponding threaded portion of the housing. Alternatively, the threaded outer surface of the rod may mesh with a corresponding threaded portion of the drive member whereas the drive track arranged in the longitudinal direction of the rod engages with a key fixedly arranged relative to the housing.

BRIEF DESCRIPTION OF THE INVENTION

The present invention will now be explained in further details with reference to the accompanying figures wherein

FIG. **1** shows an injection device according to the present invention where the release button arranged at the top of the device is activated by the thumb of the user,

FIG. **2** shows an injection device according to the present invention where the release button arranged at the top of the device is activated by the index finger of the user,

FIG. **3** shows an injection device according to the present invention where the release button is arranged on the top surface of the dose setting member, and where the drive member is in its locked position (dial position of dose setting member),

FIG. **4** shows an injection device according to the present invention where the release button is arranged on the top surface of the dose setting member, and where the drive member is in its released position (dosing position of dose setting member),

FIG. **5** shows an expanded view of the drive member in its released position,

FIG. **6** shows an expanded view of the release member in its locked position with the dose setting member,

FIG. **7** shows an expanded view of the release member in its released position with the dose setting member,

FIG. **8** shows an expanded view of the release member in a further released position where the dose setting member is allowed to rotate,

FIG. **9** shows one way of implementing the release mechanism for releasing the energized power reservoir,

FIG. **10** shows another way of implementing the release mechanism for releasing the energized power reservoir,

FIG. **11** shows a third way of implementing the release mechanism for releasing the energized power reservoir,

FIG. **12** shows a fourth way of implementing the release mechanism for releasing the energized power reservoir, and

FIG. **13** shows a fifth way of implementing the release mechanism for releasing the energized power reservoir.

While the invention is susceptible to various modifications and alternative forms, specific embodiments have been

shown by way of example in the drawings and will be described in detail herein. It should be understood, however, that the invention is not intended to be limited to the particular forms disclosed. Rather, the invention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the appended claims.

DETAILED DESCRIPTION OF THE INVENTION

FIGS. **1** and **2** show the present invention in its most general aspect. In FIG. **1** a handheld injection device **1** is shown. The injection device has an injection needle **2** fastened to one of its ends, whereas a release button **3** is arranged at the opposite end of the injection device. When the release button **3** is actuated by provided a force to it along the axial direction of the device energy is released from an internal power reservoir whereby a set dose of medicine is injected from the injection device. In FIG. **1** the release button is actuated by the thumb **4** of the user, whereas in FIG. **2** the release button is actuated by the index finger **5** of the user.

The medicine to be injected is contained in a medical reservoir typically formed as a cylindrical ampoule.

The energy released when the release button **3** is mechanical energy. The power reservoir can be a resilient member, such as a torsion spring, the resilient member being, when released, adapted to press out a set dose of medicine from the medical reservoir through the injection needle. The release button is operatively connected to some sort of release mechanism adapted to release the resilient member when the release button is actuated.

FIG. **3** shows a cross-sectional view of one embodiment of the present invention. The injection device shown in FIG. **3** comprises a housing **6**, a dose setting member **7**, a drive member **8**, a piston rod **9**, a torsion spring **10**, a biasing spring **11**, a cylindrical ampoule **12** and a release member **13**. FIG. **3** shows the injection device in a state where the dose setting member **7** is in its dose setting position.

A dose is set by rotating the dose setting member **7** a certain angle or a certain number of turns. By rotating the dose setting member **7** the torsion spring **10** is strained because the two ends of the torsion spring **10** are fixed to the housing **6** and to the dose setting member **7**, respectively. The dose setting member **7** is operatively connected to the drive member **8** via a ratchet (not shown). This ratchet prevents that the dose setting member **7** returns to its initial position upon straining the torsion spring **10**. Since the drive member **8** engages the housing **6** via a key/keyway connection or a gear wheel, the drive member **8** is not allowed to rotate relative to the housing **6** as long as the dose setting member **7** is in its dose setting position as illustrated in FIG. **3**. In order to keep the dose setting member **7** and the drive member **8** in the dose setting position, the drive member **8** and the dose setting member **7** is biased in a direction towards the top end of the injection device. This biasing is provided by a spring element, such as a linear spring **11**, arranged between the drive member **8** and part of the housing **6**. Thus, in order to release the drive member **8** from its engagement with the housing **6**, a force needs to be provided in order move the dose setting member **7** and the drive member **8** towards the medicine ampoule **12**. A miner cavity **14** ensures that this forward movement of the dose setting member **7** and the drive member **8** can be performed. Similarly, since the drive member **7** and the piston rod **9** engage via a key connection the drive member **8** is allowed to move axially relative to the piston rod **9**.

The drive member **8** has been released from its engagement with the housing **6** in FIG. **4**. In order to achieve this releasing a force, indicated by arrow **15**, has been provided to the release member **13** whereby the release member **13**, the dose member **7** and the drive member **8** have all been moved a distance towards the medicine ampoule **12**. The force indicated by arrow **15** would normally be provided by the thumb or the index finger of the user.

As seen in FIG. **4** the engaging region **16** of the housing is now separated from the engaging region **17** of the drive member **8**. This disengagement allows that the strained torsion spring **10** can release its energy to the dose setting member **7**. The dose setting member **7** and the drive member **8** are fixedly related via the intermediate ratchet (not shown). Thus, when a disengagement between engaging regions **16** and **17** has been established, the dose setting member **7** and the drive member **9** will rotate until the torsion spring **10** reaches an unstrained state. Since the drive member **8** and the piston rod **9** is connected via a key connection the rotation of the dose setting member **7** and the drive member **8** will cause the piston rod **9** to rotate as well. The piston rod **9** has an outer threaded surface which engages with a corresponding threaded portion **18** of the housing whereby the piston rod **9**, upon rotation thereof, will perform a translational movement along the axial direction of the injection device in the direction of the ampoule **12**.

Thus, the force provided to the release member **13** will release accumulated energy in the torsion spring. This energy is converted to a translational movement of the piston rod towards the ampoule whereby a set dose of medicine can be injected from the injection device.

FIG. **5** shows a cut half illustration of the housing **6** of the injection device. As seen, the drive member **8** comprises an engagement region/part **17** formed as gear wheel. Similarly, the housing **6** comprises a corresponding engagement region/part **16** adapted to receive and engage with the teeth of the gear wheel **17**.

FIG. **6** shows another embodiment of the present invention. In contrast to the embodiment shown in FIGS. **3-5** the embodiment shown in FIG. **6** contains no rotating exterior parts or elements. All rotating parts or elements are positioned inside the housing **19**. FIG. **6** shows a release member **20** (formed as a push button) which is mechanically biased towards the end of the injection device by spring element **22**. The release member **20** and dose setting member **21** are forced into engagement as long as the dose setting member **21** is in its dose setting position. The dose setting member **21** is mechanically biased towards the same end of the injection device as the release member **20** due to a spring element (shown as spring element **11** in FIG. **3**) acting on the drive member (shown as drive member **8** in FIG. **3**) which again acts on dose setting member **21**. As seen in FIG. **6** the dose setting member **21** is biased against a mechanical stop **24** where a shoulder formed in the dose setting member **21** abuts a part of the housing **19**.

In FIG. **7** an intermediate stage is illustrated. Here the release member **20** has been pushed an axial distance sufficient to release the release member **20** from the dose setting member **21**. Note that the engagement region **25** and **26** are disengaged, but since the shoulder of the dose setting member still abuts the housing part no axial movement of the dose setting member **21** has been achieved at this stage. Thus, the dose setting member **21** is prevented from rotating since the drive member (not shown) is still engaging the housing.

In FIG. **8** the dose setting member **21** has been moved an axial distance towards the ampoule (not shown) whereby the dose setting member is allowed to rotate freely causing the piston rod **27** push a set dose of medicine out of the ampoule (not shown). Note that the release member **20** and the dose setting member **21** are disengaged in FIG. **8**. This means that the release member **20** is not rotating relative to the housing during injection of a set dose. Then the set dose has been injected the user removes his thumb or index finger from the release member whereby the release member and the dose setting member return to their respective positions as illustrated in FIG. **6**, but now with the spring element **23** being in a relaxed state.

In case the user wants to set a new dose, the user rotates the release member which engages the dose setting member whereby the new dose can be set. Injecting the set dose is achieved by following the steps illustrated in FIGS. **7** and **8**.

FIGS. **9-13** show various embodiments of release mechanisms for releasing the energized power reservoir.

In FIG. **9** a torsion spring (not shown) is energized by rotating a ratchet **28** which is operatively connected to the housing **30** of the injection device when the dose to be injected is being set. In the dose setting position the ratchet **28** is operatively connected with housing part **31** via ratchet arm **32**. Energy accumulated in the torsion spring is released by displacing the ratchet **28** axially whereby it is released from its connection with housing part **31** in that the ratchet arm **32** is moved into housing part **33** whereby the piston rod **34** is allowed to rotate thereby expelling a set dose of medicament.

In the embodiment depicted in FIG. **9** a dose indicator barrel (not shown) moves in the direction away from the push-button (not shown) during setting of a dose. Obviously, the dose indicator barrel may be adapted to move in the opposite direction during setting of a dose, i.e. towards the push-button.

In the embodiment depicted in FIG. **10** the ratchet **35** is only in indirect operation with the housing **39**. The drive member of the embodiment depicted in FIG. **10** is constituted by three part—one part **36** being adapted to corporate with the housing **39**, another part **38** being adapted to drive the piston rod **40** and a flexible member **37** connecting parts **36** and **38**. The flexible member **37** is flexible in the axial direction but establishes a substantially stiff connection between parts **36** and **38** when these parts are rotated relative to each other. Thus, the flexible member **37** ensures that parts **36** and **38** are not rotatably arranged relative to each other. Thus, when the ratchet **35** is moved towards the needle end of the injection device the part **36** is disconnected from the housing **39** whereby parts **36**, **37** and **38** are allowed to rotate thereby rotating the piston rod **40**. The rotating piston rod **40** causes a set dose of medicament to be expelled from the injection device.

The embodiment depicted in FIG. **11** is similar to the embodiment in FIG. **9** except that the piston rod is moved forward by having guiding tracks arranged in the housing (instead of in the drive member) and a threaded engagement between piston rod and the drive member (instead of a threaded engagement between piston rod and housing).

FIGS. **12** and **13** show other release mechanisms between ratchet, drive member and housing.

The invention claimed is:

1. A handheld injection device, comprising:

a rotatable dose setting member,

a power reservoir comprising a torsion spring for storing energy to expel a dose of medication from the injection device,

a release member axially arranged relative to the injection device, wherein the release member forms a push button like release member,

the injection device further comprising a multi-component driver (**36**, **37**, **38**) having at least a part (**38**) adapted to drive a piston rod, and a further part (**36**) being axial movable into a position disconnected from the housing releasing the energy accumulated in the power reservoir, the further part (**36**) being axially movable by the user applying a force onto the push button like release member, wherein the release member is located at the most proximal portion of the proximal end of the injection device, opposite an end of the device wherein a needle may be mounted, and

wherein the injection device further comprises a display member adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member.

2. A handheld injection device according to claim **1**, wherein the amount of power provided to the power reservoir (**10**) depends on the angle of rotation of the dose setting member (**7**).

3. A handheld injection device according to claim **1**, wherein the release member is operatively connected to the dose setting member of the injection device.

4. A handheld injection device according to claim **3**, wherein the release member engages the dose setting member via a key/keyway connection when the dose setting member is in a dose setting position.

5. A handheld injection device according to claim **4**, wherein the release member is released from the key/keyway connection with the dose setting member when the dose setting member is in a dose injecting position.

6. A handheld injection device according to claim **1**, wherein when energy from the torsion spring is released it is adapted to expel a set dose of medicine from a medicine containing reservoir through the injection needle.

7. A handheld injection device according to claim **1**, further comprising a rotatably arranged drive member (**8**) being adapted to at least partly engage with at least part of a drive track of an associated piston rod (**9**), the drive member (**8**) being adapted to be positioned in a first axial position when the dose setting member (**7**) is in a dose setting position, the drive member (**8**) further being adapted to be positioned in a second axial position when the dose setting member (**7**) is in a dose injection position, the drive member (**8**) being adapted to release energy accumulated in the power reservoir (**10**) when the drive member (**8**) is in its second axial position.

8. A handheld injection device according to claim **7**, wherein the drive member is adapted to rotate the associated piston rod upon releasing the accumulated energy in the power reservoir.

9. A handheld injection device according to claim **7**, wherein the drive member is prevented from rotating when it is in its first axial position.

10. A handheld injection device according to claim **7**, further comprising a resilient member, such as a linear spring, for biasing the drive member in a direction towards the dose setting member.

11. A handheld injection device according to claim **7**, wherein the dose setting member is adapted to be moved a distance along an axial direction of the injection device so as to move the drive member between the first and second axial positions, the drive member being movable from the first to the second axial position by applying a force to the dose

setting member, the force being applied along the axial direction of the injection device.

12. A handheld injection device according to claim **7**,

wherein the dose setting member is rotatably mounted and rotatable about a longitudinal axis of a housing of the injection device, and

wherein the display member is rotatably mounted and rotatable over an angle corresponding to at least one revolution of the display member, the display member comprising a dose indicator barrel having numerals arranged along a substantially helical path on an outer surface thereof.

13. A handheld injection device according to claim **7**, further comprising the associated the piston rod, the piston rod having a threaded outer surface with the drive track arranged in a longitudinal direction of the outer surface of the piston rod.

14. A handheld injection device according to claim **7**, wherein the drive member is operatively connected to the dose setting member via a ratchet.

15. A handheld injection device according to claim **1**, wherein the multi-component driver (**36**, **37**, **38**) is rotatably arranged.

* * * * *

EXHIBIT N

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Eiland et al.

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(54) **SYRINGE DEVICE WITH A DOSE LIMITING MECHANISM AND AN ADDITIONAL SAFETY MECHANISM**

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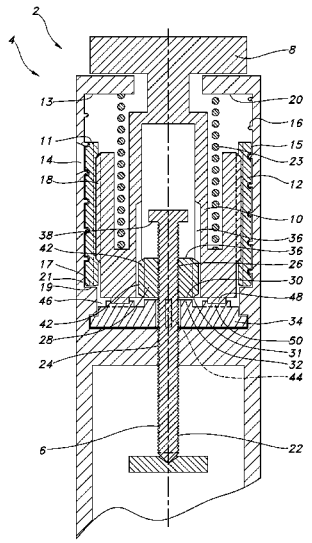
(57) **ABSTRACT**

A syringe device for ejecting a dose of a medicament, the syringe device comprising: a dose limiting mechanism arranged to interact with a dose ejecting mechanism to prevent ejection of a dose exceeding a set dose, and a safety mechanism, which is arranged such with respect to the dose ejecting mechanism that, if the dose limiting mechanism fails, the safety mechanism prevents ejection of a dose exceeding the set dose.

7 Claims, 1 Drawing Sheet



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See application file for complete search history.

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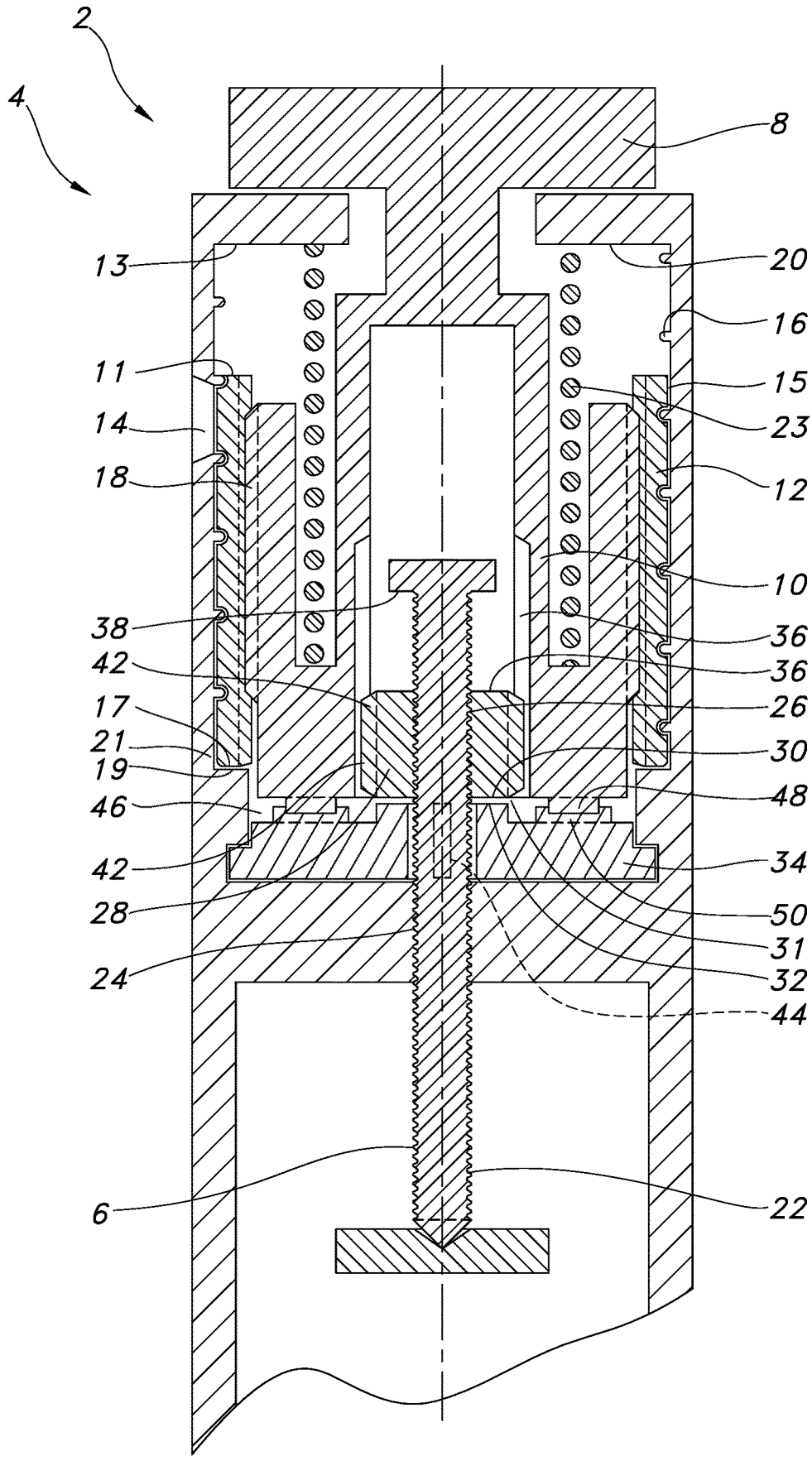
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SYRINGE DEVICE WITH A DOSE LIMITING MECHANISM AND AN ADDITIONAL SAFETY MECHANISM

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a Continuation of U.S. application Ser. No. 11/996,397, filed Mar. 20, 2008, which is a 35 U.S.C. § 371 national stage application of International Patent Application PCT/EP2006/007006 (published as WO 2007/017053), filed Jul. 17, 2006, which claimed priority of European Patent Application 05016286.6, filed Jul. 27, 2005; this application further claims priority under 35 U.S.C. § 119 of U.S. Provisional Application 60/708,211, filed Aug. 15, 2005. The contents of all above-named applications are incorporated herein by reference.

FIELD OF THE INVENTION

The present invention relates to a syringe device comprising a mechanism for preventing ejection of a dose exceeding a set dose. In particular the present invention relates to a syringe device comprising two independent mechanisms for preventing ejection of a dose exceeding a set dose.

BACKGROUND OF THE INVENTION

When drugs are to be injected into the human body, it may have serious or even lethal consequences if the injected dose exceeds the set dose. Accordingly, it is important that the syringe devices comprises means for limiting ejection to the set dose.

It is an object of the present invention to provide a syringe device comprising means for prevention ejection of a dose exceeding the set dose. Furthermore, as such means may fail, it is an object of the present invention to provide a syringe device comprising a safety mechanism adapted to prevent ejection of a dose exceeding the set dose if the means for preventing fails.

SUMMARY OF THE INVENTION

The present invention relates to a syringe device for ejecting a dose of a medicament, the syringe device comprising:

- a housing,
- a dose ejecting mechanism comprising:
  - a dose setting member being rotatable in relation to the housing so as to set a dose to be ejected,
  - a piston rod arranged with respect to the housing such that translational movement of the piston rod in a distal direction causes the dose to be ejected,
  - means for transforming translational movement of the dose setting member into translational movement of the piston rod,
- a dose limiting mechanism arranged to interact with the dose ejecting mechanism to prevent ejection of a dose exceeding the set dose, and
- a safety mechanism, which is arranged such with respect to the dose ejecting mechanism that, if the dose limiting mechanism fails, the safety mechanism prevents ejection of a dose exceeding the set dose.

An advantage of the present invention is that if a dose limiting mechanism fails to limit the ejected dose, the security mechanism is activated, and, thus, provides an extra safety for the patient.

In one embodiment the dose limiting mechanism and the safety mechanism are two independent mechanisms working independently from each other.

In one embodiment the two mechanisms are adapted to simultaneously prevent ejection of a dose exceeding the set dose. In another embodiment the safety mechanism is only activated if the dose limiting mechanism fails to prevent ejection of a dose exceeding the set dose. In one embodiment the two mechanisms are arranged such that even if the dose limiting mechanism fails, the safety mechanism is activated instantaneously such that the ejected dose does not exceed the set dose. In another embodiment the ejected dose is insignificantly larger than the set dose, if the dose limiting mechanism fails and the safety mechanism is activated. By insignificantly larger is meant that the change in dose is too small to have serious or fatal consequences.

The housing may define a passage for the piston rod, the passage may have a threaded inner surface for engagement with a threaded outer surface of the piston rod, the piston rod may be arranged with respect to the housing such that rotation of the piston rod relative to the housing causes the piston rod to be displaced translationally relative to the housing.

In one embodiment at least one of the dose limiting mechanism and the safety mechanism is adapted to limit relative rotational movement between the piston rod and the housing, to a rotation corresponding to ejection of the set dose. This may be the case, when the piston rod comprises a threaded outer surface adapted to engage a threaded inner surface of the housing. Accordingly, rotational locking of the piston rod (relative to the housing) results in a translational locking of the piston rod relative to the housing.

The dose limiting mechanism may comprise at least one first stopping surface adapted to engage at least one corresponding second stopping surface of the housing. Furthermore, rotation of the dose setting member during dose setting may cause the first stopping surface to move away from the second stopping surface and rotation during dose ejection may cause the first and the second surface(s) to move towards each other. Furthermore, ejection of a dose may be prevented when the first stopping surface abut the second stopping surface. The dose setting member may comprise the at least one first stopping surface. Alternatively, or as a supplement, the dose setting member may be coupled to a cylinder comprising a first stopping surface, and said cylinder may be adapted to indicate the set dose. The first and second stopping surfaces may be substantially plane surfaces which may extend in a direction parallel with the axial direction of the syringe device. Alternatively, the stopping surfaces may extend in a plane transverse to the axial direction, such as a plane orthogonal to the axial direction.

In one embodiment the safety mechanism comprises: a limiter defining a passage for the piston rod, the passage of the limiter defining a threaded inner surface for engagement with the threaded outer surface of the piston rod, and a driver defining a passage for the limiter, the driver being rotationally retained in relation to the limiter, the driver being coupled to the dose setting member such that rotation of the dose setting member during dose setting causes the driver to rotate, wherein relative rotation between the drive and the piston rod during dose setting causes the limiter to move away from a stopping position wherein the limiter prevents ejection of a dose.

In one embodiment the syringe device is adapted to prevent setting of a dose which exceeds the amount of a medicament in a reservoir of the syringe device. In such

embodiments, the piston rod may comprise an end-of-dose stopping surface adapted engage a corresponding surface of the limiter, when the set dose corresponds to the amount of the medicament in the reservoir of the device. Accordingly, in such embodiments the limiter serves two functions, a first function being prevention of setting of a dose exceeding the amount of the medicament left in the reservoir and a second function being a security function adapted to prevent ejection of a dose exceeding the set dose.

Moreover, the syringe device may comprise an ejection assisting system for providing an ejection force for assisting an operator of the device in forcing the piston in said distal direction so as to eject the set dose. The ejection assisting system may be adapted to force the piston in the distal direction so as to eject the dose, without the aid of the user, when the user has initiated the ejection.

The ejection assisting system may comprise a spring, such as a torsional spring which is arranged to rotate the driver relative to the housing. The spring may be pre-strained when limiter is in the stopping position. Especially when the spring is pre-strained, the redundant security system of the present invention is advantageous, as accidental un-straining of the pre-strained spring, may cause the piston rod to rotate (and thus move translationally) corresponding to a lethal dose, such as 100 IU of insulin.

DESCRIPTION OF THE DRAWINGS

The invention will now be described in further detail with reference to FIG. **1**, which discloses a syringe device according to the present invention.

FIG. **1** shows a syringe device **2** comprising a housing **4** and a piston rod **6**. The syringe device **2** also comprises a dose setting member **8** and a driver **10**, which in the FIGURE are combined into one single unit. The syringe device further comprises a scale drum **12** for indicating a set dose through a window **14**. The scale drum **12** has a threaded outer surface **15** adapted to engage a corresponding threaded inner surface **16** of the housing. The scale drum **12** is rotationally retained relative to the driver **10** through a grove-tongue engagement **18**. The drum scale **12** comprises a first stopping surface **17** adapted to engage a second stopping surface **19** of the housing. The first stopping surface **17** and the second stopping surface **19** constitutes the dose limiting mechanism **21**. The first stopping surface is moved away from the second stopping surface **19** during dose setting and towards each other during dose ejecting. When the two surfaces abut each other, the device is prevented from ejecting the medicament.

FIG. **1** further shows an example of a dose setting member **8** rotatable and longitudinally fixed in relation to the housing **4** so as to set a dose to be injected.

The syringe device comprises an ejection assisting system in the form of a pre-strained torsional spring **23** extending between the driver **10** and a proximal part **20** of the housing. Accordingly, when the dose setting member **8** is rotated to set a dose, the spring is strained even further.

The piston rod **6** comprises a threaded outer surface **22** adapted to engage a corresponding threaded inner surface of the housing **24** and accordingly rotation of the piston rod relative to the housing causes the piston rod to move translationally in relation to the housing. The threaded outer surface **22** of the piston rod also engages a threaded inner surface **26** of a limiter **28**, which in FIG. **1** is positioned in a stopping position wherein a bottom surface **30** of the limiter engages an upper surface **32** of a piston rod guide **34**. The bottom surface **30** and the upper surface **32** constitute the safety mechanism **31**. An air gap may be provided between the bottom surface **30** and the upper surface **32** which allows the limiter and the piston rod to rotate an angel corresponding an insignificant increase in the injected dose e.g. 3 IU of insulin, if the dose limiting mechanism **21** fails during dose injection.

Moreover, an upper end-of-content surface **36** of the limiter **28** is adapted to engage a lower end-of-content surface **38** of a T-shaped end part **40** of the piston rod. The end-of-content surfaces are adapted to engage, when the set dose corresponds to the amount of a medicament remaining in a reservoir (not shown) of the device. Accordingly, the engagement of the end-of-content surfaces prevents setting of a dose exceeding the amount of a medicament remaining in the reservoir. It will be appreciated that the distance between the end-of-content surfaces thus corresponds to the amount of the medicament remaining in the reservoir.

Moreover, an upper surface **11** of the drum **12** may be adapted to engage a lower surface **13** of the housing, when the maximum dose is set. The maximum dose is the largest dose which may be set for each ejection (provided that the syringe device comprises the required amount of medicament). The maximum dose does not correspond to the end-of-content dose which relates the remaining amount of a medicament in the device. Accordingly, as long as the remaining amount of medicament in the device is larger than the maximum dose, the end-of-content surfaces will not abut each other during dose setting, whereas when the remaining amount of medicament in the device is lower than the maximum dose, the maximum dose surfaces will not abut each other during dose setting, as the end-of-content surfaces prevents further rotation.

The limiter **28** and the driver **10** are locked for relative rotation by means of grove-tongue engagement **42**. Thus, when the piston rod is locked for rotation relative to the housing, a relative rotation between the driver **8** and the piston rod **6** causes the limiter to move away from the stopping position and towards the t-shaped end part **40** (i.e. upwards in the FIGURE). The piston rod is locked for rotation relative to the housing when the piston rod guide **34** is locked for rotation relative to the housing (not shown), as the piston rod guide **34** and the piston rod are locked for relative rotation due to the grove-tongue engagement **44**.

The driver **12** and the piston rod guide **34** are interconnected by a two-way ratchet mechanism **46** comprising at least one first retaining member **48** defined by the driver **12** and at least one second retaining member **50** defined by the piston rod guide **34**. The two-way ratchet mechanism is adapted to allow relative rotational movement between the driver **12** and the piston rod guide **34** during dose setting and to ensure that rotational movement of the driver during dose ejection is transferred to the piston rod guide **34**.

The use of the device is as follows. Initially the piston rod guide is locked for rotation relative to the housing. Then the dose setting member is rotated, which causes the driver and the drum scale to rotate and the pre-strained spring to be strained even further. At the same time the limiter moves towards the T-shaped end part. If the user tries to set a dose exceeding the amount of medicament in the device, the limiter abuts the T-shaped end part whereby an even larger dose cannot be set. The dose is ejected by removing the rotational lock between the piston rod guide **34** and the housing whereby the strained spring forces the driver to rotate. The rotating driver forces the piston rod guide to rotate which again forces the piston rod to rotate. Due to the grove-tongue engagement **44** and the threaded interconnection between the piston rod and the housing, the rotating

piston rod is forced to move forward and thus the medicament is expelled from the device.

The invention claimed is:

1. A syringe device for ejecting a dose of a medicament, the syringe device comprising:

a housing;

a dose ejecting mechanism comprising:

a dose setting member rotatable in relation to the housing so as to set a dose to be ejected,

a piston rod arranged with respect to the housing such that axial movement of the piston rod in a distal direction causes the set dose to be ejected,

structure for transforming rotational movement of the dose setting member into axial movement of the piston rod during ejection of the set dose in the form of an ejection assisting system comprising a pre-strained torsional spring arranged to rotate a driver relative to the housing, the pre-strained torsional spring providing an ejection force forcing the piston rod in the distal direction so as to eject the set dose without the aid of a user, when the user has initiated the injection of the set dose;

a dose limiting mechanism operably connected with the dose ejecting mechanism to prevent ejection of a dose exceeding the set dose, wherein the dose limiting mechanism comprises a first stopping surface adapted to engage a corresponding second stopping surface of the housing, and wherein rotation of the dose setting member during dose setting causes the first stopping surface to move away from the second stopping surface and wherein ejection of a dose is prevented when the first stopping surface abuts the second stopping surface; and

a safety mechanism structure operably connected to the dose ejecting mechanism such that if the dose limiting mechanism fails, the safety mechanism structure prevents ejection of a dose exceeding the set dose.

2. A syringe device according to claim **1**, wherein the housing defines a passage for the piston rod, the passage having a threaded inner surface for engagement with a threaded outer surface of the piston rod, the piston rod being arranged with respect to the housing such that rotation of the piston rod relative to the housing causes the piston rod to be displaced axially relative to the housing.

3. A syringe device according to claim **1**, wherein at least one of the dose limiting mechanism and the safety mechanism structure is adapted to limit relative rotational movement between the piston rod and the housing, to a rotation corresponding to ejection of the set dose.

4. A syringe device according to claim **1**, wherein the dose setting member comprises the first stopping surface.

5. A syringe device according to claim **1**, wherein the dose setting member is coupled to a cylinder comprising the first stopping surface, said cylinder being adapted to indicate the set dose.

6. A syringe device according to claim **1**, wherein the safety mechanism structure comprises:

a limiter defining a passage for the piston rod, the passage of the limiter defining a threaded inner surface for engagement with a threaded outer surface of the piston rod; and

the driver defining a passage for the limiter, the driver being rotationally retained in relation to the limiter, the driver being coupled to the dose setting member such that rotation of the dose setting member during dose setting causes the driver to rotate;

wherein relative rotation between the driver and the piston rod during dose setting causes the limiter to move away from a stopping position wherein the limiter prevents ejection of a dose exceeding the set dose.

7. A syringe device according to claim **1**, wherein the torsional spring is prestrained when the dose limiting mechanism is in a stopping position.

* * * * *

EXHIBIT O

US011311679B2

(12) **United States Patent**
Markussen

(10) **Patent No.: US 11,311,679 B2**
(45) **Date of Patent: *Apr. 26, 2022**

(54) **AUTOMATIC INJECTION DEVICE WITH A TOP RELEASE MECHANISM**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 13 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **16/452,049**

(22) Filed: **Jun. 25, 2019**

(65) **Prior Publication Data**

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(30) **Foreign Application Priority Data**

Jan. 21, 2005 (DK) ..... PA 2005 00113

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A61M 5/315 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC ***A61M 5/31551*** (2013.01); ***A61M 5/20*** (2013.01); ***A61M 5/3156*** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC A61M 5/315–31596; A61M 5/2033; A61M 5/326; A61M 2005/206; A61M 2005/208
See application file for complete search history.

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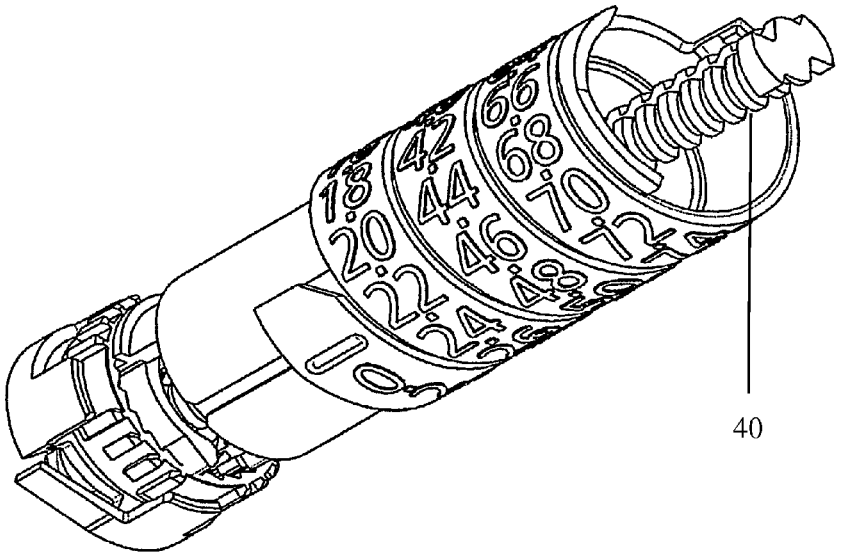
Primary Examiner — Laura A Bouchelle
(74) *Attorney, Agent, or Firm* — Wesley Nicolas

(57) **ABSTRACT**

The present invention relates to a handheld mechanical injection device by which set doses of a liquid medicament can be injected from a medical reservoir. The medicament is expelled through an injection needle by release of a power reservoir in the device, the power reservoir being fully or partially released by actuation of a user operable release member being positioned at or near an upper end of the injection device, the upper end being that end of the injection device which is opposite the injection needle.

6 Claims, 13 Drawing Sheets



Related U.S. Application Data

continuation of application No. 14/797,350, filed on Jul. 13, 2015, now Pat. No. 9,616,180, which is a continuation of application No. 13/326,738, filed on Dec. 15, 2011, now Pat. No. 9,108,002, which is a continuation of application No. 11/813,435, filed as application No. PCT/DK2006/000032 on Jan. 20, 2006, now Pat. No. 8,096,978.

(60) Provisional application No. 60/647,320, filed on Jan. 26, 2005.

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A61M 5/24 (2006.01)

(52) **U.S. Cl.**
CPC ***A61M 5/31525*** (2013.01); ***A61M 5/31528*** (2013.01); ***A61M 5/31553*** (2013.01); ***A61M 5/31585*** (2013.01); *A61M 5/24* (2013.01); *A61M 5/31583* (2013.01); *A61M 5/31593* (2013.01); *A61M 2005/202* (2013.01); *A61M 2005/3126* (2013.01)

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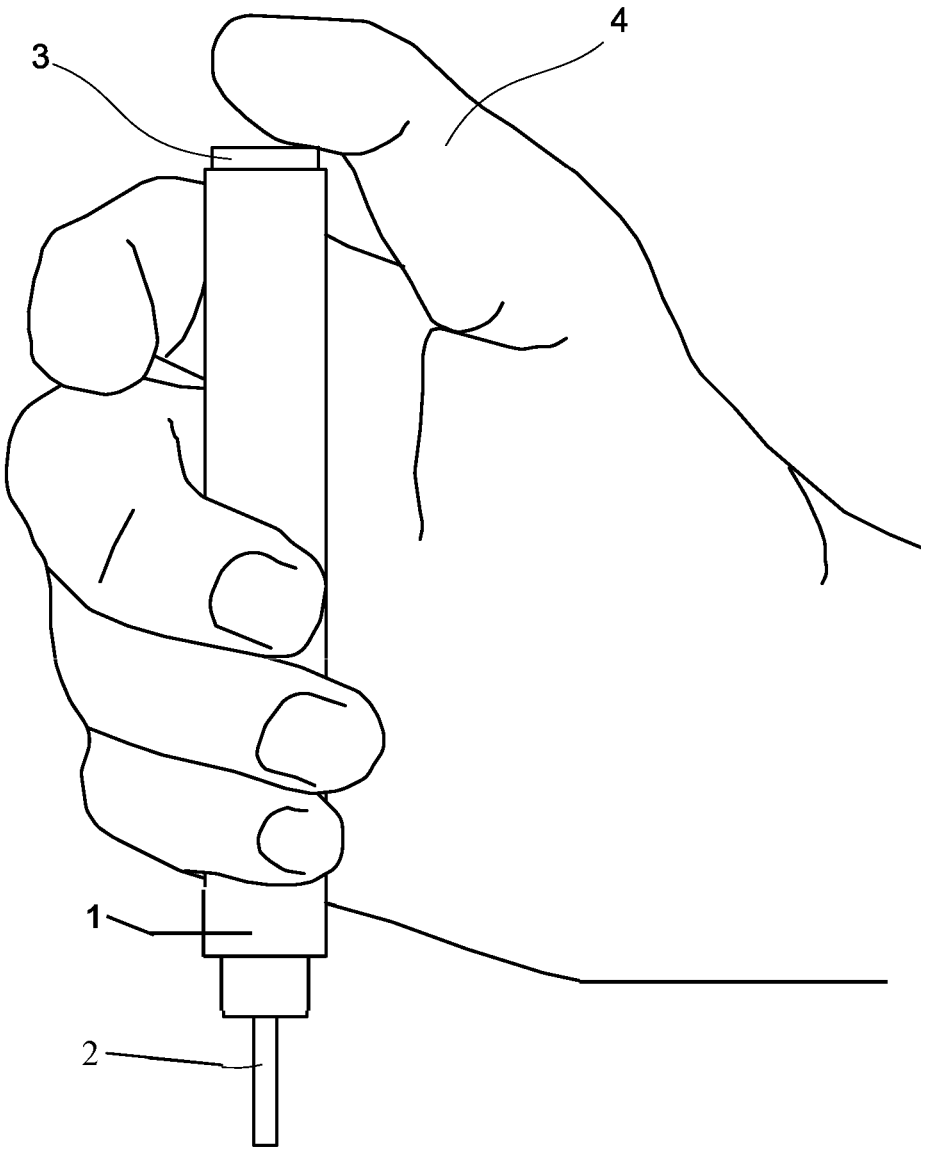


FIG. 1

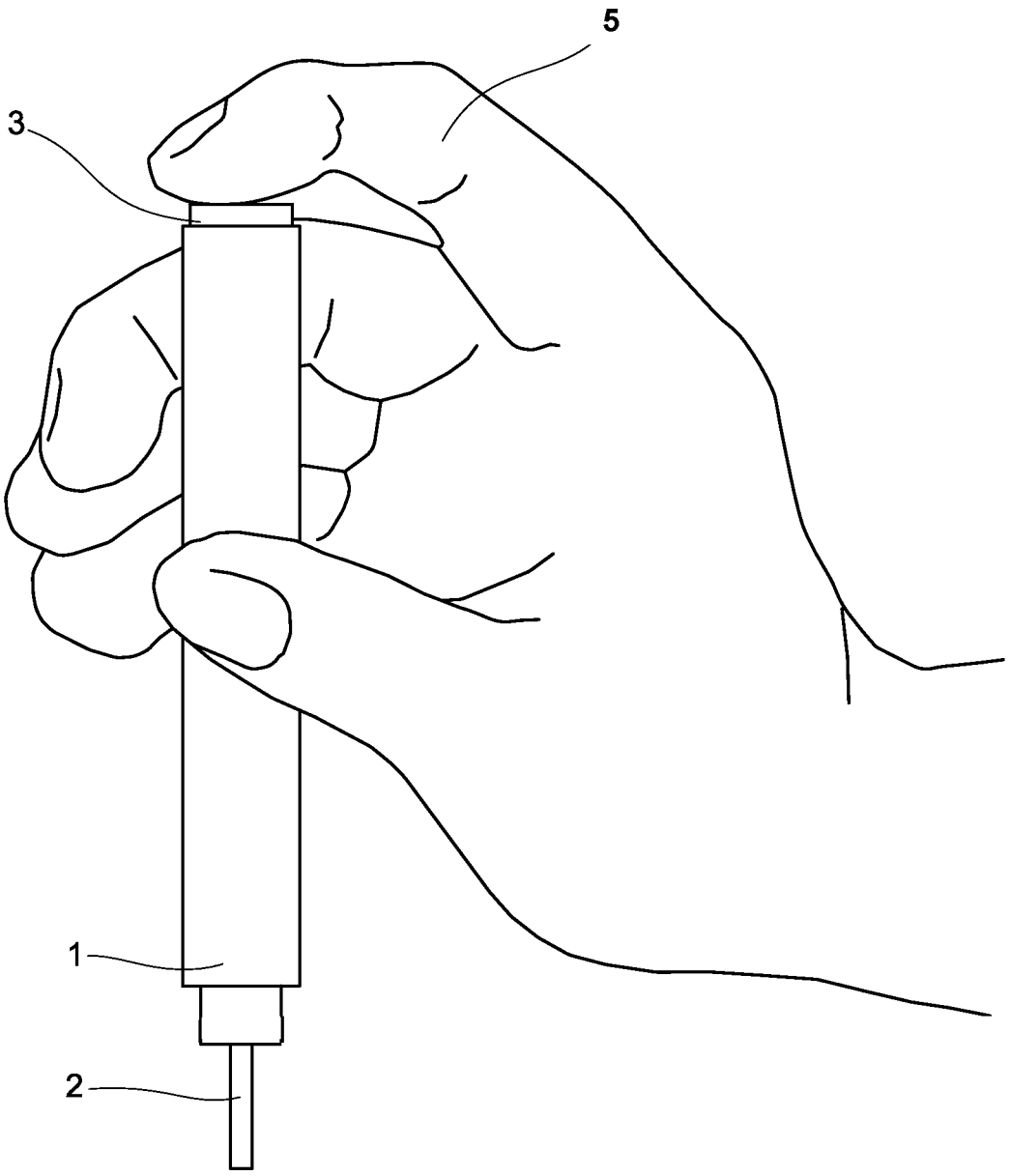


FIG. 2

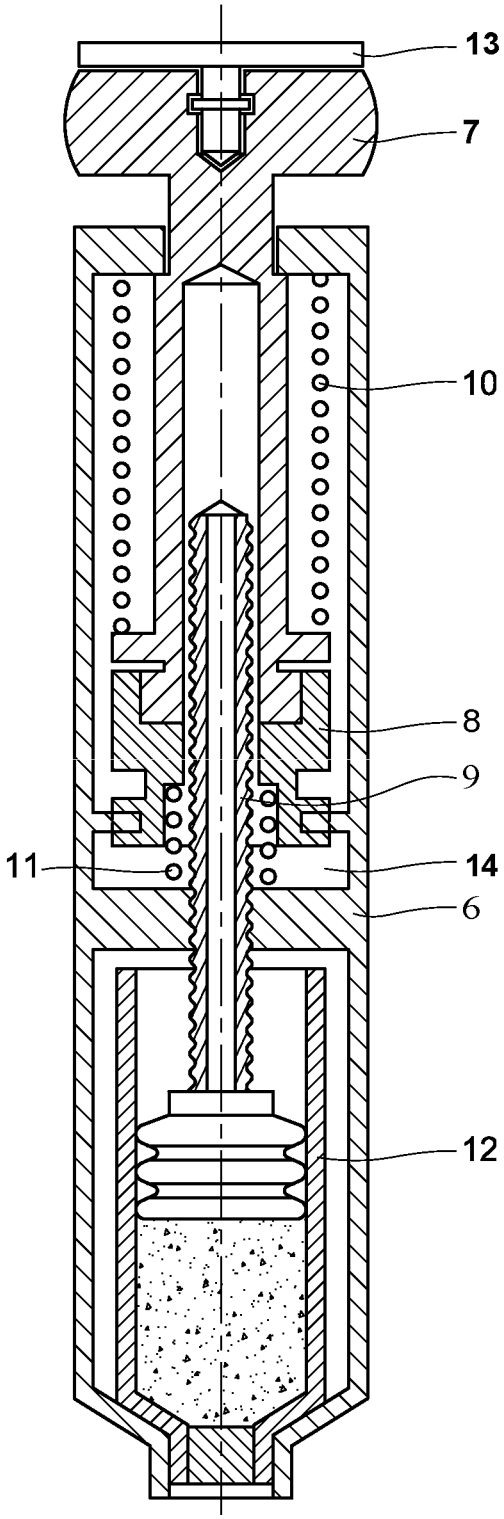
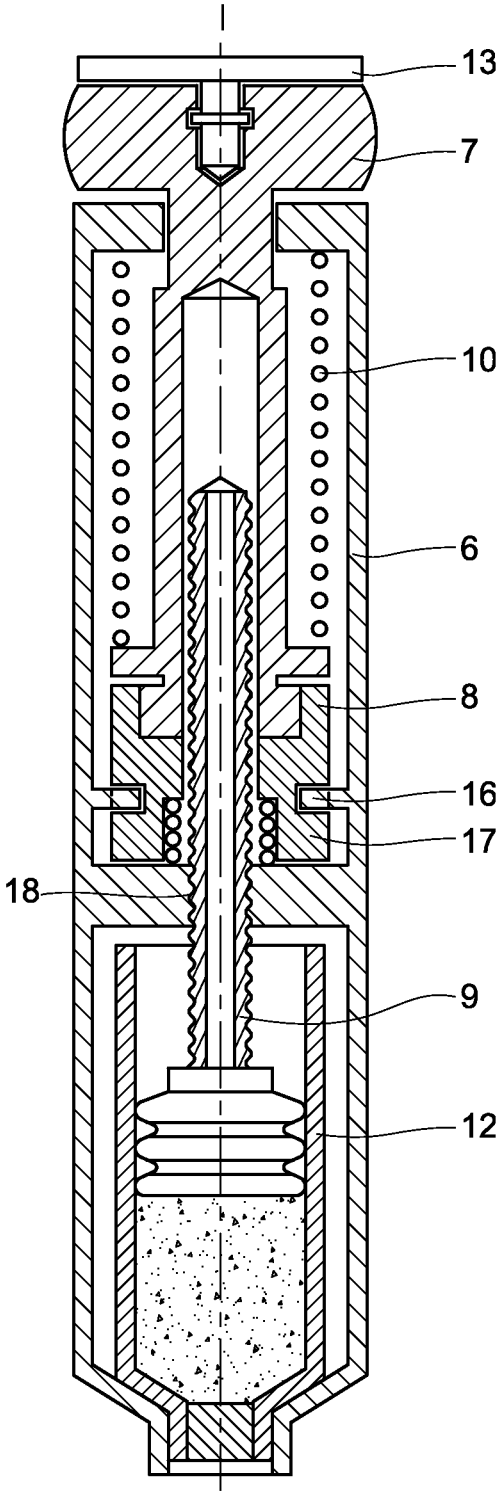


FIG. 3



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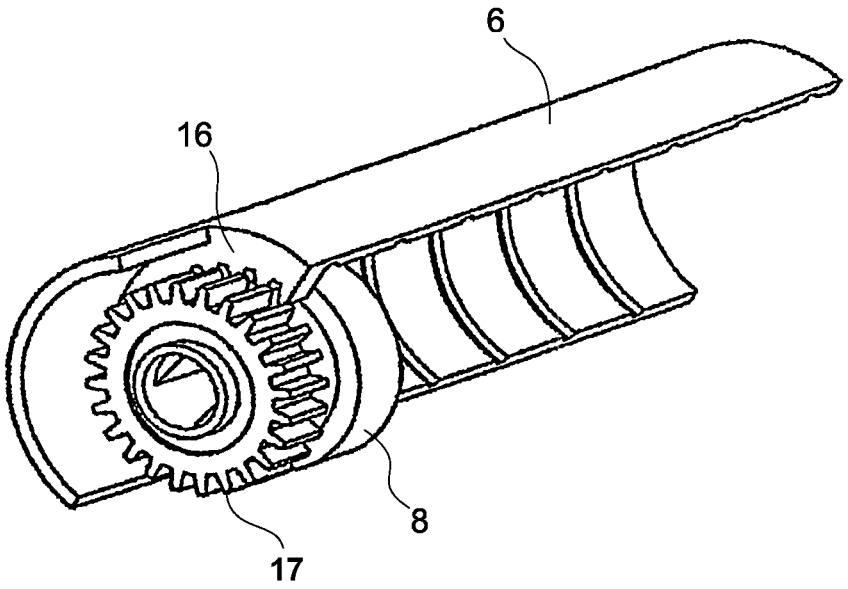

FIG. 5

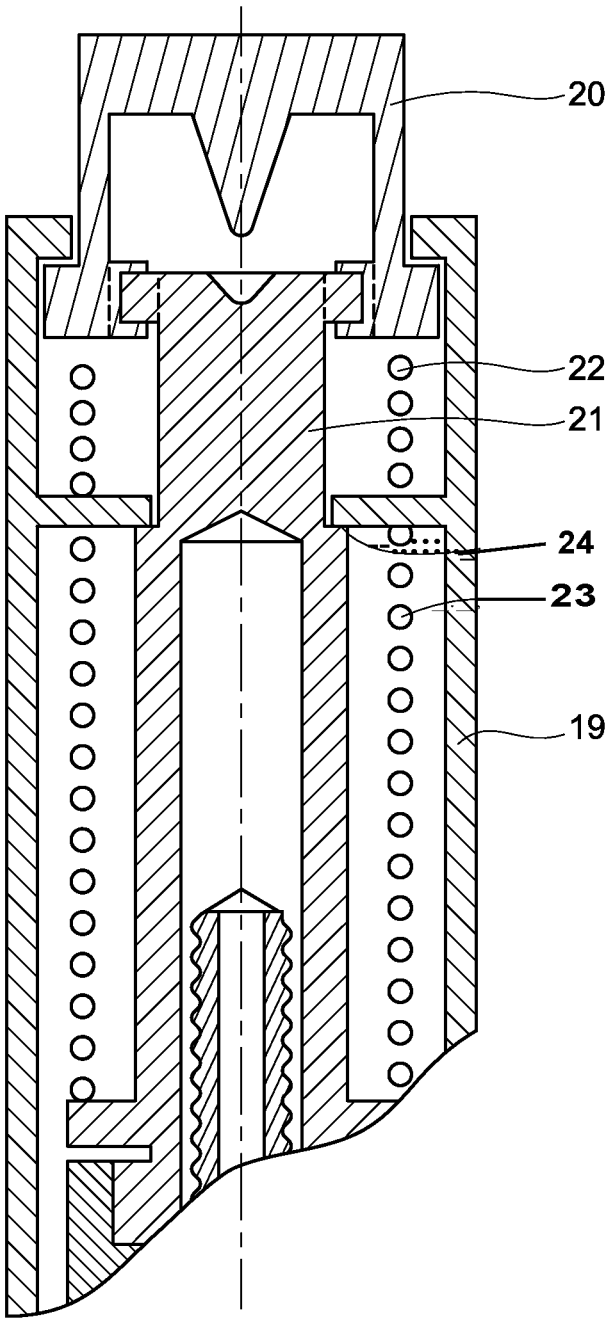

FIG. 6

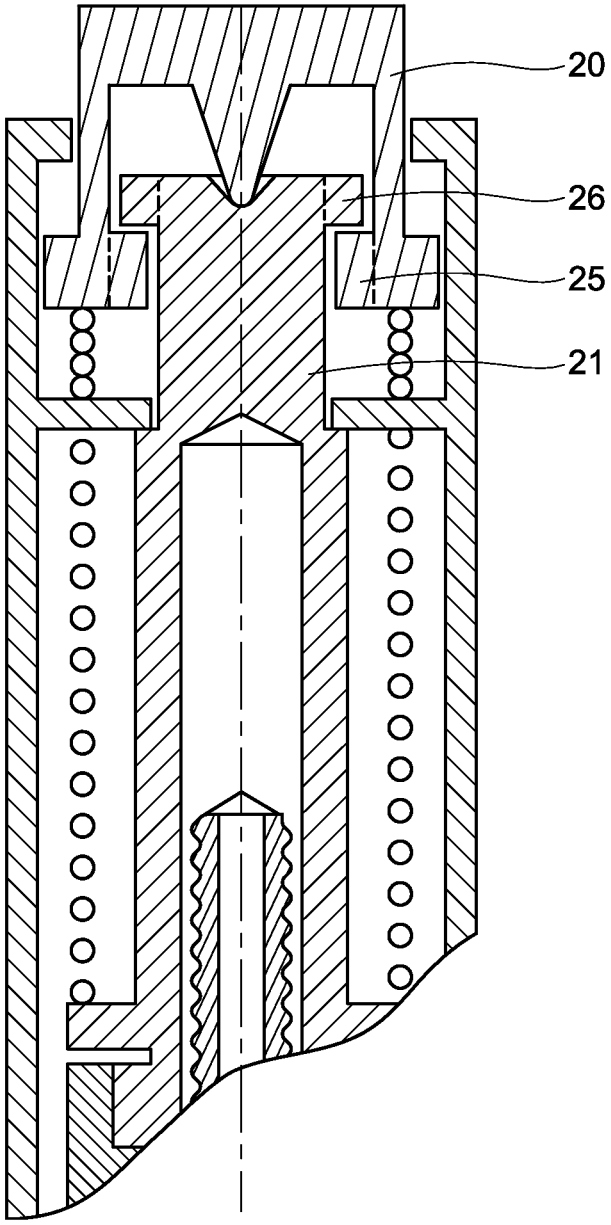

FIG. 7

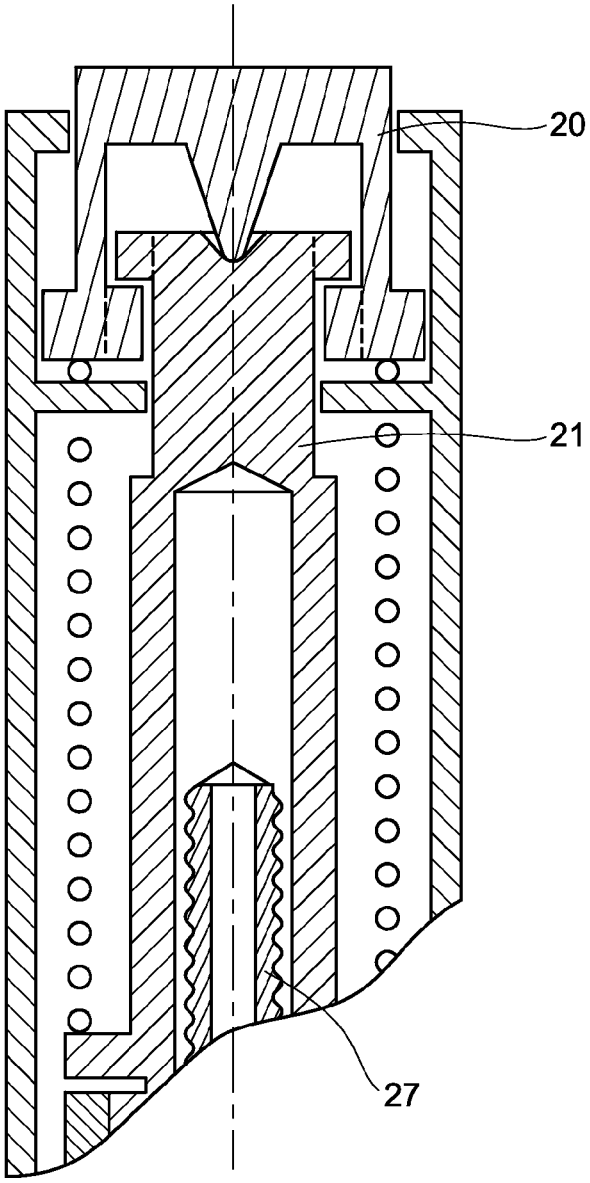

FIG. 8

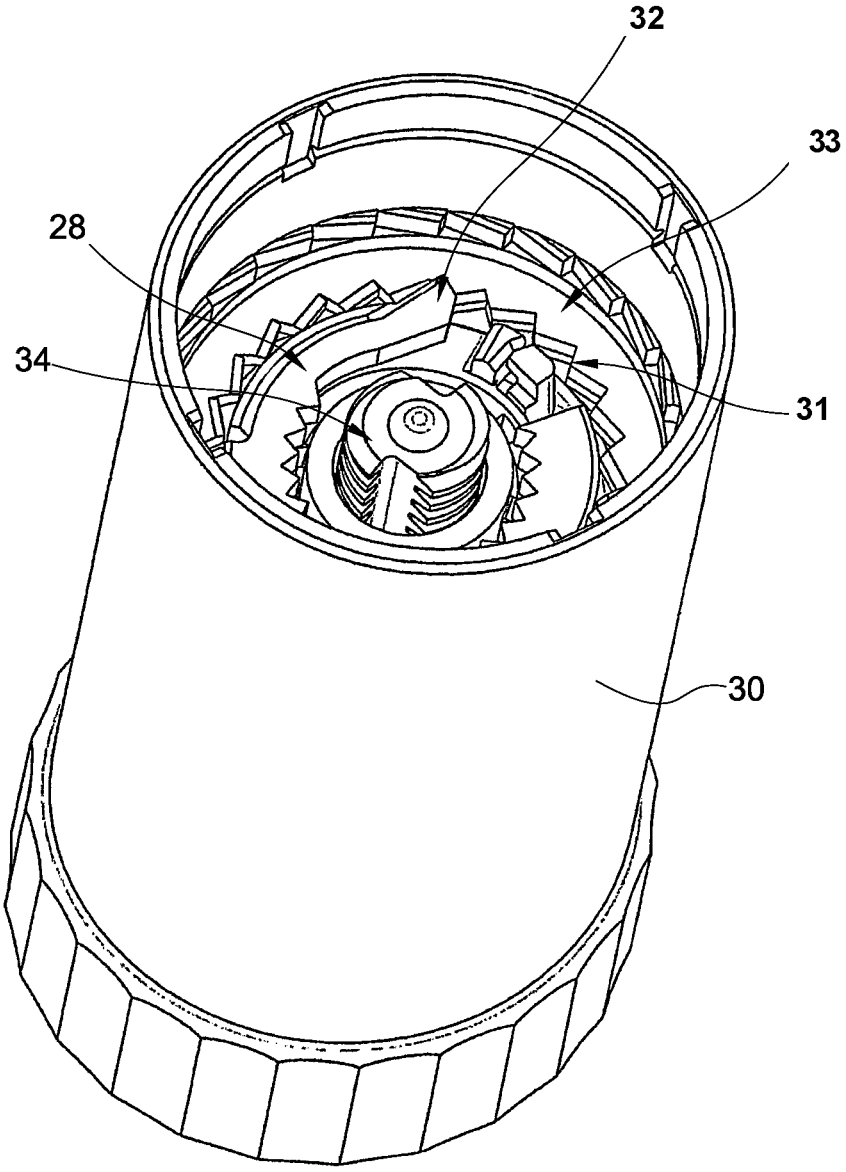

FIG. 9

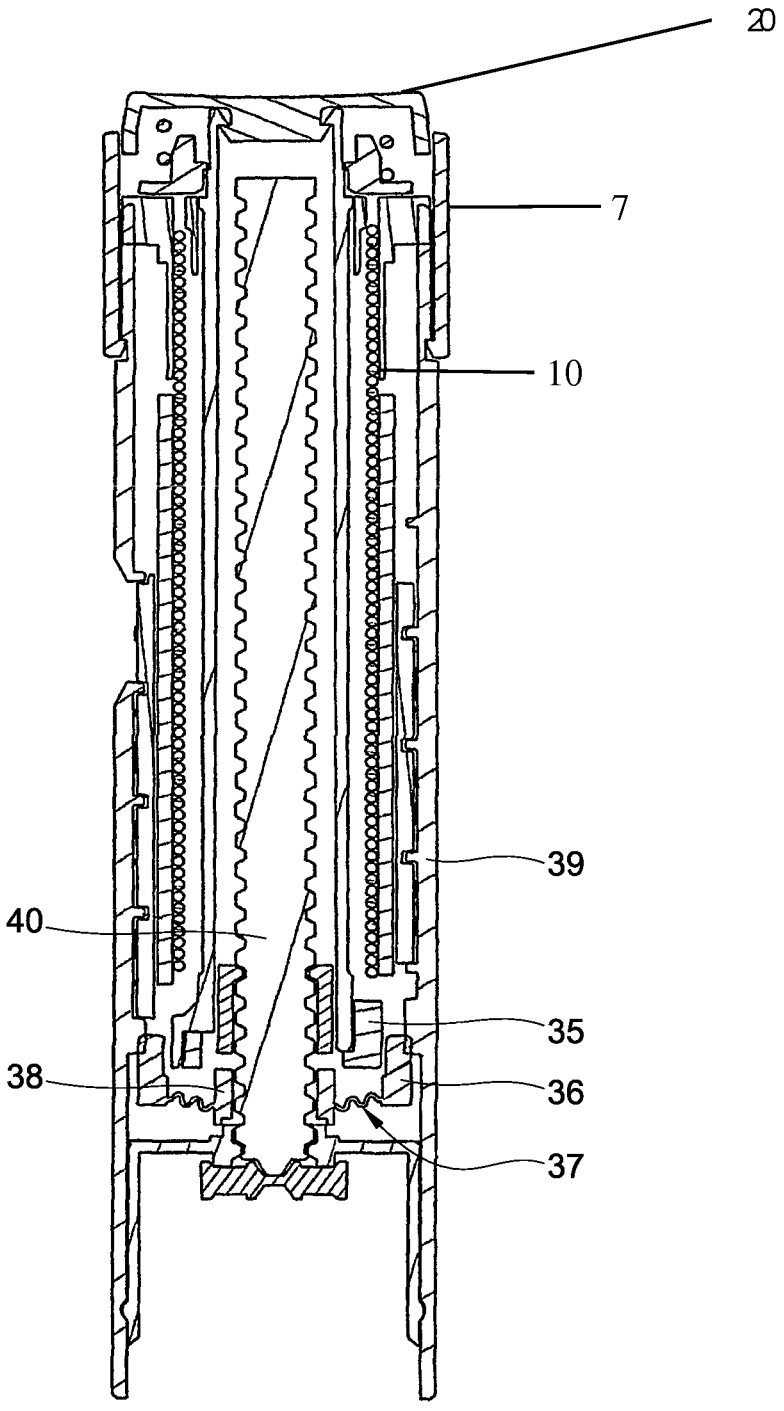

FIG. 10

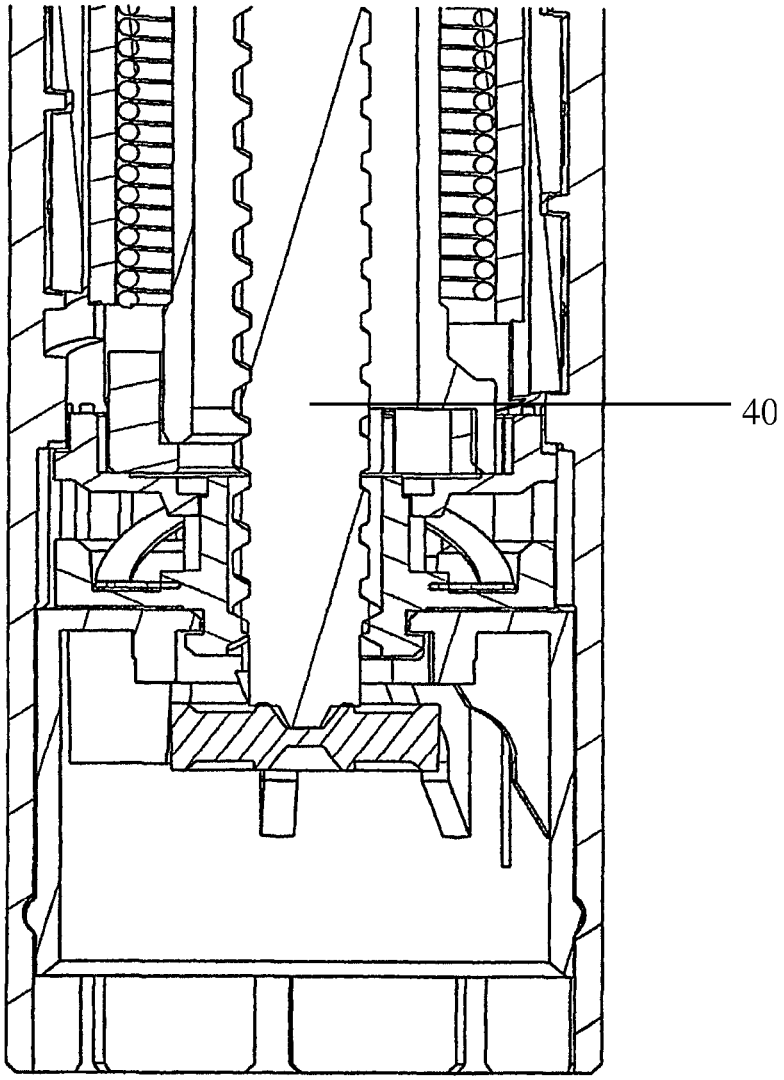

FIG. 11

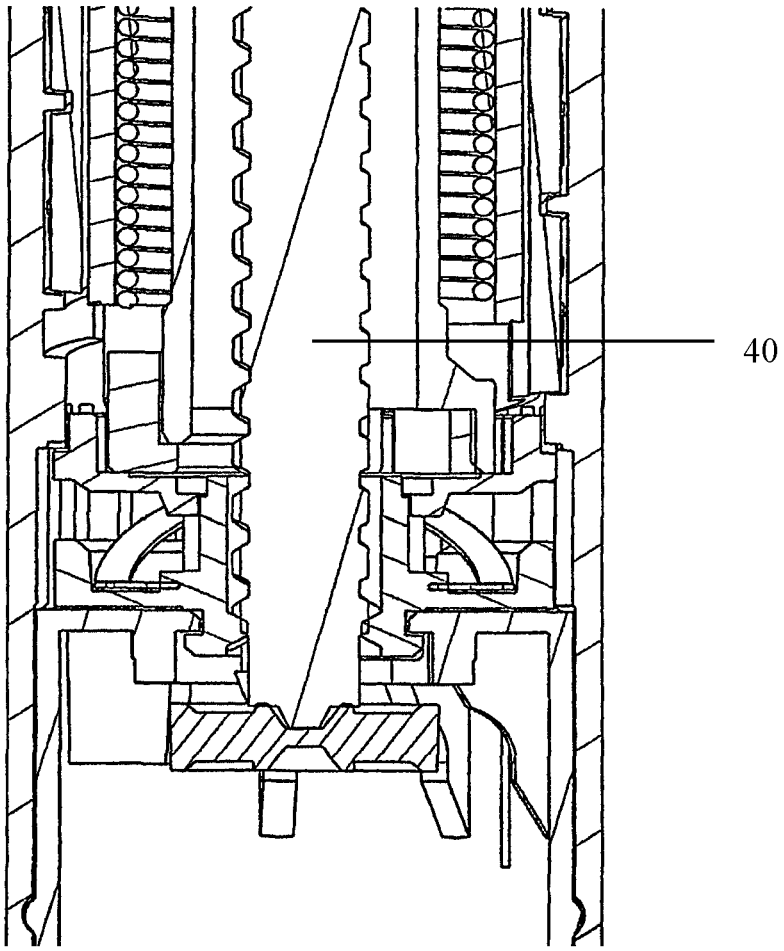

FIG. 12

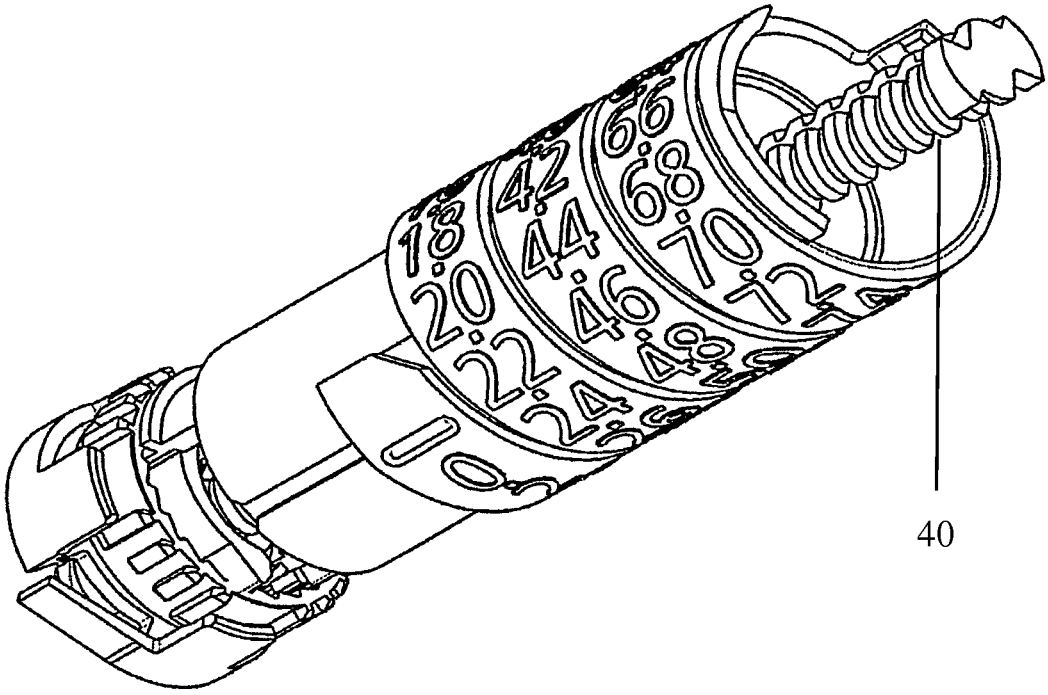

FIG. 13

AUTOMATIC INJECTION DEVICE WITH A TOP RELEASE MECHANISM

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 15/441,638, filed Feb. 24, 2017, which is a continuation of U.S. patent application Ser. No. 14/797,350, filed Jul. 13, 2015 (U.S. Pat. No. 9,616,180), which is a continuation of U.S. patent application Ser. No. 13/326,738, filed Dec. 15, 2011 (U.S. Pat. No. 9,108,002) which is a continuation of U.S. patent application Ser. No. 11/813,435 filed Jun. 2, 2008 (U.S. Pat. No. 8,096,978) which is a 35 U.S.C. § 371 national stage application of International Patent Application PCT/DK2006/000032 (published as WO 2006/076921), filed Jan. 20, 2006, which claimed priority of Danish Patent Application PA 2005 00113, filed Jan. 21, 2005; this application further claims priority under 35 U.S.C. § 119 of U.S. Provisional Application 60/647,320, filed Jan. 26, 2005; the contents of which are incorporated herein by reference.

The present invention relates to an automatic and handheld mechanical injection device where an injection of a set dose of medicament is initiated by actuating a release member being arranged at or near the top of the injection device.

BACKGROUND OF THE INVENTION

Automatic injection devices have previously been disclosed in the patent literature. Automatic injection devices contain some sort of power reservoir where electrical or mechanical energy can be accumulated. The accumulated energy is easily released by actuating a release mechanism whereby the accumulated energy assists the user in injecting a set dose of medicine and/or assisting needle insertion.

For example, EP 0 516 473 A1 discloses an injection device having a needle which, when the device is operated, is first caused to project, then liquid is forced out through it, and finally the needle is automatically retracted. The needle extends forwardly from a capsule that can slide longitudinally within a barrel-like body, a relatively weak spring normally maintaining the capsule and needle retracted. A more powerful spring acts oppositely on a plunger which, when released, shoots the capsule forward by acting on the liquid therein, and then forces the liquid out through the projecting needle. At the end of the forward stroke the plunger and capsule are decoupled and the weak spring returns the exhausted capsule and its needle to the retracted position. The spring acting on the plunger can be released by a release button positioned on the outer surface of the injection device.

In WO 01/41838 discloses a handheld injection device by which set doses of a liquid medicament can be injected from a medical reservoir, such as cylinder ampoule, by release of a power reservoir in the device. The power reservoir can either be an electric battery by which a motor can be energized to press out a set dose of medicine, or a strained spring maintained in its strained position by a detent which spring when released can press out a set dose of medicine. When the power reservoir is released, the liquid medicine will be pressed out from the cylinder ampoule through an injection needle mounted on the cylinder ampoule or on the injection device carrying the cylinder ampoule. The power reservoir is released fully or partially by activating a release button, such as an electric switch, located on the housing of the injection device and in the distal half of the length of the injection device. By making at least a part of the distal third of the injection device of an ergonomic shaped cross section, the user can grip the injection device as a pencil is gripped by a thumb, an index finger and a long finger.

In both EP 0 516 473 A1 and WO 01/41838 the release buttons are positioned on an outer surface of the injection devices. In EP 0 516 473 A1 the release button is position on the outer side of the cylindrical body, whereas in WO 01/41838 the release button is positioned close to the injection needle of the injection device. However, it may be advantageous to position the release button or mechanism so that the injection device can be activated by providing a force to the upper region of the injection device—preferably to a release button or mechanism arranged axially with the injection device.

It is an object of the present invention to provide an automatic and handheld mechanical injection device having a combined release member and dose setting member

It is a further object of the present invention to provide an automatic and handheld mechanical injection device where an injection of a set dose can be initiated using the thumb or the index finger of the hand handling the injection device by providing an axial force to an upper region of the injection device.

It is a still further object of the present invention to provide an automatic and handheld mechanical injection device having an exterior design very similar to conventional manual injection devices.

SUMMARY OF THE INVENTION

The above-mentioned objects are complied with by providing, in a first aspect, a handheld injection device by which set doses of a liquid medicament can be injected from a medical reservoir through an injection needle by release of a power reservoir in the device, the power reservoir being adapted to be fully or partially released by actuation of a user operable release member positioned at or near an upper end of the injection device, the upper end being that end of the injection device which is opposite the injection needle, the power reservoir being adapted to be powered by rotation of a rotatably mounted dose setting member.

The amount of power provided to the power reservoir may depend on the angle of rotation of the dose setting member. Thus, a rather limited rotation of the dose setting member provides a relatively small amount energy to the power reservoir, whereas a large rotation of the dose setting member provides a relatively large amount of energy to the power reservoir.

The release member may be positioned less than one fifth or one sixth of the length of the injection device from the upper end. Alternatively, the release member may be axially arranged relative to the injection device so that the release member forms a push button like release member on the top of the injection device.

The release member may be operatively connected to a dose setting member of the injection device in that the release member may engage the dose setting member via a key/keyway connection when the dose setting member is in a dose setting position. The release member may be released from the key/keyway connection with the dose setting member when the dose setting member is in a dose injecting position. With this arrangement, the handheld injection device has no rotating exterior parts or elements.

The power reservoir may be a resilient member, such as a torsion spring or a linear spring, the resilient member

being, when released, adapted to press out a set dose of medicine from the medical reservoir through the injection needle. The release member may be operatively connected to a release mechanism adapted to release the resilient member when said release member is actuated. The release member may have a shape which is ergonomic shaped to be activated by a thumb or an index finger of the user.

The medical reservoir may be a cylindrical ampoule comprising a first and a second end of which the first end is closed by a pierceable membrane which may be pierced by a first end of the injection needle when this needle is mounted on the device. The other end of the injection needle may be sharp so as to be able to pierce the skin at the position where an injection is to be made. The second end of the ampoule may be closed by a piston which may be forced into the ampoule so as to expel medicament through the needle.

The handheld injection device may further comprise a rotatably arranged drive member being adapted to at least partly engage with at least part of a drive track of an associated piston rod, the drive member being adapted to be positioned in a first axial position when the dose setting member is in a dose setting position, the drive member further being adapted to be positioned in a second axial position when the dose setting member is in a dose injection position, the drive member being adapted to release energy accumulated in the power reservoir when the drive member is in its second axial position.

The drive member may be adapted to rotate the associated piston rod upon releasing the accumulated energy in the power reservoir. However, in its first axial position, the drive member is prevented from rotating because the drive member engages at least part of a housing of the injection device. The injection device may further comprise a resilient member, such as a linear spring, for biasing the drive member in a direction towards the dose setting member. The linear spring operatively connects the drive member and the housing.

The dose setting member may be adapted to be moved a distance along an axial direction of the injection device so as to move the drive member between the first and second axial positions. The drive member may be adapted to be moved from the first to the second axial position by applying a force to the dose setting member, the force being applied along the axial direction of the injection device.

The injection device may, as already mentioned, further comprise a push button axially arranged with the dose setting member, the push button being adapted to engage with the dose setting member when the dose setting member is in its dose setting position, and disengage from the dose setting member when the dose setting member is in its dose injection position. By disengage is meant that the push button and the dose setting member are mutually rotatable when this disengaged state is reached. The injection device may further comprise a resilient member, such as a linear spring, for axially biasing the push button in a direction away from the drive member.

The handheld injection device may further comprise a rotatably mounted display member adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member, the rotatably mounted display member being rotatable over an angle corresponding to at least one revolution of the display member. The display member may comprise a dose indicator barrel having numerals arranged along a substantially helical path on an outer surface thereof. Alternatively or in addition, the display member may comprise a counting device having two or more display wheels having numerals arranged on an outer surface thereof.

The handheld injection device may further comprise the associated the piston rod, the piston rod having a threaded outer surface with the drive track arranged in a longitudinal direction of the outer surface of the piston rod. The drive member may be operatively connected to the dose setting member via a ratchet.

The power reservoir may be arranged between the housing and the dose setting member in such a way that when the dose setting member is rotated, energy is accumulated in the power reservoir. The power reservoir may comprise a torsion spring formed as a helical spring extending coaxially with the associated piston rod.

It is to be noted that the interaction between the drive member, the piston rod and the housing may be implemented in various ways. Above, the piston rod has a threaded outer surface and a drive track arranged in the longitudinal direction of the rod. A key arranged on the drive member engages the drive track of the rod and the forward movement of the rod relative to the housing is caused by the threaded outer portion of the rod which meshes with a corresponding threaded portion of the housing. Alternatively, the threaded outer surface of the rod may mesh with a corresponding threaded portion of the drive member whereas the drive track arranged in the longitudinal direction of the rod engages with a key fixedly arranged relative to the housing.

BRIEF DESCRIPTION OF THE INVENTION

The present invention will now be explained in further details with reference to the accompanying figures wherein

FIG. **1** shows an injection device according to the present invention where the release button arranged at the top of the device is activated by the thumb of the user,

FIG. **2** shows an injection device according to the present invention where the release button arranged at the top of the device is activated by the index finger of the user,

FIG. **3** shows an injection device according to the present invention where the release button is arranged on the top surface of the dose setting member, and where the drive member is in its locked position (dial position of dose setting member),

FIG. **4** shows an injection device according to the present invention where the release button is arranged on the top surface of the dose setting member, and where the drive member is in its released position (dosing position of dose setting member),

FIG. **5** shows an expanded view of the drive member in its released position,

FIG. **6** shows an expanded view of the release member in its locked position with the dose setting member,

FIG. **7** shows an expanded view of the release member in its released position with the dose setting member,

FIG. **8** shows an expanded view of the release member in a further released position where the dose setting member is allowed to rotate,

FIG. **9** shows one way of implementing the release mechanism for releasing the energized power reservoir,

FIG. **10** shows another way of implementing the release mechanism for releasing the energized power reservoir,

FIG. **11** shows a third way of implementing the release mechanism for releasing the energized power reservoir,

FIG. **12** shows a fourth way of implementing the release mechanism for releasing the energized power reservoir, and

FIG. **13** shows a fifth way of implementing the release mechanism for releasing the energized power reservoir.

While the invention is susceptible to various modifications and alternative forms, specific embodiments have been shown by way of example in the drawings and will be described in detail herein. It should be understood, however, that the invention is not intended to be limited to the particular forms disclosed. Rather, the invention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the appended claims.

DETAILED DESCRIPTION OF THE INVENTION

FIGS. **1** and **2** show the present invention in its most general aspect. In FIG. **1** a handheld injection device **1** is shown. The injection device has an injection needle **2** fastened to one of its ends, whereas a release button **3** is arranged at the opposite end of the injection device. When the release button **3** is actuated by provided a force to it along the axial direction of the device energy is released from an internal power reservoir whereby a set dose of medicine is injected from the injection device. In FIG. **1** the release button is actuated by the thumb **4** of the user, whereas in FIG. **2** the release button is actuated by the index finger **5** of the user.

The medicine to be injected is contained in a medical reservoir typically formed as a cylindrical ampoule.

The energy released when the release button **3** is mechanical energy. The power reservoir can be a resilient member, such as a torsion spring, the resilient member being, when released, adapted to press out a set dose of medicine from the medical reservoir through the injection needle. The release button is operatively connected to some sort of release mechanism adapted to release the resilient member when the release button is actuated.

FIG. **3** shows a cross-sectional view of one embodiment of the present invention. The injection device shown in FIG. **3** comprises a housing **6**, a dose setting member **7**, a drive member **8**, a piston rod **9**, a torsion spring **10**, a biasing spring **11**, a cylindrical ampoule **12** and a release member **13**. FIG. **3** shows the injection device in a state where the dose setting member **7** is in its dose setting position.

A dose is set by rotating the dose setting member **7** a certain angle or a certain number of turns. By rotating the dose setting member **7** the torsion spring **10** is strained because the two ends of the torsion spring **10** are fixed to the housing **6** and to the dose setting member **7**, respectively. The dose setting member **7** is operatively connected to the drive member **8** via a ratchet (not shown). This ratchet prevents that the dose setting member **7** returns to its initial position upon straining the torsion spring **10**. Since the drive member **8** engages the housing **6** via a key/keyway connection or a gear wheel, the drive member **8** is not allowed to rotate relative to the housing **6** as long as the dose setting member **7** is in its dose setting position as illustrated in FIG. **3**. In order to keep the dose setting member **7** and the drive member **8** in the dose setting position, the drive member **8** and the dose setting member **7** is biased in a direction towards the top end of the injection device. This biasing is provided by a spring element, such as a linear spring **11**, arranged between the drive member **8** and part of the housing **6**. Thus, in order to release the drive member **8** from its engagement with the housing **6**, a force needs to be provided in order move the dose setting member **7** and the drive member **8** towards the medicine ampoule **12**. A miner cavity **14** ensures that this forward movement of the dose setting member **7** and the drive member **8** can be performed. Similarly, since the drive member **7** and the piston rod **9** engage via a key connection the drive member **8** is allowed to move axially relative to the piston rod **9**.

The drive member **8** has been released from its engagement with the housing **6** in FIG. **4**. In order to achieve this releasing a force, indicated by arrow **15**, has been provided to the release member **13** whereby the release member **13**, the dose member **7** and the drive member **8** have all been moved a distance towards the medicine ampoule **12**. The force indicated by arrow **15** would normally be provided by the thumb or the index finger of the user.

As seen in FIG. **4** the engaging region **16** of the housing is now separated from the engaging region **17** of the drive member **8**. This disengagement allows that the strained torsion spring **10** can release its energy to the dose setting member **7**. The dose setting member **7** and the drive member **8** are fixedly related via the intermediate ratchet (not shown). Thus, when a disengagement between engaging regions **16** and **17** has been established, the dose setting member **7** and the drive member **9** will rotate until the torsion spring **10** reaches an unstrained state. Since the drive member **8** and the piston rod **9** is connected via a key connection the rotation of the dose setting member **7** and the drive member **8** will cause the piston rod **9** to rotate as well. The piston rod **9** has an outer threaded surface which engages with a corresponding threaded portion **18** of the housing whereby the piston rod **9**, upon rotation thereof, will perform a translational movement along the axial direction of the injection device in the direction of the ampoule **12**.

Thus, the force provided to the release member **13** will release accumulated energy in the torsion spring. This energy is converted to a translational movement of the piston rod towards the ampoule whereby a set dose of medicine can be injected from the injection device.

FIG. **5** shows a cut half illustration of the housing **6** of the injection device. As seen, the drive member **8** comprises an engagement region/part **17** formed as gear wheel. Similarly, the housing **6** comprises a corresponding engagement region/part **16** adapted to receive and engage with the teeth of the gear wheel **17**.

FIG. **6** shows another embodiment of the present invention. In contrast to the embodiment shown in FIGS. **3-5** the embodiment shown in FIG. **6** contains no rotating exterior parts or elements. All rotating parts or elements are positioned inside the housing **19**. FIG. **6** shows a release member **20** (formed as a push button) which is mechanically biased towards the end of the injection device by spring element **22**. The release member **20** and dose setting member **21** are forced into engagement as long as the dose setting member **21** is in its dose setting position. The dose setting member **21** is mechanically biased towards the same end of the injection device as the release member **20** due to a spring element (shown as spring element **11** in FIG. **3**) acting on the drive member (shown as drive member **8** in FIG. **3**) which again acts on dose setting member **21**. As seen in FIG. **6** the dose setting member **21** is biased against a mechanical stop **24** where a shoulder formed in the dose setting member **21** abuts a part of the housing **19**.

In FIG. **7** an intermediate stage is illustrated. Here the release member **20** has been pushed an axial distance sufficient to release the release member **20** from the dose setting member **21**. Note that the engagement region **25** and **26** are disengaged, but since the shoulder of the dose setting member still abuts the housing part no axial movement of the dose setting member **21** has been achieved at this stage.

Thus, the dose setting member **21** is prevented from rotating since the drive member (not shown) is still engaging the housing.

In FIG. **8** the dose setting member **21** has been moved an axial distance towards the ampoule (not shown) whereby the dose setting member is allowed to rotate freely causing the piston rod **27** push a set dose of medicine out of the ampoule (not shown). Note that the release member **20** and the dose setting member **21** are disengaged in FIG. **8**. This means that the release member **20** is not rotating relative to the housing during injection of a set dose. Then the set dose has been injected the user removes his thumb or index finger from the release member whereby the release member and the dose setting member return to their respective positions as illustrated in FIG. **6**, but now with the spring element **23** being in a relaxed state.

In case the user wants to set a new dose, the user rotates the release member which engages the dose setting member whereby the new dose can be set. Injecting the set dose is achieved by following the steps illustrated in FIGS. **7** and **8**.

FIGS. **9-13** show various embodiments of release mechanisms for releasing the energized power reservoir.

In FIG. **9** a torsion spring (not shown) is energized by rotating a ratchet **28** which is operatively connected to the housing **30** of the injection device when the dose to be injected is being set. In the dose setting position the ratchet **28** is operatively connected with housing part **31** via ratchet arm **32**. Energy accumulated in the torsion spring is released by displacing the ratchet **28** axially whereby it is released from its connection with housing part **31** in that the ratchet arm **32** is moved into housing part **33** whereby the piston rod **34** is allowed to rotate thereby expelling a set dose of medicament.

In the embodiment depicted in FIG. **9** a dose indicator barrel (not shown) moves in the direction away from the push-button (not shown) during setting of a dose. Obviously, the dose indicator barrel may be adapted to move in the opposite direction during setting of a dose, i.e. towards the push-button.

In the embodiment depicted in FIG. **10** the ratchet **35** is only in indirect operation with the housing **39**. The drive member of the embodiment depicted in FIG. **10** is constituted by three part—one part **36** being adapted to corporate with the housing **39**, another part **38** being adapted to drive the piston rod **40** and a flexible member **37** connecting parts **36** and **38**. The flexible member **37** is flexible in the axial direction but establishes a substantially stiff connection between parts **36** and **38** when these parts are rotated relative to each other. Thus, the flexible member **37** ensures that parts **36** and **38** are not rotatably arranged relative to each other. Thus, when the ratchet **35** is moved towards the needle end of the injection device the part **36** is disconnected from the housing **39** whereby parts **36**, **37** and **38** are allowed to rotate thereby rotating the piston rod **40**. The rotating piston rod **40** causes a set dose of medicament to be expelled from the injection device.

The embodiment depicted in FIG. **11** is similar to the embodiment in FIG. **9** except that the piston rod is moved forward by having guiding tracks arranged in the housing (instead of in the drive member) and a threaded engagement between piston rod and the drive member (instead of a threaded engagement between piston rod and housing).

FIGS. **12** and **13** show other release mechanisms between ratchet, drive member and housing.

The invention claimed is:

1. A handheld injection device by which set doses of a liquid medicament can be injected from a medical reservoir through an injection needle,

comprising:

a rotatable dose setting member,

a power reservoir comprising a torsion spring for storing energy to expel the set doses of medication from the injection device,

a user operable release member positioned at or near an upper end of the injection device (**1**), the upper end being that end of the injection device (**1**) which is opposite the injection needle,

the injection device further comprising a multi-component driver having at least a part (**38**) adapted to drive a piston rod, and a further part (**36**) being axial movable into a position disconnected from the housing releasing the energy accumulated in the power reservoir, the further part (**36**) being axially movable by the user applying a force onto the release member, and

wherein the injection device further comprises a display member adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member,

the display member being rotatably mounted and rotatable over an angle corresponding to at least one revolution of the display member and which display member comprises a dose indicator barrel having numerals arranged along a substantially helical path on an outer surface thereof.

2. A handheld injection device according to claim **1**, wherein the amount of power provided to the power reservoir (**10**) depends on the angle of rotation of the dose setting member (**7**).

3. A handheld injection device according to claim **1**, wherein the release member is operatively connected to the dose setting member of the injection device.

4. A handheld injection device according to claim **3**, wherein the release member engages the dose setting member via a key/keyway connection when the dose setting member is in a dose setting position.

5. A handheld injection device according to claim **4**, wherein the release member is released from the key/keyway connection with the dose setting member when the dose setting member is in a dose injecting position.

6. A handheld injection device according to claim **1**, wherein when energy from the torsion spring is released it is adapted to expel a set dose of medicine from a medicine containing reservoir through the injection needle.

* * * * *

EXHIBIT P

US011446443B2

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Moeller et al.

(10) **Patent No.: US 11,446,443 B2**
(45) **Date of Patent: *Sep. 20, 2022**

(54) **INJECTION DEVICE WITH TORSION SPRING AND ROTATABLE DISPLAY**

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(73) Assignee: **Novo Nordisk A/S**, Bagsvaerd (DK)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

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A61M 5/20 (2006.01)
A61M 5/315 (2006.01)
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CPC ***A61M 5/31535*** (2013.01); ***A61M 5/14566*** (2013.01); ***A61M 5/20*** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC A61M 5/31535; A61M 5/3155; A61M 5/31553; A61M 5/31556; A61M 5/20;
(Continued)

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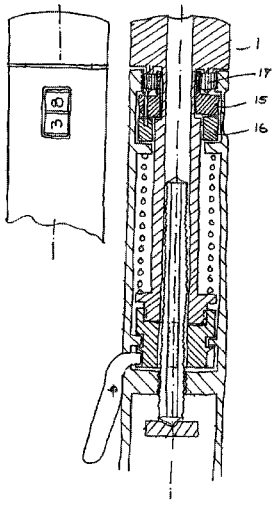
(57) **ABSTRACT**

The present invention relates to an injection device comprising a torsion spring operatively connected to a dose setting member being adapted to set a dose to be ejected from the injection device. A rotatably mounted display member adapted to display the dose to be ejected in accordance with a setting of the dose setting member is also provided. The rotatably mounted display member is adapted to be rotated over an angle corresponding to at least one revolution of the display member. The display member may be implemented as a dose indicator barrel having numerals arranged along a helical path on an outer surface thereof, or alternatively, as a counting device having two or more display wheels having numerals arranged on an outer surface thereof.

19 Claims, 5 Drawing Sheets



Related U.S. Application Data

continuation of application No. 14/167,558, filed on Jan. 29, 2014, now Pat. No. 9,687,611, which is a continuation of application No. 13/626,541, filed on Sep. 25, 2012, now Pat. No. 8,684,969, which is a continuation of application No. 11/665,571, filed as application No. PCT/EP2005/011287 on Oct. 20, 2005, now Pat. No. 8,357,120.

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A61M 5/31 (2006.01)

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CPC ***A61M 5/3155*** (2013.01); ***A61M 5/31553*** (2013.01); *A61M 5/31556* (2013.01); *A61M 5/31583* (2013.01); *A61M 5/31593* (2013.01); *A61M 2005/202* (2013.01); *A61M 2005/3125* (2013.01)

(58) **Field of Classification Search**
CPC A61M 5/14566; A61M 5/31583; A61M 5/31593; A61M 2005/3125
See application file for complete search history.

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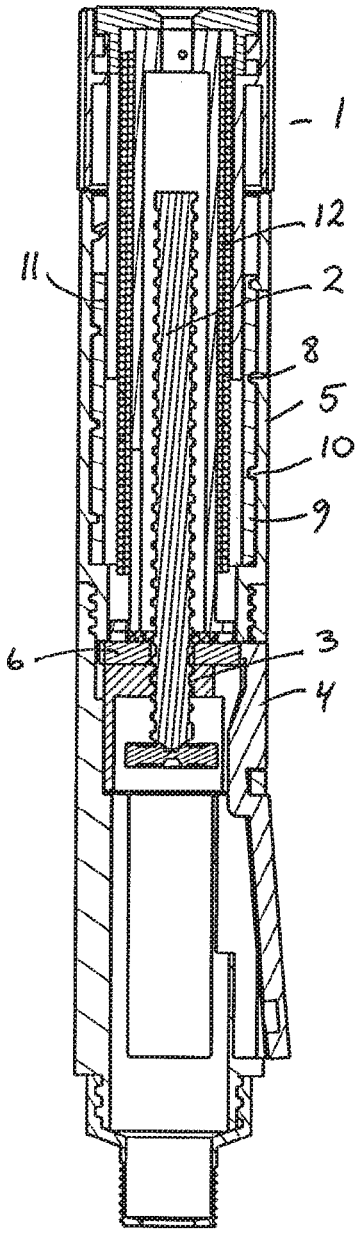

Fig. 1

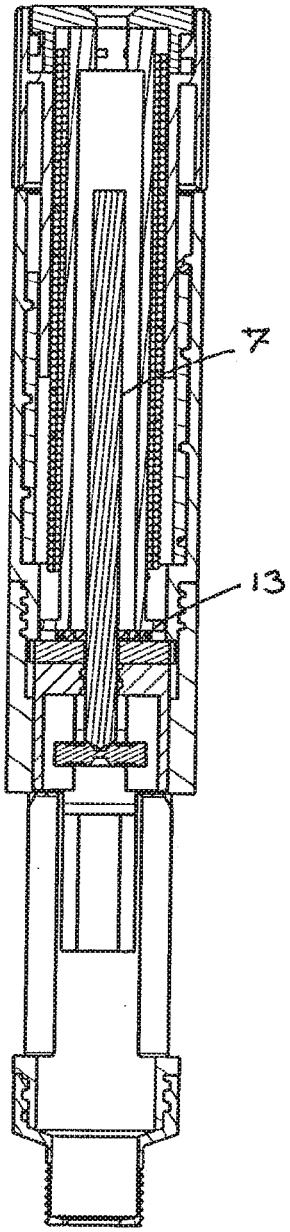

Fig. 2

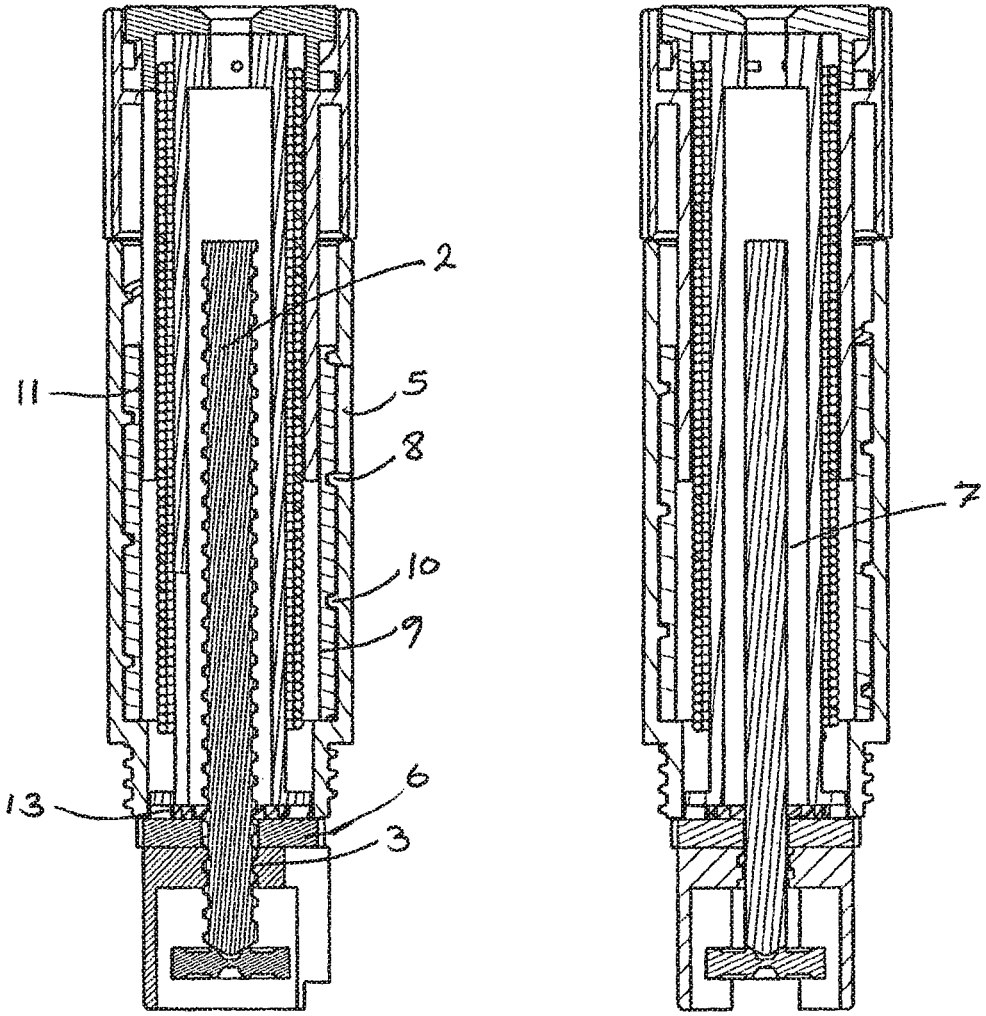

Fig. 3

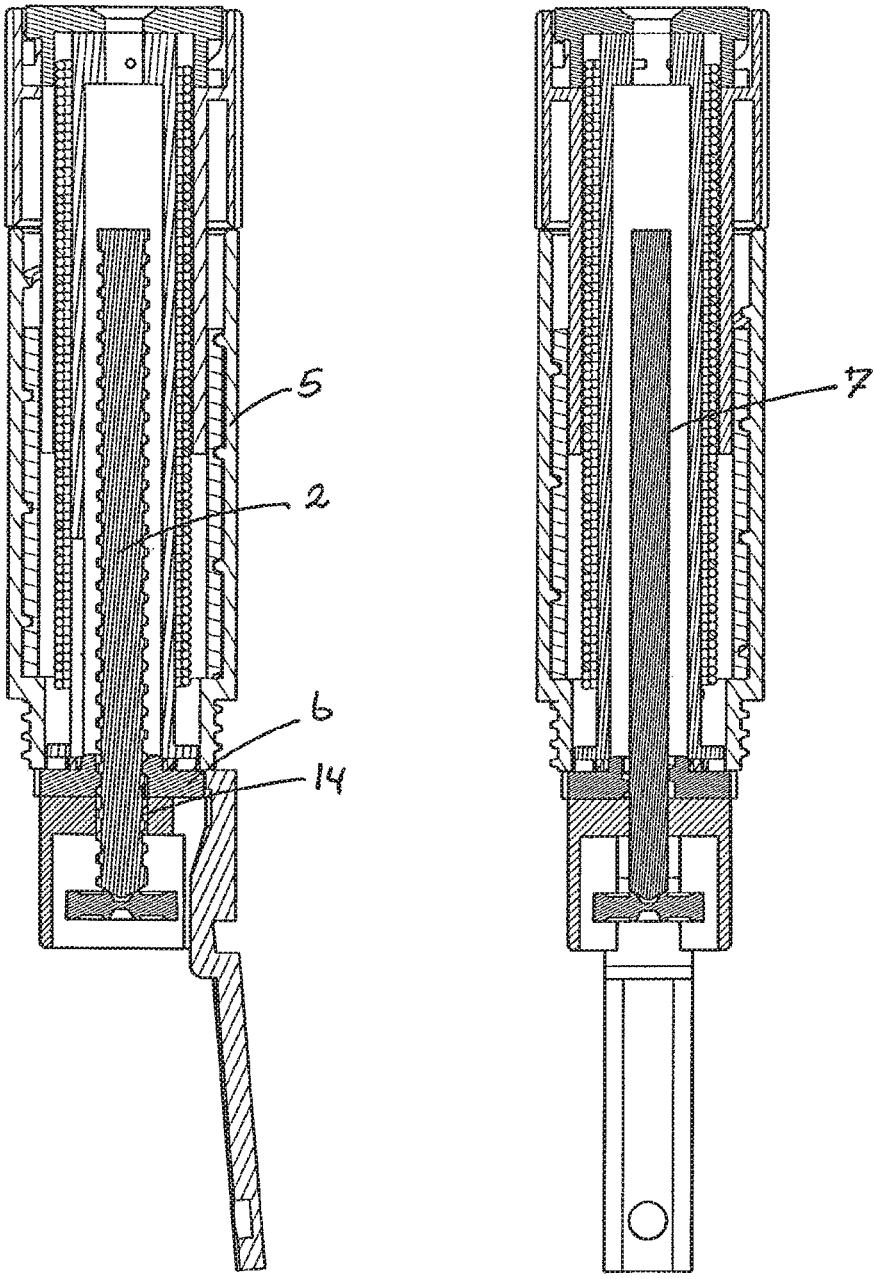

Fig. 4

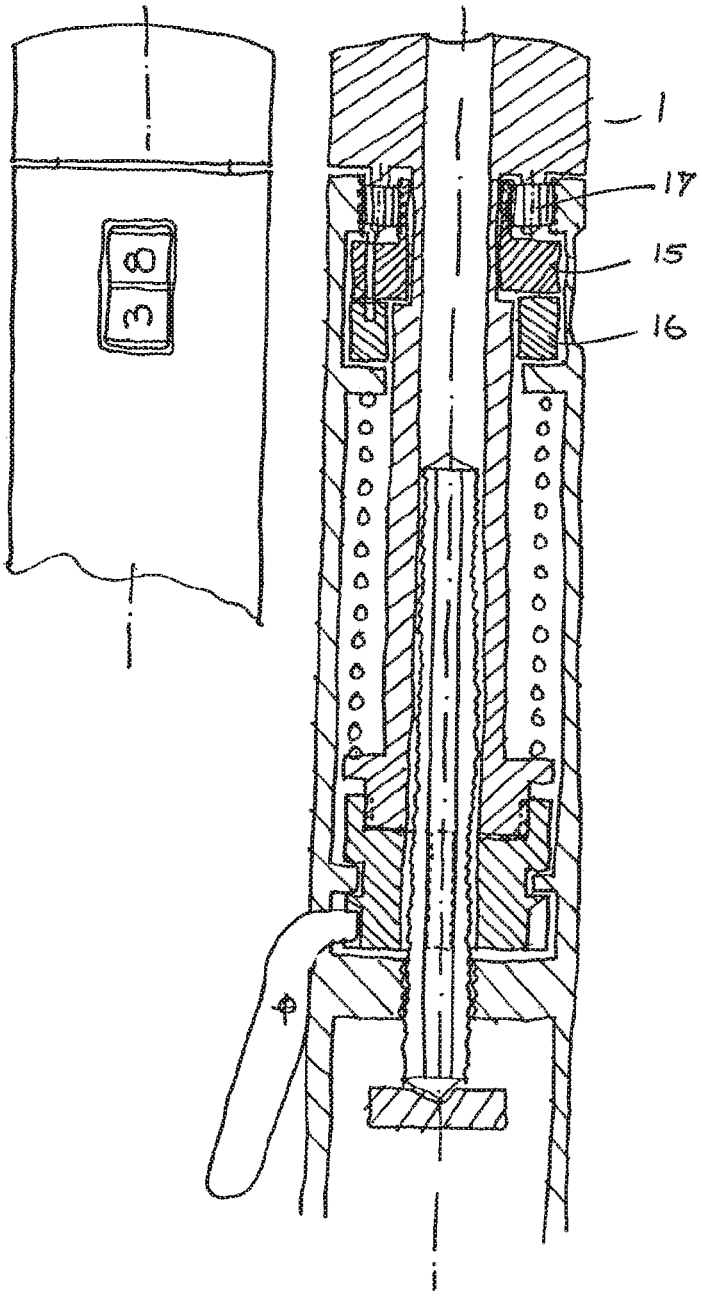

Fig. 5

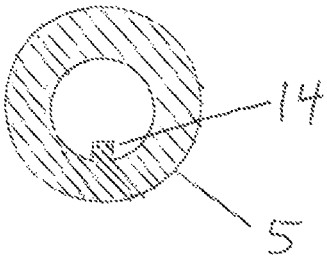

Fig. 6

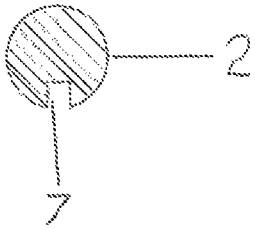

Fig. 7

INJECTION DEVICE WITH TORSION SPRING AND ROTATABLE DISPLAY

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. application Ser. No. 15/606,147, filed May 26, 2017, (Notice of Allowance mailed), which is a continuation of U.S. application Ser. No. 14/167,558, filed Jan. 29, 2014 (U.S. Pat. No. 9,687,611), which is a continuation of U.S. application Ser. No. 13/626,541, filed Sep. 25, 2012 (U.S. Pat. No. 8,684,969), which is a continuation of U.S. application Ser. No. 11/665,571, filed Dec. 5, 2007 (U.S. Pat. No. 8,357,120), which is a 35 U.S.C. § 371 national stage application of International Patent Application PCT/EP2005/011287 (published as WO 2006/045528), filed Oct. 20, 2005, which claims priority of European Patent Application 04077899.5, filed Oct. 21, 2004; this application further claims priority under 35 U.S.C. § 119 of U.S. Provisional Application 60/626,271, filed Nov. 9, 2004, all of which are hereby incorporated by reference.

FIELD OF THE INVENTION

The present invention relates to an injection device, such as a wind-up pen, wherein numerals indicating the dose to be ejected from the injection device are displayed over an angle of rotation exceeding one revolution. In particular, the numerals indicating the dose to be ejected are arranged along a helical path, or alternatively, numerals indicating the dose to be ejected are displayed on a counting device. The present invention ensures that an increased accuracy in dose setting may be obtained.

BACKGROUND OF THE INVENTION

Various types of automatic injection devices have been described in the literature. A majority of these automatic injection devices apply dose indicator barrels, dose indicator wheels or the like which, during dose setting, are only allowed to rotate less than one single revolution. The fact that the dose indicator barrel is only allowed to rotate less than one revolution during dose setting puts a limit to the obtainable angular resolution. This limited angular resolution also limits the accuracy of the dose setting procedure.

In prior art injection devices the dose setting scale arranged on the outer surface of the barrels or wheels contains only up to 42 scale units with an incremental of 2. Thus, the accuracy when setting a dose is limited by this rather rough incremental.

Examples of "one revolution" barrels or wheel may for example be found in U.S. Pat. No. 5,725,508, EP 0 338 806 or U.S. Pat. No. 5,104,380.

WO 02/053214 discloses an automatic injection device having a dose indicator barrel capable of rotating more than one revolution. However, the injection device according to WO 02/053214 applies a linear spring to move a piston rod in the distal direction of the injection device. Evidently, an injection device applying a linear spring has a built-in axial displacement due to compressions and extensions of the linear spring along the axial direction of the injection device. This linear movement may easily be utilized to provide axial movements of the dose indicator barrel. However, it is a disadvantage that linear springs are highly non-linear in terms of force vs. compression. In addition, a linear spring exhibits relative high mechanical looses. Thus, due to the problems relating to the non-linear properties and relatively high looses there is a need for injection devices having linear and more efficient injection assisting systems.

The above-mentioned problems may be solved by applying a torsion spring instead of the linear spring. An injection device applying a torsion spring is conceptually different from linear spring-based devices in that torsion-based systems do not have a built-in axial movement of the spring assisting the user in injecting a dose of medicament from the injection device. The advantages of torsion-based injection devices are many, the greatest of these probably being that torsion springs respond in a linear manner over a large working range.

Thus, there is a need for a torsion spring-based injection device providing an improved and more user friendly dose setting procedure. It is an object of the present invention to provide such torsion spring-based injection device having an expanded dose scale with a high resolution.

SUMMARY OF THE INVENTION

The above-mentioned object is complied with by providing, in a first aspect, an injection device comprising

- a torsion spring operatively connected to a dose setting member, the dose setting member being adapted to set a dose to be ejected from the injection device, and
- a rotatably mounted display member adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member, the rotatably mounted display member being rotatable over an angle corresponding to at least one revolution of the display member.

The display member may be adapted to be moved between two end positions. These two end positions may define or set an axial operation range of the display member. The axial operation range of the display member may be associated with a substantially linear working range of the torsion spring. The working range of the torsion spring utilized to move the display member between the two end positions may constitute only a fraction of the available working range provided by the torsion spring. Thus, by applying a torsion spring only a small and linear working range of the available working range is utilized.

The display member may comprise a dose indicator barrel having numerals arranged along a helical path on an outer surface thereof.

According to a first embodiment of the present invention, the injection device may further comprise

- a housing,
- a piston rod having a threaded outer surface with a drive track arranged in a longitudinal direction of the outer surface of the piston rod,

wherein the dose setting member is rotatably mounted and defines a passage for the piston rod, the dose setting member further having a guiding track arranged on an inner surface thereof,

- a rotatable drive member being adapted to at least partly engage with at least part of the drive track of the piston rod so as to drive the piston rod,

wherein the dose indicator barrel has a part engaging at least part of the guiding track of the dose setting member, the dose setting member and the dose indicator barrel being movable in relation to each other, the dose indicator barrel further having a threaded outer surface cooperating with a threaded inner portion of the housing whereby the dose indicator barrel undergoes a combined translational and

rotational movement in relation to the housing upon rotation of the dose setting member, and

wherein the injection device has a threaded portion cooperating with the threaded outer surface of the piston rod so that rotation of the piston rod relative to the housing results in a longitudinal movement of the piston rod.

It is to be understood that the drive track dose not necessarily extend over the full length of the piston rod. For example, the drive track may in some cases only extend over a part of the full length of the piston rod. Also, the drive track arranged in the piston rod may be an indentation or groove in the longitudinal direction of the piston rod. Alternatively, it may also be a planar surface or two opposing planar surfaces.

Similarly, it is to be understood that other arrangements in terms of the positioning of the threaded portion of for example the dose indicator barrel may be arranged differently.

According to a second embodiment of the present invention, the injection device further comprises

a housing,

a piston rod having a threaded outer surface with a track arranged in a longitudinal direction of the outer surface of the piston rod,

wherein the dose setting member is rotatably mounted and defines a passage for the piston rod, the dose setting member further having a guiding track arranged on an inner surface thereof,

a rotatable drive member having a threaded portion cooperating with at least part of the threaded outer surface of the piston rod,

wherein the dose indicator barrel has a part engaging at least part of the guiding track of the dose setting member, the dose setting member and the dose indicator barrel being movable in relation to each other, the dose indicator barrel further having a threaded outer surface cooperating with a threaded inner portion of the housing whereby the dose indicator barrel undergoes a combined translational and rotational movement in relation to the housing upon rotation of the dose setting member, and

wherein the injection device has a portion at least partly engaging the track of piston rod so that rotation of the drive member relative to the housing results in a longitudinal movement of the piston rod.

The drive member may be adapted to be connected to the dose setting member via a ratchet. This ratchet allows the dose setting member to be rotated in both directions so that a given dose may be either increased or reduced. Due to the force provided by the torsion spring onto the ratchet, the dose setting member will remain in any position—i.e. dose value—to which it has been brought.

The dose setting member may be adapted to be separated from the driving member. This separation may be achieved in several ways. In one way the separation may be obtained by a retraction of the dose setting member in the axial direction of the injection device. The retraction of the dose setting member must be over a distance sufficient to detach the dose setting member or the drive member from the teeth of the ratchet. Other separation mechanisms, such as pushing the dose setting member or twisting the dose setting member are also applicable.

The torsion spring may be arranged between the housing and the dose setting member in such a way that when the dose setting member is rotated around the piston rod, the torsion spring is strained. The torsion spring may be a helical spring which extends coaxially with the piston rod, and which interconnects the housing and the dose setting member in such a way that rotation of the dose setting member, in order to set the dose, strains the torsion spring.

The injection device may further comprise a locking member adapted to fixate the piston rod in such a way that no relative rotation of the piston rod and the housing is possible when the locking member is in its locking position. This fixation may be provided by a direct engagement of the locking member into the track of the piston rod, or via the drive member. The injection device may further comprise a release button adapted to release the locking member from its locking position. Preferably, the release button is positioned in the distal half of the length of the injection device.

The injection device may further comprise a first stopping member for defining an outer position of the dose indicator barrel. This outer position of the dose indicator barrel may correspond to a maximum obtainable dose. Another outer position of the dose indicator barrel, given by a second stopping member, may define a stop for providing further doses. The stopping members may form integral parts of the inner surface of the housing.

In a third embodiment, the display member may comprise a counting device having two or more display wheels having numerals arranged on an outer surface thereof. In this second embodiment the counting device may have a first and a second wheel. When the dose setting member is rotated, the first wheel is rotated via an optional gear mechanism, such as a planet gear. This first wheel may contain numerals with an incremental of one. The total scale on this wheel may be from 0 to 9. The second wheel next to the first wheel also contains numerals with an incremental of 1. However, this second wheel "counts" the number of revolutions of the first wheel, or alternatively, it "counts" the tens of the first wheel with an incremental of one.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will now be described in further details with reference to the accompanying figures, wherein

FIG. **1** shows a cross-sectional view of a first embodiment of the injection device according to the present invention,

FIG. **2** shows a cross-sectional view (rotated 90 degrees compared to FIG. **1**) of a first embodiment of the injection device according to the present invention,

FIG. **3** shows a detailed cross-sectional view of a first embodiment of the present invention,

FIG. **4** shows a detailed cross-sectional view of a second embodiment of the present invention, and

FIG. **5** shows a detailed cross-sectional view of a third embodiment of the present invention.

FIG. **6** shows a cross-section of a key in a housing component.

FIG. **7** shows a cross-section view of a piston rod with a track.

While the invention is susceptible to various modifications and alternative forms, specific embodiments have been shown by way of example in the drawings and will be described in detail herein. It should be understood, however, that the invention is not intended to be limited to the particular forms disclosed. Rather, the invention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the appended claims.

DETAILED DESCRIPTION OF THE INVENTION

In its most general aspect the present invention relates to an injection device comprising a torsion spring in combi-

nation with a rotatable dose indicator mechanism capable of being rotated at least one revolution—i.e. over an angle larger than 360 degrees. For example, the dose indicator mechanism may be implemented as a barrel (see FIGS. **1-4**) or as interconnected wheels (see FIG. **5**), the latter being operated as a counting device. In order to increase the angular resolution compared to known dose indicator mechanisms the dose indicator mechanism of the present invention is rotatable over an angle of rotation corresponding to at least one revolution. The fact that the dose to be ejected is displayed over at least one revolution allows that the dose setting scale may contain at least 50, 60, 70, 80, 90, 100 units with an incremental of one.

FIGS. **1-3** show a cross-sectional view of the injection device according to a first embodiment of the present invention. The dose of medicament to be ejected from the injection device is set by rotating dose setting member **1**. The dose setting member **1** is attached to the housing **5** of the injection device via torsion spring **12**. When the dose setting member **1** is rotated in order to set a dose to be ejected from the injection device, energy is accumulated in torsion spring **12**. This energy may be released by releasing locking member **4** whereby the piston rod **2** will rotate and move in the distal direction of the injection device. The distal movement of the piston rod **2** is caused by a rotational movement of the piston rod **2** itself in that the piston rod **2** has a threaded outer surface. The threads of the piston rod **2** engage and co-operate with a threaded portion **3** of the injection device causing the piston rod **2** to perform the distal and axial movement.

The inner surface of housing **5** of the injection device is provided with threads **10**. These threads are adapted to engage and co-operate with outer threads **8** of a dose indicator barrel **9**. The dose indicator barrel **9** engages with sliding track **11** of the dose setting member **1** in such a way that the dose indicator barrel **9** is able to slide in said sliding track **11** in an axial direction of the injection device.

When the dose setting member **1** is rotated in order to set a dose, the dose indicator barrel **9** rotates with the dose setting member **1** causing the dose indicator barrel **9** to be axially displaced relative to the housing **5**. A window is provided in the housing **5** of the injection device. Through this window, the user of the injection device may view the actual dose setting level from numerals (not shown) provided on an exterior surface of the dose indicator barrel **9**. The numerals are arranged along a helical path.

An advantage of having the numerals arranged along a helical-like path is that a higher angular resolution is obtainable when a dose is to be set. Due to this higher angular resolution a dose can be set with a significantly higher accuracy. This greater accuracy is obtained since the helical-like path allows for more numerals to be arranged on the dose indicator barrel **9** compared to numerals arranged at the same height on the surface of the dose indicator barrel **9**.

When a dose has been ejected from the injection device, the dose indicator barrel **9** is adapted to be rotated back to its initial position and it is thereby ready to be set to a new dose. The same applies for an injection device applying a counting device as a dose meter.

As already mentioned, the piston rod **2** has a threaded outer surface. This threaded outer surface engages and co-operates with a threaded portion **3** of the injection device. The piston rod **2** is driven by the drive member **6** that engages a track in piston rod **2**. The axial movement of the piston rod **2** is provided by rotating piston rod **2** in the threaded portion **3** of the injection device. Drive member **6** may be locked by the locking member **4**. In its locked position, drive member **6** is prevented from rotating. In order to release the drive member **6**, the user of the injection device may activate a spring-loaded push button **15** whereby drive member **6** causes the piston rod **2** to rotate in threaded part **3** of the housing whereby the piston rod **2** rotates and travels in the distal direction of the injection device. Thus, when the drive member **6** is released, the injection device ejects automatically. During ejection, the dose indicator barrel returns to zero dose.

The dose setting member **1** and the drive member **6** are mechanically connected via a self-tightening ratchet **13**. Preferably, the self-tightening ratchet **13** has saw-toothed teeth with approximately vertical oriented flanks as the self-tightening flanks.

In order to reset or reduce an already set dose, the dose setting member **1** is arranged to be axially retractable over a distance corresponding to the height of the teeth of the one-way ratchet **13**. Thus, by pulling the dose setting member **1** back, and thereby disengage the dose setting member **1** from the drive member **6**, an already set dose can be reduced or even reset. The amount of reduction obviously depends on the angle of rotation (in the opposite rotation direction as when a dose is set) of the dose setting member **1**.

The self-tightening ratchet may be formed as a separate component having first and second engaging parts. Alternatively, one of these parts may form an integral part of the dose setting member **1**, or alternatively, an integral part the drive member **6**.

FIG. **4** shows a second embodiment of the present invention. Compared to the first embodiment, the drive member **6** has a threaded portion cooperating with the threaded outer surface of the piston rod **2**. The main difference compared to the first embodiment is that the piston rod **2** is no longer rotatable relative to the housing **5**. This non-rotatable relationship is ensured in that the housing of the injection device has a key **14** which at least partly engages the track **7** of piston rod **2**. Thus, when the drive member **6** is free to rotate relative to the housing **5** the piston rod **2** will undergo a translational movement along the axial direction of the injection device.

FIG. **5** shows a third embodiment of the present invention. In this embodiment the dose indicator barrel of the first and second embodiment has been replaced by a counting device having two wheels **15**, **16**. In principle the number of wheels may be chosen arbitrary, but for simplicity, a counting device having only two wheels is illustrated in FIG. **5**. The counting device is operated as follows: When the dose setting member **1** is rotated, the wheel closest to the dose setting member **15** is rotated via an optional planet gear **17**. This wheel contains numerals with an incremental of one. The total scale on this wheel may contain 10 units distributed over a scale from 0 to 9, or alternatively, the total scale may contain for example 20 units distributed over two scales each having a scale from 0 to 9.

The second wheel **16** next to the first wheel **15** also contains numerals with an incremental of 1. However, this second wheel "counts" the number of revolutions of the first wheel, or alternatively, it "counts" the tens of the first wheel with an incremental of one. Alternatively, the second wheel "counts" the number of half resolutions of the first wheel in case the first wheel contains a scale having 20 units.

The invention claimed is:

1. An injection device comprising:

a housing (**5**) with an inner surface provided with threads (**10**),

a dose setting member (**1**) adapted to set a dose to be ejected from the injection device,

a torsion spring (**12**) operatively connected to the dose setting member (**1**), such that energy is accumulated in the torsion spring (**12**) upon rotation of the dose setting member (**1**) and released to eject automatically,

wherein,

a rotatably mounted display member threadedly engaged with threads (**10**) of the housing (**5**) and operatively connected with the dose setting member (**1**) and adapted to display the dose to be ejected from the injection device in accordance with a setting of the dose setting member (**1**), and

the rotatably mounted display member is rotatable over an angle corresponding to at least one revolution of the display member.

2. The injection device according to claim **1**, wherein the display member is adapted to be moved between two end positions, said two end positions defining an operation range of the display member, said operation range being associated with a substantially linear working range of the torsion spring.

3. The injection device according to claim **1**, wherein the display member comprises a dose indicator barrel (**9**) having numerals arranged along a helical path on an outer surface thereof.

4. The injection device according to claim **3**, further comprising:

a piston rod (**2**) having a threaded outer surface with a drive track (**7**) arranged in a longitudinal direction of said outer surface,

wherein the dose setting member (**1**) is rotatably mounted and defines a passage for the piston rod (**2**), the dose setting member (**1**) further having a guiding track (**11**) arranged on an inner surface thereof,

a rotatable drive member (**6**) being adapted to at least partly engage with at least part of the drive track (**7**) of the piston rod (**2**) so as to drive the piston rod,

wherein the dose indicator barrel (**9**) has a part engaging at least part of the guiding track (**11**) of the dose setting member (**1**), the dose setting member (**1**) and the dose indicator barrel (**9**) being movable in relation to each other, the dose indicator barrel (**9**) further having a threaded outer surface (**8**) cooperating with a threaded inner portion (**10**) of the housing (**5**) whereby the dose indicator barrel (**9**) undergoes a combined translational and rotational movement in relation to the housing (**5**) upon rotation of the dose setting member (**1**), and

wherein the injection device has a threaded portion (**3**) cooperating with the threaded outer surface of the piston rod (**2**) so that rotation of the piston rod (**2**) relative to the housing (**5**) results in a longitudinal movement of the piston rod (**2**).

5. The injection device according to claim **3**, further comprising:

a piston rod (**2**) having a threaded outer surface with a track (**7**) arranged in a longitudinal direction of said outer surface,

wherein the dose setting member (**1**) is rotatably mounted and defines a passage for the piston rod (**2**), the dose setting member (**1**) further having a guiding track (**11**) arranged on an inner surface thereof,

a rotatable drive member (**6**) having a threaded portion cooperating with at least part of the threaded outer surface of the piston rod (**2**),

wherein the dose indicator barrel (**9**) has a part engaging at least part of the guiding track (**11**) of the dose setting member (**1**), the dose setting member (**1**) and the dose indicator barrel (**9**) being movable in relation to each other, the dose indicator barrel (**9**) further having a threaded outer surface (**8**) cooperating with a threaded inner portion (**10**) of the housing (**5**) whereby the dose indicator barrel (**9**) undergoes a combined translational and rotational movement in relation to the housing (**5**) upon rotation of the dose setting member (**1**), and

wherein the injection device has a portion at least partly engaging the track (**7**) of piston rod (**2**) so that rotation of the drive member (**6**) relative to the housing (**5**) results in a longitudinal movement of the piston rod (**2**).

6. The injection device according to claim **4**, wherein the drive member (**6**) is adapted to be connected to the dose setting member (**1**) via a ratchet (**13**).

7. The injection device according to claim **5**, wherein the drive member (**6**) is adapted to be connected to the dose setting member (**1**) via a ratchet (**13**).

8. The injection device according to claim **4**, wherein the torsion spring (**12**) is arranged between the housing (**5**) and the dose setting member (**1**) in such a way that when the dose setting member (**1**) is rotated around the piston rod (**2**), the torsion spring (**12**) is strained.

9. The injection device according to claim **5**, wherein the torsion spring (**12**) is arranged between the housing (**5**) and the dose setting member (**1**) in such a way that when the dose setting member (**1**) is rotated around the piston rod (**2**), the torsion spring (**12**) is strained.

10. The injection device according to claim **8**, wherein the torsion spring (**12**) is a helical spring which extends coaxially with the piston rod (**2**).

11. The injection device according to claim **9**, wherein the torsion spring (**12**) is a helical spring which extends coaxially with the piston rod (**2**).

12. The injection device according to claim **4**, further comprising a locking member (**4**) adapted to fixate the piston rod (**2**) in such a way that no relative rotation between of the piston rod (**2**) and the housing (**5**) is possible when the locking member (**4**) is in its locking position.

13. The injection device according to claim **5**, further comprising a locking member (**4**) adapted to fixate the piston rod (**2**) in such a way that no relative rotation between of the piston rod (**2**) and the housing (**5**) is possible when the locking member (**4**) is in its locking position.

14. The injection device according to claim **12**, further comprising a release button adapted to release the locking member (**4**) from its locking position.

15. The injection device according to claim **13**, further comprising a release button adapted to release the locking member (**4**) from its locking position.

16. The injection device according to claim **14**, wherein the release button is positioned in the distal half of the length of the injection device.

17. The injection device according to claim **15**, wherein the release button is positioned in the distal half of the length of the injection device.

18. The injection device according to claim **4**, further comprising a stopping member for defining an outer position of the dose indicator barrel (**9**), the outer position of the dose indicator barrel (**9**) corresponding to a maximum obtainable dose.

19. The injection device according to claim **5**, further comprising a stopping member for defining an outer position of the dose indicator barrel (**9**), the outer position of the dose indicator barrel (**9**) corresponding to a maximum obtainable dose.

* * * * *

EXHIBIT Q

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(12) **Reissued Patent**
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(54) **DIAL-DOWN MECHANISM FOR WIND-UP PEN**

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§ 371 (c)(1),
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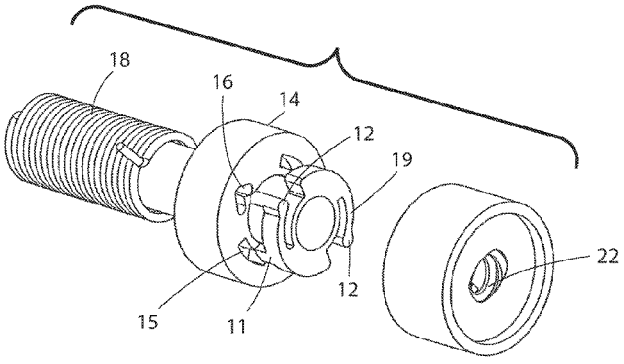
(57) **ABSTRACT**

The present invention relates to a dial-down mechanism for an injection device comprising a torsion spring for assisting injection of a dose of medicament from the injection device, the dial-down mechanism comprising dial-up cam arranged to receive and engage with a dial-up key, wherein the dial-up cam and the dial-up key are adapted to, upon rotation of a dose setting member in a first direction, cooperate to strain the torsion spring of the injection device, and a dial-down cam arranged to receive and engage with a dial-down key, wherein the dial-down cam and the dial-down key are

(Continued)



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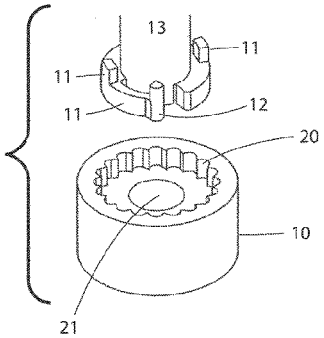

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adapted to, upon rotation of the dose setting member in a second direction, cooperate to release the torsion spring of the injection device, the second rotation direction being opposite to the first rotation direction.

11 Claims, 5 Drawing Sheets

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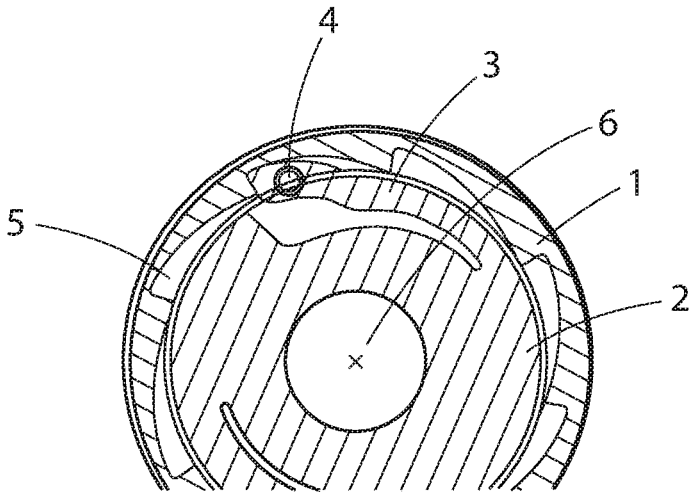

Fig. 1A Amended

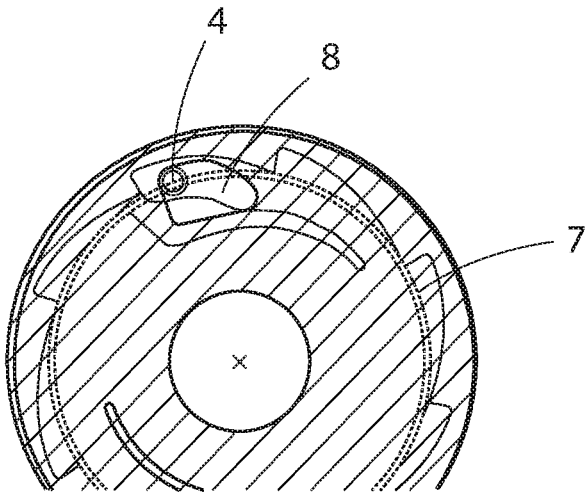

Fig. 1B Amended

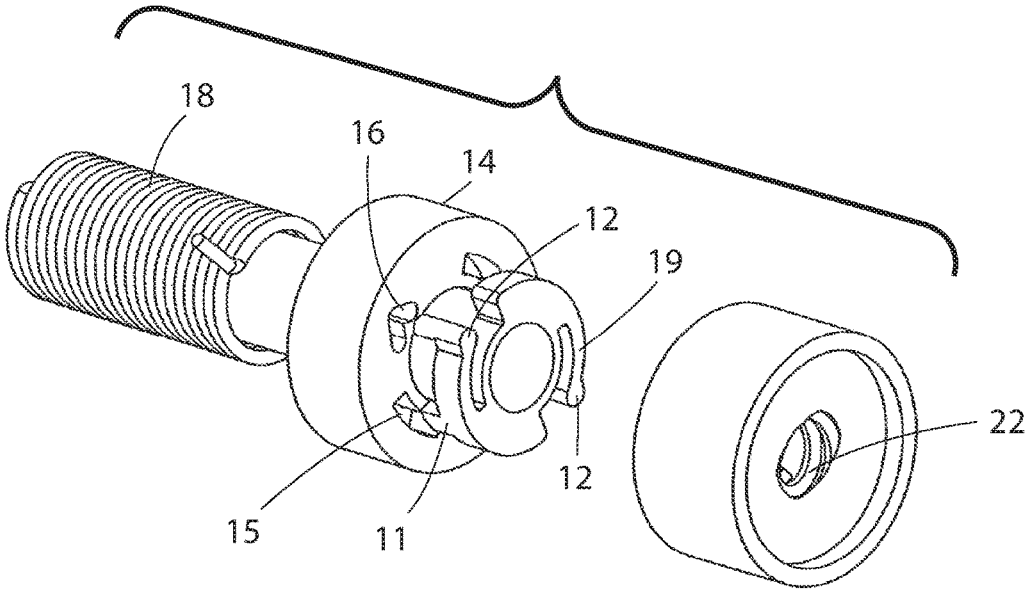

Fig. 2A Amended

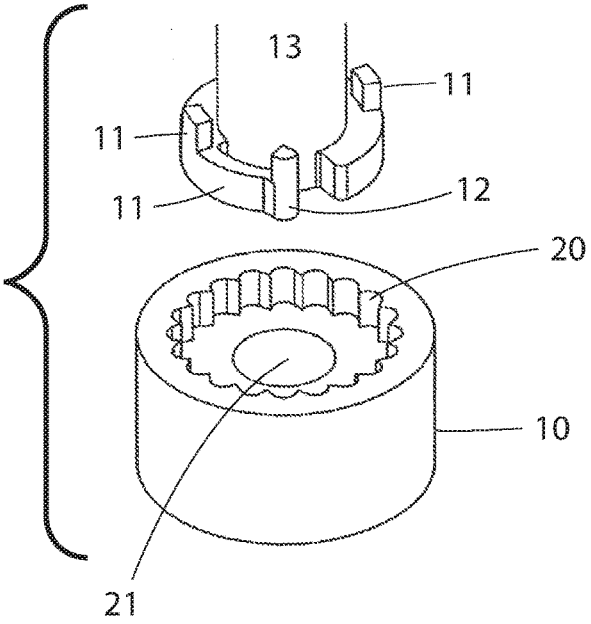

Fig. 2B Amended

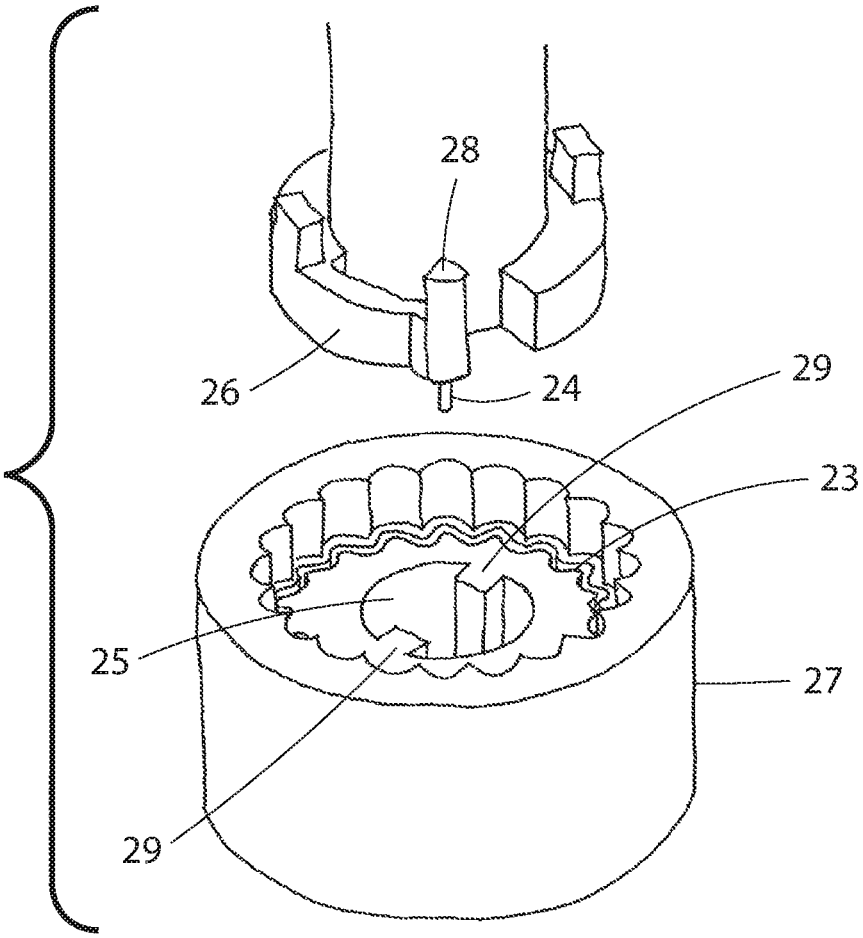

Fig. 3 Amended

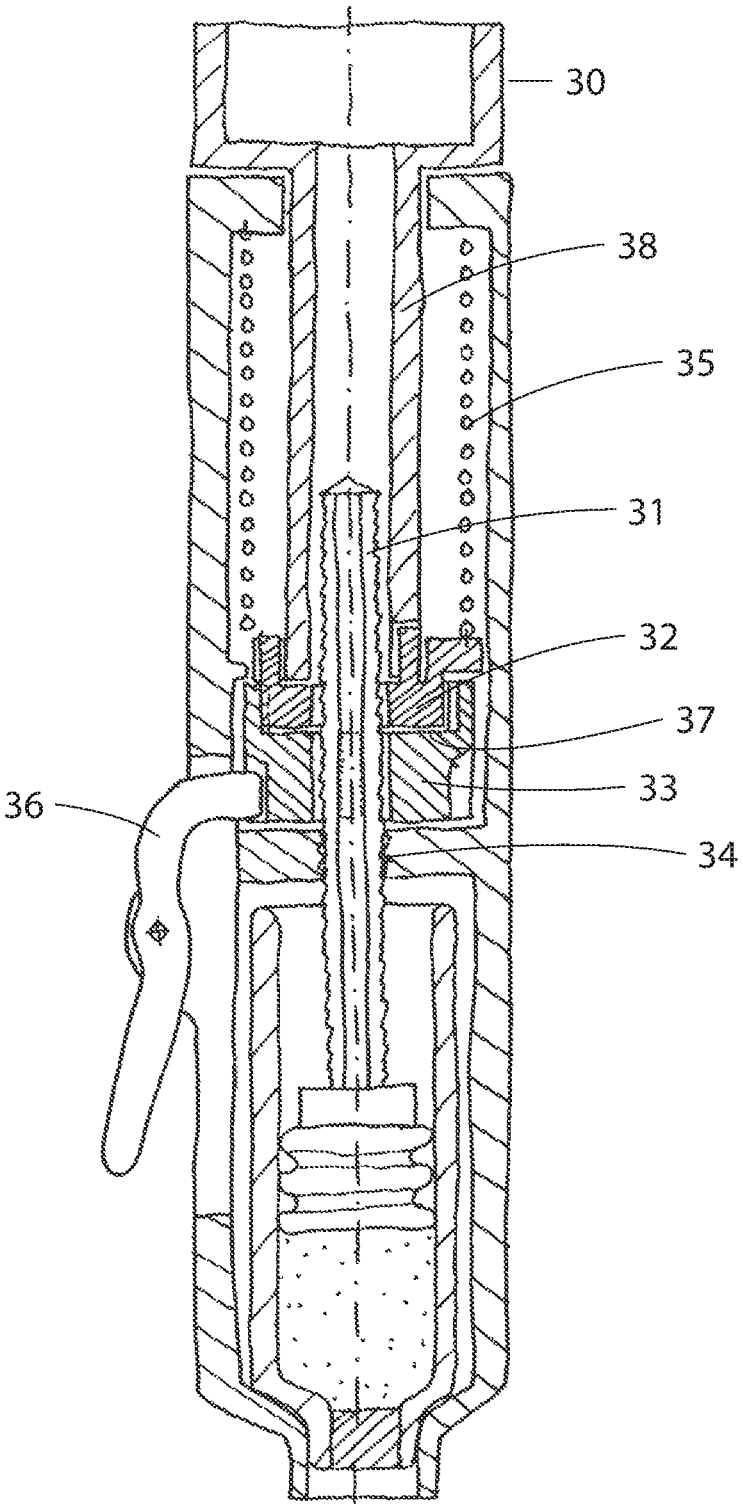

Fig. 4 Amended

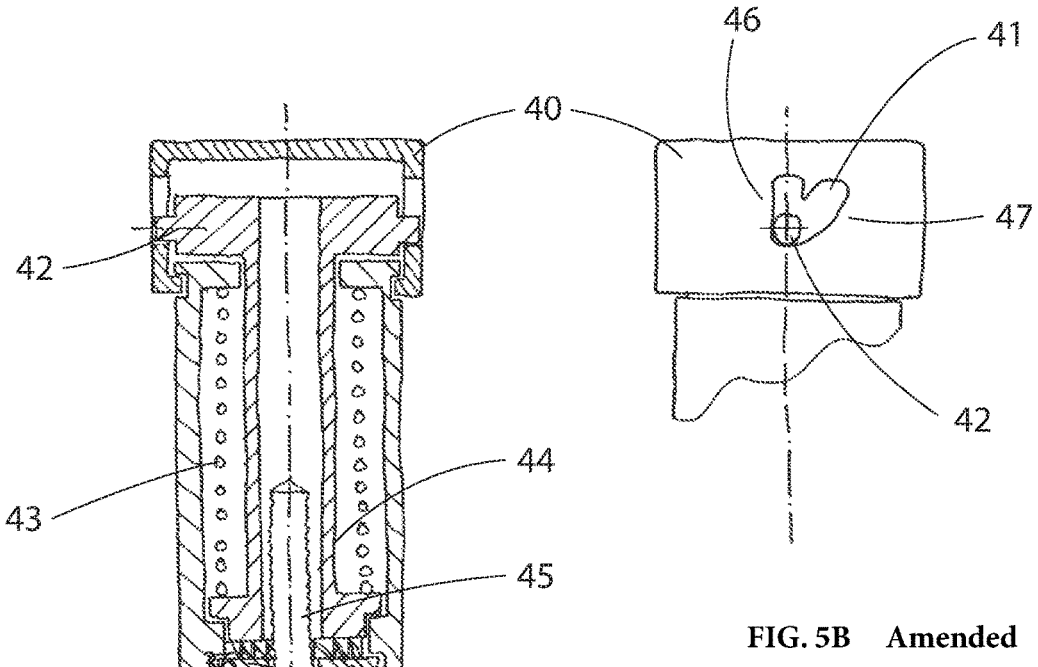

FIG. 5B Amended

FIG. 5A Amended

DIAL-DOWN MECHANISM FOR WIND-UP PEN

Matter enclosed in heavy brackets [ ] appears in the original patent but forms no part of this reissue specification; matter printed in italics indicates the additions made by reissue; a claim printed with strikethrough indicates that the claim was canceled, disclaimed, or held invalid by a prior post-patent action or proceeding.

CROSS-REFERENCE TO RELATED APPLICATIONS

[This application is a 35 U.S.C. § 371 national stage application of International Patent Application PCT/EP2005/011285 (published as WO 2006/045526), filed Oct. 20, 2005, which claimed priority of European Patent Application 04077900.1, filed Oct. 21, 2004; this application further claims priority under 35 U.S.C. § 119 of U.S. Provisional Application 60/626,270, filed Nov. 9, 2004.] *This application is a Divisional Reissue of U.S. application Ser. No. 13/431,019, filed Mar. 27, 2012, which is an Application for Reissue of U.S. Pat. No. 7,686,786, issued Mar. 30, 2010 (U.S. application Ser. No. 11/665,486, filed Oct. 11, 2007), which is a 35 U.S.C. §371 national stage application of International Patent Application PCT/EP2005/011285 (published as WO2006/045526), filed Oct. 20, 2005, which claimed priority of European Patent Application 04077900.1, filed Oct. 21, 2004; this application further claims priority under 35 U.S.C. §119 of U.S. Provisional Application 60/626,270, filed Nov. 9, 2004, incorporated herein by reference.*

FIELD OF THE INVENTION

The present invention relates to a dial-down mechanism for automatic wind-up pens. In particular, the present invention relates to integrated axial and radial dial-down mechanisms for wind-up pens.

BACKGROUND OF THE INVENTION

In known injection devices, such as wind-up pens, based on torsion springs, the use of dial-down mechanisms rely on that the user of the injection device applies a force to a rotatable dose setting member of the injection device. The force must be applied in order to axially withdraw the dose setting member a certain distance to release the dose setting member from a toothing mechanism or ratchet positioned within the body of the injection device. By releasing the dose setting member from this toothing mechanism the dose setting member can be reversed by rotation and set at a new and lower dose.

An example of a known wind-up pen applying a torsion spring may for example be found in U.S. Pat. No. 5,104,380. However, the pen suggested in U.S. Pat. No. 5,104,380 does not offer a dial-down mechanism. A dial-down mechanism is provided in WO 02/053214. However, the proposed solution in WO 02/053214 involves a linear spring.

It is a disadvantage of known torsion spring-based dial-down systems that the user must apply a force to withdraw the dose setting member a certain axial distance and, at the same time, adjust the angular position of the dose setting member. Especially for persons having reduced motoric skills or reduced finger strength, such as children, elderly people or disabled people this is a rather complicated procedure.

US 2004/199117 discloses a medication delivery pen including an arrangement where incorrect dosage settings may be corrected by a user via a dial-back feature that enables the user to reset the dose amount without expelling medication and without having to dial a dose knob to an extended, reset position. The medication delivery pen of US 2004/199117 is a so-called manual pen where the injection of a medicament from the pen is driven by a force purely provided by the user of the pen. Thus, the injection of a medicament is not assisted by any resilient member, such as a spring, and the dial-down arrangement disclosed in US 2004/199117 is not arranged to maintain a resilient member in a given strained position.

It is an object of the present invention to provide a dial-down mechanism for automatic wind-up pens. Automatic wind-up pens are here to be understood as pens having a resilient member, such as a spring, to assist injecting a medicament from an injection device.

SUMMARY OF THE INVENTION

The above-mentioned object is complied with by providing, in a first aspect, a dial-down mechanism for an injection device comprising a torsion spring for assisting injection of a dose of medicament from the injection device, the dial-down mechanism comprising

- dial-up cam arranged to receive and engage with a dial-up key, wherein the dial-up cam and the dial-up key are adapted to, upon rotation of a dose setting member in a first direction, cooperate to strain the torsion spring of the injection device, and
- a dial-down cam arranged to receive and engage with a dial-down key, wherein the dial-down cam and the dial-down key are adapted to, upon rotation of the dose setting member in a second direction, cooperate to release the torsion spring of the injection device, the second rotation direction being opposite to the first rotation direction.

Generally speaking the dial-down mechanism may be implemented as a radial dial-down mechanism or as an axial dial-down mechanism. In the radial dial-down mechanism the dial-down key or keys are arranged to move in the radial direction of the mechanism. This may also be the radial direction of the injection device. In the axial dial-down mechanism, the dial-down key or keys are arranged to move in the axial direction of the injection device.

Also it should be noted that the dial-up key or keys, and the dial-down key or keys may be different keys—i.e. physically separated keys. However, it may also be that the dial-up and dial-down key is constituted by the same key. Thus, it may be that the mechanism according to the present invention comprises only a single key which is used for both dial-up and dial down.

The dial-up and dial-down cams may be arranged as openings or indentations in an outer surface part of a disc-shaped cam member. The cam member may, alternatively, also be shaped as a substantially cylindrical member. In particular, the dial-up and dial-down cams may be arranged in a substantially plane surface part of the cam member. This substantially plane surface part may be substantially perpendicular to an axial direction of the disc or cylindrical shaped cam member. The cam member may be a hollow construction, or alternatively, the cam member may be a solid construction.

In both the radial and the axial mechanism, the dial-up cam may form a curved track, such as part of a circular, elliptical or parabolic track. The dial-down cam may form part of a V-shaped track, or alternative, it may have a rectangular shape.

The dial-down mechanism may comprise a first and a second dial-up cam. Furthermore, the dial-down mechanism may comprise a first and a second dial-up key, wherein the first dial-up key may be adapted to engage and cooperate with the first dial-up cam, and wherein the second dial-up key may be adapted to engage and cooperate with the second dial-up cam.

The dial-down mechanism may further comprise a first and a second dial-down cam, and a first and a second dial-down key. The first dial-down key may be adapted to engage and cooperate with the first dial-down cam, whereas the second dial-down key may be adapted to engage and cooperate with the second dial-down cam.

It may also be that the dial-up and dial-down cams form part of regions of the same track. Furthermore, the dial-up and dial-down keys may be constituted by the same key, said key being adapted to engage and cooperate with dial-up and dial-down cams of the same track.

In the axial mechanism, the dial-up and dial-down cams may be arranged as cams having an axial component parallel to an axial direction of the injection device. The dial-up and dial-down cams may be arranged on an outer and curved surface part of a substantially cylindrical cam member. This substantially cylindrical cam member may be the dose setting member of the injection device, or it may be a separate component cooperating with the dose setting member of the injection device.

In the axial mechanism, the dial-up cam may be substantially parallel to an axial direction of the injection device. In order to be able to release an associated ratchet from a toothing the dial-down cam may form an angle, such as around 45 degrees, to the dial-up cam.

In a second aspect, the present invention relates to an axially arranged dial-down mechanism for an injection device, the dial-down mechanism comprising

a rotatable member adapted to be rotated when a dose to be injected from the injection device is set, the rotatable member comprising a dial-up cam and a dial-down cam, wherein the dial-up cam is adapted to receive and engage with a key of a ratchet of the injection device during dose setting during dial-up, and wherein the dial-down cam is adapted to receive and engage with the key during dial-down,

wherein the dial-up cam is substantially parallel to an axial direction of the injection device.

In this second aspect of the present invention the dial-up and dial-down cams may form part of regions of the same track. The dial-up and dial-down keys may be constituted by the same key, said key being adapted to engage and cooperate with dial-up and dial-down cams of the same track.

In a third aspect, the present invention relates to a medication delivery device, such as a handheld medication delivery device, comprising a dial-down mechanism according to the first aspect of the present invention.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will now be described in further details with reference to the accompanying figures, wherein

FIG. **1** shows the principle of a radial dial-up and dial-down mechanism where the keys on the flexible arm are used for both dial-up and dial-down,

[FIG. **2** shows] *FIGS. 2A and 2B show* a radial dial-up/dial down mechanism with separate keys for dial-up and dial-down, *where FIG. 2A shows torsion spring 18 and disc 14 over ratchet 13* (*not labeled*) *and adjacent to nut 10* (*not labeled*), *and FIG. 2B also shows ratchet 13 adjacent nut 10.*

FIG. **3** shows a radial dial-up/dial down mechanism with separate keys for dial-up and dial-down where the movements of the dial-down key is determined by a track in the nut,

FIG. **4** shows an injection device having an integrated radial dial-down mechanism, and

[FIG. **5** shows] *FIGS. 5A and 5B show* an injection device having an integrated axial dial-down mechanism, *where FIG. 5A shows a cross-section of an injection device, and FIG. 5B shows a partial front or side elevation view of the same injection device.*

While the invention is susceptible to various modifications and alternative forms, specific embodiments have been shown by way of example in the drawings and will be described in detail herein. It should be understood, however, that the invention is not intended to be limited to the particular forms disclosed. Rather, the invention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the appended claims.

DETAILED DESCRIPTION OF THE INVENTION

The dial-down mechanism according to the present invention may be implemented as an axial or a radial mechanism. Both of these mechanisms may be integrated into an injection device, such as an injection pen.

A radial solution is shown in FIG. **1**. FIG. **1**a shows a rotatable inner part **2** biased against a fixed outer part **1**. The biasing force is provided by a torsion spring (not shown) in the counter-clockwise direction. The inner part **2**, which is rotatable around a center axis **6**, has one or more flexible arms **3** adapted to engage with the edges **5** in the fixed outer part **1**. FIG. **1**b shows the arrangement of FIG. **1**a with a rotatable disc **7** (hatched region) placed on top of the inner part **2** and outer part **1**. The disc **7** has an opening **8**. The edges defining the opening **8** constitute dial-up and dial-down cams. A pick-up key **4** attached to, or integrated with, the flexible arm **3** operates as a cam follower when the disc **7** is rotated relative to the outer part **1**.

The system illustrated in FIG. **1** is operated in the following manner:

When a dose is to be set (dial-up), the inner part **2** is rotated in the clockwise direction whereby the flexible arm **3** will move from one edge **5** to the neighboring edge or edges—depending on the angle of rotation. The inner part **2** is driven by disc **7**—thus, when disc **7** is rotated the inner part **2** rotates with it. During rotation in the clockwise direction, the pick-up key **4** moves in and out along the radial direction.

When the disc **7** is rotated in the counter clockwise direction (dial-down direction) the pick-up key **4**, and thereby the flexible arm **3**, is lifted out of its engaging position with the edge **5** of the outer part **1**. When the arm **3** is fully disengaged from the edge **5** the inner part **2** may be rotated in the counter clockwise direction relative to the outer part **1**. It is a characteristic of the system shown in FIG. **1** that the pick-up key **4** is used for both dial-up (increasing a dose) and dial-down (resetting or reducing a dose).

It should be noted that the directions of rotation could be reversed so that dial-up is achieved by rotating the inner

portion **2** in the counter clockwise direction. In such a configuration dial-down could be achieved by rotating disc **7** in the clockwise direction.

[FIG. **2** shows] *FIGS. 2A and 2B show* an exploded drawing of the radial embodiment of the dial-down mechanism according to the present invention. The main difference compared to the embodiment shown in FIG. **1** is that the embodiment of [FIG. **2**] *FIGS. 2A and 2B* applies different pick-up keys for dial-up (pick-up key **11**) and dial-down (pick-up key **12**). The dial-up key **11** engages with track **15** of the disc **14**, whereas dial-down key **12** engages with track **16** of the disc **14**. Tracks **15** and **16** are formed as through-going openings or indentations in a planar surface of the disc **14**. The dial-up tracks **15** take the form of curved tracks whereas the dial-down tracks **16** are V-shaped. An obvious alternative to the V-shape is a rectangular shape. It should be noted that the general idea is that the dial-up tracks **15** should be capable of transferring a momentum to a torsion spring **18**. In the same manner, the dial-down tracks **16** should be capable of releasing the dial-down keys (and thereby release energy) in case the disc **14** is rotated just a few degrees relative to the nut **10**.

The dial-down keys **12** are integrated with the flexible arms **19**. These arms are fabricated of a resilient material such as for example plastic. The flexible arms **19** with integrated dial-down keys **12** form an integral part of the ratchet **13**. Thus, the ratchet including arms and dial-down keys may preferably be fabricated of the same material, such as of plastic. In order to bias the dial-down keys **12** against the teeth **20** of the nut **10** a torsion spring **18** is arranged coaxially with the ratchet **13**. An opening **21** is provided in the center part of the nut **10**. The side wall of this opening is provided with threads **22** which are adapted to engage with a threaded outer surface of a piston rod (not shown).

FIG. **3** shows another radial embodiment according to the present invention. In this embodiment, the movement of the arm **26** is controlled by a track **23** in the nut **27**. The track **23** is engaged by the track/cam follower **24** which precisely guides the dial-down key **28** from one tooth to the neighboring tooth during dial-down. In contrast to FIG. **2** the opening **25** in the center of the nut **27** is provided with a track follower **29**. This track follower is adapted to engage with a track in the outer surface of a piston rod (not shown).

FIG. **4** shows an injection device having a radial dial-down mechanism according to the present invention. Among other components the injection device shown in FIG. **4** shows a dose setting member **30**, a piston rod **31** having a threaded outer surface and a drive track arranged in the axial direction of the piston rod, a nut **32**, a torsion spring **35**, a drive member **33**, the threaded portion **34** of the housing, a lease mechanism **36**, a toothing mechanism **37**, and ratchet **38**.

A dose is set by rotating the dose setting member **30** and the nut **32** whereby the torsion spring **35** is strained. The dose setting member **30** is prevented from returning to its initial position due the toothing mechanism **37** positioned between the nut **32** and the drive member **33**. In case the user wants to reduce a preset dose, the dose setting member **30** is simply rotated in the opposite direction. The interaction between ratchet **38** and nut **32** during dial-down is described in connection with FIG. **2**.

[FIG. **5** shows] *FIGS. 5A and 5B show* an injection device having an axial dial-down mechanism according to the present invention. Among other components the injection device shown in FIG. **[5]** *5B* comprising a dose setting member **40**, an opening **41** defining dial-up and dial-down cam surfaces, a cam follower **42**, a torsion spring **43**, a ratchet **44**, and a piston rod **45**. The general idea behind the axial dial-down mechanism is to use the torsion spring **43** to both drive and rotate the piston rod **45** and to ensure that the upper and lower parts of the toothing **48** remain together.

When a dose is to be set, the cam follower **42** engages with cam surface **46**. As a result the torsion spring **43** is strained because the ratchet **44** is prevented from reversing due to the toothing **48**. During dial-up the ratchet **44** will move up and down along cam surface **46** as the upper and lower parts of the toothing **48** rotate relative to each other. In case of dial-down the cam surface **47** will lift and thereby release the upper part of the toothing from the lower part of the toothing thereby the ratchet **44** is allowed to rotate an angle corresponding to one tooth.

The invention clamed is:

1. A dial-down mechanism for an injection device comprising a torsion spring (**18**) for assisting injection of a dose of medicament from the injection device, the dial-down mechanism comprising

dial-up cam (**15**) arranged to receive and engage with a dial-up key (**11**), wherein the dial-up cam (**15**) and the dial-up key (**11**) are adapted to, upon rotation of a dose setting member in a first direction, cooperate to strain the torsion spring (**18**) of the injection device, and

a dial-down cam (**16**) arranged to receive and engage with a dial-down key (**12**), wherein the dial-down cam (**16**) and the dial-down key (**12**) are adapted to, upon rotation of the dose setting member in a second direction, cooperate to release the torsion spring (**18**) of the injection device, the second rotation direction being opposite to the first rotation direction,

wherein the dial-up and dial-down cams form part of regions of the same track,

further comprising an arm wherein the dial-up and dial-down keys are both located on the same arm, said keys being adapted to engage and cooperate with dial-up and dial-down cams of the same track.

2. A dial-down mechanism according to claim **1**, wherein the dial-up cam (**15**) forms part of a curved track.

3. A dial-down mechanism according to claim **2**, wherein the curved dial-up cam (**15**) forms part of a circular, elliptical or parabolic track.

4. A dial-down mechanism according to claim **1** comprising a first and a second dial-up cam.

5. A dial-down mechanism according to claim **4** comprising a first and a second dial-up key, wherein the first dial-up key is adapted to engage and cooperate with the first dial-up cam, and wherein the second dial-up key is adapted to engage and cooperate with the second dial-up cam.

6. A dial-down mechanism according to claim **1**, wherein the dial-down cam (**16**) forms part of a V-shaped track.

7. A dial-down mechanism according to claim **1** comprising a first and a second dial-down cam.

8. A dial-down mechanism according to claim **7** comprising a first and a second dial-down key, wherein the first dial-down key is adapted to engage and cooperate with the first dial-down cam, and wherein the second dial-down key is adapted to engage and cooperate with the second dial-down cam.

9. A medication delivery device comprising a dial-down mechanism according to claim **1**.

10. A medication delivery device according to claim **9**, wherein the medication delivery device is a handheld medication injection pen.

11. A method for using a wind up injection pen, the method comprising the steps of

rotating a first element in a first direction, the direction being a dial up direction;

causing a second element to be rotated in the same direction as the first element;

straining a torsional spring;

moving an arm that is in engagement with one edge to a neighboring edge, wherein when the arm is engaged with an edge it prevents the torsional spring from unwinding;

rotating the first element in a second direction opposite the first direction;

moving a pick-up key and radially lifting the arm out of engagement with an edge and when the arm is fully disengaged from an edge allowing the second rotatable element to rotate in the second direction and allowing the strain on the spring to be decreased.

* * * * *