CLAIMS

What is claimed is:

1. A pharmaceutical composition for providing sustained glycemic control, comprising an effective amount of a protein comprising an insulin amino acid sequence and an amino acid sequence providing a sustained release from an injection site, and pharmaceutical excipients to achieve sustained release.

2. The pharmaceutical composition of claim 1, wherein the insulin amino acid sequence comprises an A chain and a B chain amino acid sequence, wherein the A chain and B chain have the amino acid sequence of SEQ ID NO: 13, optionally having from 1 to 8 amino acid insertions, deletions, or substitutions, collectively.

3. The pharmaceutical composition of claim 2, wherein the amino acid sequence that provides a slow absorption from the injection site is covalently bound to the insulin A chain.

4. The pharmaceutical composition of claim 2 or 3, wherein the A chain and B chain are bound by one or more disulfide bonds.

5. The pharmaceutical composition of claim 2 or 3, wherein the A chain and B chain are attached through a peptide or chemical linker.

6. The pharmaceutical composition of claim 1, wherein the amino acid sequence providing a sustained release has a substantially repeating pattern of proline residues.

7. The pharmaceutical composition of claim 6, wherein the amino acid sequence providing a sustained release is an elastin-like peptide (ELP) amino acid sequence.

8. The pharmaceutical composition of claim 7, wherein the ELP comprises repeats of VPGXG (SEQ ID NO: 3), where each X is independently selected from alanine, arginine, asparagine, aspartic acid, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, serine, threonine, tryptophan, tyrosine and valine residues.

9. The pharmaceutical composition of claim 8, wherein X is valine.

10. The pharmaceutical composition of claim 9, wherein the amino acid sequence of the ELP comprises repeats of AVGVP (SEQ ID NO: 4), IPGVG (SEQ ID NO: 6), or LPGVG (SEQ ID NO: 8).

11. The pharmaceutical composition of any one of claim 10, wherein the ELP comprises at least 15 repeats of an ELP amino acid unit.

12. The pharmaceutical composition of claim 10, wherein the ELP comprises at least 30 repeats of an ELP unit.

13. The pharmaceutical composition of claim 10, wherein the ELP comprises at least 60 repeats of an ELP unit.

14. The pharmaceutical composition of claim 10, wherein the ELP comprises at least 90 repeats of an ELP unit.

15. The pharmaceutical composition of claim 10, wherein the ELP comprises at least 120 repeats of an ELP unit.

16. The pharmaceutical composition of claim 10, wherein the ELP comprises at least 180 repeats of an ELP unit.

17. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition comprises SEQ ID NO: 14.

18. The pharmaceutical composition of claim 7, wherein the ELP has a transition temperature of just less than 37°C in normal saline.

19. The pharmaceutical composition of claim 1, wherein the amino acid sequence providing a sustained release forms a random coil or non-globular extended structure or unstructured biopolymer, including a biopolymer where at least 50% of the amino acids are devoid of secondary structure as determined by Chou-Fasman algorithm.

20. The pharmaceutical composition of claim 1, wherein the amino acid sequence is a protein having an extended, non-globular structure, or a random coil structure.

21. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition is a fusion protein.

22. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition comprises about 110mM sodium chloride and about 20mM histidine.

23. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition is formulated for administration about once per week.

24. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition is formulated for administration daily.

25. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition is formulated for administration at a dosage of about 0.5 mg/mL to about 200 mg/mL.

26. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition is formulated for administration at a dosage of about 10 mg/mL to about 50 mg/mL.

27. The use of a pharmaceutical composition in the manufacture of a medicament for the treatment of diabetes, wherein the pharmaceutical composition comprises an effective amount of a protein comprising an insulin amino acid sequence and an amino acid sequence providing a sustained release from an injection site, and pharmaceutical excipients to achieve sustained release.

28. The use of claim 27, wherein the diabetes is type 1 diabetes.

29. The use of claim 27, wherein the diabetes is type 2 diabetes.

30. The method of claim 27, wherein the pharmaceutical composition is administered at a frequency of from 1 to about 30 times per month.

31. The method of claim 27, wherein the pharmaceutical composition is administered about weekly.

32. The method of claim 27, wherein the pharmaceutical composition is administered two or three times per week.

33. The method of claim 27, wherein the pharmaceutical composition is administered about daily.

34. The method of claim 27, wherein the pharmaceutical composition is administered subcutaneously.

CLAIMS

1. A pharmaceutical composition for providing sustained glycemic control, comprising an effective amount of a fusion protein comprising the amino acid sequence of SEQ ID NO: 15 and the amino acid sequence of SEQ ID NO: 16, and an elastin-like peptide (ELP) amino acid sequence comprising at least one repeat of VPGXG (SEQ ID NO: 3), wherein administration of the fusion protein lowers fasting blood glucose levels for at least six hours following administration in a patient, and pharmaceutical excipients.

2. The pharmaceutical composition of claim 1, wherein the ELP is covalently bound to SEQ ID NO: 15.

3. The pharmaceutical composition of claim 1, wherein the amino acid sequence of SEQ ID NO: 15 and the amino acid sequence of SEQ ID NO:16 are bound by one or more disulfide bonds.

4. The pharmaceutical composition of claim 1, wherein the ELP component comprises at least 120 repeat units of VPGXG, wherein each X is independently selected from V, A, and G.

5. The pharmaceutical composition of claim 4, wherein the ELP component comprises at least 120 repeat units of VPGXG, wherein X is V, A, and G in the ratio of about V5, A2, and G3.

6. The pharmaceutical composition of claim 5, wherein the fusion protein comprises the amino acid sequences of SEQ ID NO: 15, SEQ ID NO: 16, and SEQ ID NO: 32.

7. The pharmaceutical composition of claim 1 or 6, wherein the pharmaceutical excipients comprise two or more of calcium chloride, magnesium chloride, potassium chloride, potassium phosphate monobasic, sodium chloride, and sodium phosphate dibasic.

8. The pharmaceutical composition of claim 1 or 6, wherein the pharmaceutical composition is formulated for administration about once per week.

9. The pharmaceutical composition of claim 1 or 6, wherein the pharmaceutical composition is formulated for administration daily.

10. The pharmaceutical composition of claim 1 or 6, wherein the pharmaceutical composition is formulated for administration at a dosage of about 0.5 mg/mL to about 200 mg/mL.

11. The pharmaceutical composition of claim 10, wherein the pharmaceutical composition is formulated for administration at a dosage of about 10 mg/mL to about 50 mg/mL.

12. The use of a pharmaceutical composition in the manufacture of a medicament for the treatment of diabetes, wherein the pharmaceutical composition comprises an effective amount of a fusion protein comprising the amino acid sequence of SEQ ID NO: 15 and the amino acid sequence of SEQ ID NO: 16, and an elastin-like peptide (ELP) amino acid sequence comprising at least one repeat of VPGXG (SEQ ID NO: 3), wherein administration

of the fusion protein lowers fasting blood glucose levels for at least six hours following administration in a patient, and pharmaceutical excipients.

13. The use of claim 12, wherein the ELP is covalently bound to SEQ ID NO: 15.

14. The use of claim 12, wherein the amino acid sequence of SEQ ID NO: 15 and the amino acid sequence of SEQ ID NO:16 are bound by one or more disulfide bonds.

15. The use of claim 12, wherein the ELP component comprises at least 120 repeat units of VPGXG, wherein each X is independently selected from V, A, and G.

16. The use of claim 15, wherein the ELP component comprises at least 120 repeat units of VPGXG, wherein X is V, A, and G in the ratio of about V5, A2, and G3.

17. The use of claim 16, wherein the fusion protein comprises the amino acid sequences of SEQ ID NO: 15, SEQ ID NO: 16, and SEQ ID NO: 32.

18. The use of claim 12 or 17, wherein the pharmaceutical excipients comprise two or more of calcium chloride, magnesium chloride, potassium chloride, potassium phosphate monobasic, sodium chloride, and sodium phosphate dibasic.

19. The use of claim 12 or 17, wherein the diabetes is type 1 diabetes.

20. The use of claim 12 or 17, wherein the diabetes is type 2 diabetes.

21. The use of claim 12 or 17, wherein the pharmaceutical composition is administered at a frequency of from about 1 to about 30 times per month,

22. The use of claim 21, wherein the pharmaceutical composition is administered about weekly.

23. The use of claim 21, wherein the pharmaceutical composition is administered two or three times per week.

24. The use of claim 21, wherein the pharmaceutical composition is administered about daily.

25. The use of claim 12 or 17, wherein the pharmaceutical composition is administered subcutaneously.