a. an insulin;
b. citrate, in a concentration from 5 to 25 mM;
c. treprostinil, in a concentration from 0.04 to 20 µg/mL;
d. zinc, in a concentration sufficient to provide at least 2 zinc ions per six molecules of insulin;
e. a preservative; and
f. one or more additional stabilizing agents selected from the group consisting of magnesium-containing compounds and sodium chloride;

and having a pH of 7.0 to 7.8 at room temperature.

In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising:

a. an insulin;
b. citrate, in a concentration from 5 to 25 mM;
c. treprostinil, in a concentration from 0.04 to 20 µg/mL;
d. a preservative;
e. a stabilizing agent comprising zinc, in a concentration sufficient to provide at least 2 zinc ions per six molecules of insulin; and

and having a pH of 7.0 to 7.8 at room temperature.

In a further aspect of the present disclosure, there is provided the pharmaceutical composition disclosed herein for use in therapy.

In another aspect of the present disclosure, there is provided the pharmaceutical composition disclosed herein for use in the treatment of diabetes.

WE CLAIM:

1. A pharmaceutical composition comprising:
    a. an insulin;
    b. citrate, in a concentration from 5 to 25 mM;
    c. treprostinil, in a concentration from 0.04 to 20 µg/mL;
    d. zinc, in a concentration sufficient to provide at least 2 zinc ions per six molecules of insulin;
    e. a preservative; and
    f. one or more additional stabilizing agents selected from the group consisting of magnesium-containing compounds and sodium chloride;

    and having a pH of 7.0 to 7.8 at room temperature.
2. The pharmaceutical composition of claim 1 wherein the zinc concentration is from 0.2 to 2 mM.
3. The pharmaceutical composition of any of claims 1-2 wherein the zinc concentration is from 0.2 to 1 mM.
4. The pharmaceutical composition of any of claims 1-3, wherein the zinc concentration is from 0.6 to 0.8 mM.
5. The pharmaceutical composition of any of claims 1-4, wherein the one or more additional stabilizing agents comprise a magnesium-containing compound.
6. The pharmaceutical composition of claim 5, wherein the magnesium-containing compound is present in a concentration resulting in a molar ratio of magnesium to citrate from 1:2 to 1:10.
7. The pharmaceutical composition of claim 6, wherein the molar ratio of magnesium to citrate is from 1:3 to 1:5.
8. The pharmaceutical composition of any of claims 6-7 wherein the magnesium-containing compound is magnesium chloride.
9. The pharmaceutical composition of any of claims 1-8, wherein the insulin concentration is from 100 to 300 U/mL.
10. The pharmaceutical composition of any of claims 1-9, wherein the insulin concentration is either 100 U/mL or 200 U/mL.

11. The pharmaceutical composition of any of claims 1-10, wherein the insulin is insulin lispro.
12. The pharmaceutical composition of any of claims 1-11, wherein the concentration of citrate is from 10 to 25 mM.
13. The pharmaceutical composition of any of claims 1-12, wherein the concentration of treprostinil is from 0.04 to 10 µg/mL.
14. The pharmaceutical composition of any of claims 1-13, wherein the concentration of treprostinil is from 0.5 to 2 µg/mL.
15. The pharmaceutical composition of any of claims 1-14, wherein the preservative is m-cresol.
16. The pharmaceutical composition of claim 15, wherein the concentration of m-cresol is from 2.5 to 3.8 mg/mL.
17. The pharmaceutical composition of any of claims 1-16, wherein the one or more additional stabilizing agents comprise sodium chloride.
18. The pharmaceutical composition of claim 17 wherein the sodium chloride is present in a concentration from 1 to 50 mM.
19. The pharmaceutical composition of any of claims 1-18, wherein the total concentration of chloride is from 10 to 50 mM.
20. The pharmaceutical composition of any of claims 1-19, further comprising a tonicity agent.
21. The pharmaceutical composition of claim 20, wherein the tonicity agent is glycerol.
22. The pharmaceutical composition of claim 21, wherein the concentration of glycerol is from 1 to 15 mg/mL.
23. The pharmaceutical composition of claim 1 comprising:
    a. insulin lispro, in a concentration from 100 to 200 U/mL;
    b. citrate, in a concentration from 5 to 25 mM;
    c. treprostinil, in a concentration from 0.5 to 2 µg/mL; and
    d. zinc, in a concentration from 0.2 mM to 2 mM.
24. The pharmaceutical composition of claim 23, wherein the concentration of citrate is from 15 to 25 mM.
25. The pharmaceutical composition of any of claims 23-24, wherein the concentration of zinc is from 0.6 to 0.9 mM.

26. The pharmaceutical composition of any of claims 23-25, further comprising a magnesium-containing compound, in a concentration resulting in a molar ratio of magnesium to citrate from 1:3 to 1:5.

27. The pharmaceutical composition of any of claims 1-26 having a pH of about 7.4.

28. The pharmaceutical composition of claim 23 wherein:

a. insulin lispro is in a concentration of about 100 U/mL;
b. citrate is in a concentration of about 15 mM;
c. treprostinil is in a concentration of about 1 µg/mL; and
d. zinc is in a concentration of about 0.6 mM;

and further comprising:

e. magnesium chloride in a concentration of about 5 mM;
f. m-cresol, in a concentration of about 3.15 mg/mL;
g. glycerol, in a concentration of about 12 mg/mL;

and having a pH of about 7.4.

29. The pharmaceutical composition of claim 23 wherein:

a. insulin lispro is in a concentration of about 200 U/mL;
b. citrate is in a concentration of about 15 mM;
c. treprostinil is in a concentration of about 1 µg/mL; and
d. zinc is in a concentration of about 0.8 mM;

and further comprising:

e. magnesium chloride in a concentration of about 5 mM;
f. m-cresol, in a concentration of about 3.15 mg/mL; and
g. glycerol, in a concentration of about 12 mg/mL;

and having a pH of about 7.4.

30. A pharmaceutical composition comprising:
    a. an insulin;
    b. citrate, in a concentration from 5 to 25 mM;
    c. treprostinil, in a concentration from 0.04 to 20 µg/mL;
    d. a preservative;
    e. a stabilizing agent comprising zinc, in a concentration sufficient to provide at least 2 zinc ions per six molecules of insulin; and

and having a pH of 7.0 to 7.8 at room temperature.

31. The pharmaceutical composition of any one of Claims 1-30 for use in therapy.

32. The pharmaceutical composition of any one of Claims 1-30 for use in the treatment of diabetes.

33. Use of the pharmaceutical composition of any one of Claims 1-30 in the manufacture of a medicament for the treatment of diabetes.

34. An article of manufacture comprising any one of the pharmaceutical compositions of Claims 1-30.

35. The article of manufacture of Claim 34 which is a multi-use vial.

36. The article of manufacture of Claim 34 which is a multi-use cartridge.

37. The article of manufacture of Claim 34 which is a re-usable pen injector.

38. The article of manufacture of Claim 34 which is a disposable pen device.

39. The article of manufacture of Claim 34 which is a pump device for continuous subcutaneous insulin infusion therapy.

40. The article of manufacture of Claim 34 which is a container closure system for use in a pump device for continuous subcutaneous insulin infusion therapy.