CLAIMS

1. An insulin analog comprising an A chain peptide and a B chain peptide, wherein the B chain comprises an aromatic or large aliphatic residue at a position corresponding to amino acid number 20 of the B chain of human insulin and/or an aromatic or large aliphatic residue at a position corresponding to amino acid number 15 of the B chain of human insulin, wherein the analog comprises at least one amino acid found in human insulin but lacking in the corresponding position of *Conus geographus* venom insulin, and wherein the A chain peptide and the B chain peptide are bonded together across at least one pair of cysteine residues.

2. The insulin analog of claim 1, wherein the aromatic or large aliphatic residue at a position corresponding to amino acid number 20 of the B chain of human insulin is selected from the group consisting of tyrosine, phenylalanine, 4 methylphenylalanine, histidine, tryptophan, methionine, cyclopentylalanine and cyclohexylalanine.

3. The insulin analog of claim 1 or claim 2, wherein the B chain is truncated at the C terminal end when compared to human insulin.

4. The insulin analog of claim 3, wherein the B chain is lacking one or more or all of the nine C terminal amino acids of human insulin.

5. The insulin analog of claim 3 or claim 4, wherein the B chain is at least lacking Phe_{B24} of human insulin.

6. The insulin analog according to any one of claims 1 to 5, wherein the B chain is at least lacking the human B chain aromatic triplet (amino acids Phe_{B24} Phe_{B25} Tyr_{B26}).

7. The insulin analog according to any one of claims 1 to 6, comprising:

an A chain peptide comprising the sequence Gly-X_{A2}-X_{A3}-X_{A4}-X_{A5}-Cys_{A6}-Cys_{A7}-X_{A8}-X_{A9}-X_{A10}-Cys_{A11}-X_{A12}-X_{A13}-X_{A14}-X_{A15}-X_{A16}-X_{A17}-X_{A18}-X_{A19}-Cys_{A20}-X_{A21}-X_{A22}-X_{A23}-X_{A24}-X_{A25}-X_{A26}-X_{A27}-X_{A28}-X_{A29}-X_{A30}-X_{A31}-X_{A32}-X_{A33}-X_{A34},

wherein X_{A2} = Val or Ile; X_{A3} = Val or Ala; X_{A4} = Glu, Asp, Cys or gamma carboxyglutamate; X_{A5} = Gln, Glu, gamma carboxyglutamate, His or Val; Cys_{A6}, Cys_{A7}, and

~~Cys_{A11} are independently Cys or selenocysteine; X_{A8} = Thr, His, Asp, Gln, Tyr, Lys, Ala or Val; X_{A9} = Ser, Arg, Asn, Gly, His or Lys; X_{A10} = Ile, Pro, Tyr, Ala, Ser, Val, Phe, His or Thr; X_{A12} = Ser or Thr; X_{A13} = Leu, Asn, Val, Arg or Asp; X_{A14} = Tyr, Ala, Gln, His, Asp or Glu; X_{A15} = Gln, Glu or Thr; X_{A16} = Phe, Leu, or Ala; X_{A17} = Glu, Gln, Lys, Arg, Ile, Met, Thr or Ser; X_{A18} = Lys, Ser, Thr, Asn, Gln or Glu; X_{A19} = Tyr or Phe; Cys_{A20} = Cys, selenocysteine, amidated Cys, or amidated selenocysteine; X_{A21} = Asn, Pro, His, Ser, Gly, Ala, or is absent; X_{A22} = Pro, Asn, Thr, Leu, Ser or is absent; X_{A23} = Thr, Leu, Val, Ser or is absent; X_{A24} = Arg, Thr, Met, Gln, Leu or is absent; X_{A25} = Glu, Gly or is absent; from X_{A26} = Ser, Leu or is absent; X_{A27} to X_{A31} are independently Ser or are absent; X_{A32} = Ala, Ser or is absent; X_{A33} = Ala, Val or is absent; and X_{A34} = Ala or is absent (SEQ ID NO: 1); and**

a B chain peptide comprising the sequence X_{B1}-X_{B2}-X_{B3}-X_{B4}-X_{B5}-X_{B6}-X_{B7}-X_{B8}-Cys_{B9}-X_{B10}-X_{B11}-X_{B12}-X_{B13}-X_{B14}-X_{B15}-X_{B16}-X_{B17}-X_{B18}-X_{B19}-X_{B20}-Cys_{B21}-X_{B22}-X_{B23}-X_{B24}-X_{B25}-X_{B26}-X_{B27}-X_{B28}-X_{B29}-X_{B30}-X_{B31}-X_{B32}-X_{B33}-X_{B34}-X_{B35}-X_{B36}-X_{B37}-X_{B38}-X_{B39},

**wherein X_{B1} = Thr, Asn, Ser or is absent; X_{B2} = Phe, Ser, Asn, Thr, Gln or is absent; X_{B3} = Ala, Asp, Gly, Pro, Leu, Phe, or His; X_{B4} = Ala, Thr, Pro, Asp, Val or Gly; X_{B5} = Asn, Pro, His, Thr, Arg, Lys, Ser or hydroxyproline; X_{B6} = Lys, Glu, Asn, Asp, Arg, Gln or Gly; X_{B7} = His, Tyr, Arg or Ile; X_{B8} = Arg, Thr, Ile, Ser, Leu, Tyr or Lys; Cys_{B9} = Cys or selenocysteine; X_{B10} = Gly, Gln or Asp; X_{B11} = Ser, Leu, Gly or Pro; X_{B12} = His, Glu, gamma carboxyglutamate, Asp, or Asn; X_{B13} = Ile, Leu, Asp, Val or Ala; X_{B14} = Thr, Ala, Pro, Val or Arg; X_{B15} = Asn, Asp, Ala, Val, Thr, Pro or Glu; X_{B16} = Ala, Ser, Gln, His, Thr, Tyr, Arg or Gly; X_{B17} = Thr, Tyr, Pro, Leu or Gly; X_{B18} = Tyr, Met, Val, Gln, Ile, Asp, Gly, Asn or Leu; X_{B19} = Leu, Asp, Gln, Gly, Lys, Glu, Arg, Ser or Thr; X_{B20} = Val, Leu or Lys; C_{B21} = Cys, amidated Cys, selenocysteine or amidated selenocysteine; X_{B22} = Val, Tyr, Phe, His, Gly, Gln, Leu, amidated His, amidated Val or is absent; X_{B23} = Glu, Asp, Arg, Ser, Gly or is absent; X_{B24} = Arg, Asp, Val or is absent; X_{B25} = Gly, Leu, Val or is absent; X_{B26} = Phe, Val, Ile or is absent; X_{B27} = Phe, Asn, Pro, Glu or is absent; X_{B28} = Tyr, Cys, His or is absent; X_{B29} = Thr, His, Ile, Leu, Ser, Tyr or is absent; X_{B30} = Pro, Glu, Leu, Ile, Arg or is absent; X_{B31} = Ile, Lys or is absent; X_{B32} = Ala, Asp, Ser, Thr, Lys, Leu, Gln or is absent; X_{B33} = Cys or is absent; X_{B34} = Glu, Pro, Val or is absent; X_{B35} = Glu, Gly or is absent; X_{B36} = Glu, Gly or is absent; X_{B37} = Glu, Val or is absent; X_{B38} = Ala, Asp or is absent; and X_{B39} = Ala or is absent (SEQ ID NO: 2).~~

8. The insulin analog of claim 7, wherein the B-chain peptide comprises the sequence X_{B1}-X_{B2}-X_{B3}-X_{B4}-X_{B5}-X_{B6}-X_{B7}-X_{B8}-Cys_{B9}-X_{B10}-X_{B11}-X_{B12}-X_{B13}-X_{B14}-X_{B15}-X_{B16}-X_{B17}-X_{B18}-X_{B19}-X_{B20}-Cys_{B21}-X_{B22}-X_{B23}-X_{B24}-X_{B25}-X_{B26}-X_{B27}-X_{B28}-X_{B29}-X_{B30}-X_{B31}-X_{B32}-X_{B33}-X_{B34}-X_{B35}-X_{B36}-X_{B37}-X_{B38}-X_{B39},

wherein X_{B1} = Thr, Asn, Ser or is absent; X_{B2} = Phe, Ser, Asn, Thr, Gln or is absent; X_{B3} = Asp, Gly, Pro, Leu, Phe, or His; X_{B4} = Thr, Pro, Asp, Val or Gly; X_{B5} = Asn, Pro, His, Thr, Arg, Ser or hydroxyproline; X_{B6} = Lys, Glu, Asn, Asp, Arg, Gln or Gly; X_{B7} = His, Tyr, Arg or Ile; X_{B8} = Arg, Thr, Ile, Ser, Leu, Tyr or Lys; Cys_{B9} = Cys or selenocysteine; X_{B10} = Gly, Gln or Asp; X_{B11} = Ser, Leu, Gly or Pro; X_{B12} = His, Glu, gamma-carboxyglutamate, Asp, or Asn; X_{B13} = Ile, Leu, Asp, Val or Ala; X_{B14} = Thr, Ala, Pro, Val or Arg; X_{B15} = Asn, Asp, Ala, Val, Thr, Pro or Glu; X_{B16} = Ala, Ser, Gln, His, Tyr, Arg or Gly; X_{B17} = Tyr or Leu; X_{B18} = Tyr, Met, Val, Gln, Ile, Asp, Gly, Asn or Leu; X_{B19} = Leu, Asp, Gln, Gly, Lys, Glu, Arg or Thr; X_{B20} = Val, Leu or Lys; C_{B21} = Cys, amidated Cys, selenocysteine or amidated selenocysteine; X_{B22} = Tyr, Phe or His; X_{B23} = Glu, Arg, Ser, Gly or is absent; X_{B24} = Arg, Asp, Val or is absent; X_{B25} = Gly, Leu, Val or is absent; X_{B26} = Phe, Val, Ile or is absent; X_{B27} = Phe, Asn, Pro, Glu or is absent; X_{B28} = Tyr, Cys, His or is absent; X_{B29} = Thr, His, Leu, Tyr or is absent; X_{B30} = Pro, Glu, Leu, Ile, Arg or is absent; X_{B31} = Ile, Lys or is absent; X_{B32} = Thr, Lys, Leu, Gln or is absent; X_{B33} = Cys or is absent; X_{B34} = Glu, Pro, Val or is absent; X_{B35} = Glu, Gly or is absent; X_{B36} = Glu, Gly or is absent; X_{B37} = Glu, Val or is absent; X_{B38} = Ala, Asp or is absent; and X_{B39} = Ala or is absent (SEQ ID NO: 3).

9. The insulin analog of claim 7 or claim 8, wherein the B-chain peptide comprises the sequence X_{B1}-X_{B2}-X_{B3}-X_{B4}-X_{B5}-X_{B6}-X_{B7}-X_{B8}-Cys_{B9}-X_{B10}-X_{B11}-X_{B12}-X_{B13}-X_{B14}-X_{B15}-X_{B16}-X_{B17}-X_{B18}-X_{B19}-X_{B20}-Cys_{B21}-X_{B22}-X_{B23}-X_{B24}-X_{B25}-X_{B26}-X_{B27}-X_{B28}-X_{B29}-X_{B30}-X_{B31}-X_{B32}-X_{B33}-X_{B34}-X_{B35}-X_{B36}-X_{B37}-X_{B38}-X_{B39},

wherein X_{B1} = Thr, Asn, Ser or is absent; X_{B2} = Phe, Ser, Asn, Thr, Gln or is absent; X_{B3} = Asp, Gly, Pro, Leu, Phe, or His; X_{B4} = Thr, Pro, Asp, Val or Gly; X_{B5} = Asn, Pro, His, Thr, Arg, Ser or hydroxyproline; X_{B6} = Lys, Glu, Asn, Asp, Arg, Gln or Gly; X_{B7} = His, Tyr, Arg or Ile; X_{B8} = Arg, Thr, Ile, Ser, Leu, Tyr or Lys; Cys_{B9} = Cys or selenocysteine; X_{B10} = Gly, Gln or Asp; X_{B11} = Ser, Leu, Gly or Pro; X_{B12} = His, Glu, gamma-carboxyglutamate, Asp, or Asn; X_{B13} = Ile, Leu, Asp, Val or Ala; X_{B14} = Thr, Ala, Pro, Val or Arg; X_{B15} = Asn, Asp, Ala, Val, Thr, Pro or Glu; X_{B16} = Ala, Ser, Gln, His, Tyr, Arg or Gly; X_{B17} = Tyr or Leu;

~~X_{B18} = Tyr, Met, Val, Gln, Ile, Asp, Gly, Asn or Leu; X_{B19} = Leu, Asp, Gln, Gly, Lys, Glu, Arg or Thr; X_{B20} = Val, Leu or Lys; C_{B21} = Cys, amidated Cys, selenocysteine or amidated selenocysteine; X_{B22} = Tyr, Phe or His; X_{B23} = Glu, Arg, Ser, Gly or is absent; and X_{B24}, X_{B25}, X_{B26}, X_{B27}, X_{B28}, X_{B29}, X_{B30}, X_{B31}, X_{B32}, X_{B33}, X_{B34}, X_{B35}, X_{B36}, X_{B37}, X_{B38} and X_{B39} are absent (SEQ ID NO: 4).~~

~~10. The insulin analog of claim 7 or claim 8, wherein the B-chain peptide comprises the sequence X_{B1}-X_{B2}-X_{B3}-X_{B4}-X_{B5}-X_{B6}-X_{B7}-X_{B8}-Cys_{B9}-Gly-Ser-X_{B12}-X_{B13}-X_{B14}-X_{B15}-X_{B16}-X_{B17}-X_{B18}-X_{B19}-X_{B20}-Cys_{B21}-X_{B22}-X_{B23}-X_{B24}-X_{B25}-X_{B26}-X_{B27}-X_{B28}-X_{B29}-X_{B30}-X_{B31}-X_{B32}-X_{B33}-X_{B34}-X_{B35}-X_{B36}-X_{B37}-X_{B38}-X_{B39},~~

~~where X_{B1} = Thr, Asn, Ser or is absent; X_{B2} = Phe, Ser, Asn, Thr, Gln or is absent; X_{B3} = Asp, Gly, Pro, Leu, Phe, or His; X_{B4} = Thr, Pro, Asp, Val or Gly; X_{B5} = Asn, Pro, His, Thr, Arg, Ser or hydroxyproline; X_{B6} = Lys, Glu, Asn, Asp, Arg, Gln or Gly; X_{B7} = His, Tyr, Arg or Ile; X_{B8} = Arg, Thr, Ile, Ser, Leu, Tyr or Lys; Cys_{B9} = Cys or selenocysteine; X_{B12} = His, Glu, gamma-carboxyglutamate, Asp, or Asn; X_{B13} = Ile, Leu, Asp, Val or Ala; X_{B14} = Thr, Ala, Pro, Val or Arg; X_{B15} = Asn, Asp, Ala, Val, Thr, Pro or Glu; X_{B16} = Ala, Ser, Gln, His, Tyr, Arg or Gly; X_{B17} = Tyr or Leu; X_{B18} = Tyr, Met, Val, Gln, Ile, Asp, Gly, Asn or Leu; X_{B19} = Leu, Asp, Gln, Gly, Lys, Glu, Arg or Thr; X_{B20} = Val, Leu or Lys; C_{B21} = Cys, amidated Cys, selenocysteine or amidated selenocysteine; X_{B22} = Tyr, Phe or His; X_{B23} = Glu, Arg, Ser, Gly or is absent; X_{B24} = Arg, Asp, Val or is absent; X_{B25} = Gly, Leu, Val or is absent; X_{B26} = Phe, Val, Ile or is absent; X_{B27} = Phe, Asn, Pro, Glu or is absent; X_{B28} = Tyr, Cys, His or is absent; X_{B29} = Thr, His, Leu, Tyr or is absent; X_{B30} = Pro, Glu, Leu, Ile, Arg or is absent; X_{B31} = Ile, Lys or is absent; X_{B32} = Thr, Lys, Leu, Gln or is absent; X_{B33} = Cys or is absent; X_{B34} = Glu, Pro, Val or is absent; X_{B35} = Glu, Gly or is absent; X_{B36} = Glu, Gly or is absent; X_{B37} = Glu, Val or is absent; X_{B38} = Ala, Asp or is absent; and X_{B39} = Ala or is absent (SEQ ID NO: 5).~~

~~11. The insulin analog of claim 7 or claim 8, wherein the B-chain peptide comprises the sequence X_{B1}-X_{B2}-X_{B3}-X_{B4}-X_{B5}-X_{B6}-X_{B7}-X_{B8}-Cys_{B9}-Gly-Ser-X_{B12}-X_{B13}-X_{B14}-X_{B15}-X_{B16}-X_{B17}-X_{B18}-X_{B19}-X_{B20}-Cys_{B21}-X_{B22}-X_{B23}-X_{B24}-X_{B25}-X_{B26}-X_{B27}-X_{B28}-X_{B29}-X_{B30}-X_{B31}-X_{B32}-X_{B33}-X_{B34}-X_{B35}-X_{B36}-X_{B37}-X_{B38}-X_{B39},~~

where X_{B1} = Thr, Asn, Ser or is absent; X_{B2} = Phe, Ser, Asn, Thr, Gln or is absent; X_{B3} = Asp, Gly, Pro, Leu, Phe, or His; X_{B4} = Thr, Pro, Asp, Val or Gly; X_{B5} = Asn, Pro, His, Thr, Arg, Ser or hydroxyproline; X_{B6} = Lys, Glu, Asn, Asp, Arg, Gln or Gly; X_{B7} = His or Tyr; X_{B8} = Arg, Thr, Ile, Ser, Leu, Tyr or Lys; Cys_{B9} = Cys or selenocysteine; X_{B12} = His, Glu, gamma carboxyglutamate, Asp, or Asn; X_{B13} = Ile, Leu, Asp, Val or Ala; X_{B14} = Thr, Ala, Pro, Val or Arg; X_{B15} = Asn, Asp, Ala, Val, Thr, Pro or Glu; X_{B16} = Ala, Ser, Gln, His, Tyr, Arg or Gly; X_{B17} = Tyr or Leu; X_{B18} = Tyr, Met, Val, Gln, Ile, Asp, Gly, Asn or Leu; X_{B19} = Leu, Asp, Gln, Gly, Lys, Glu, Arg or Thr; X_{B20} = Val or Leu; C_{B21} = Cys, amidated Cys, selenocysteine or amidated selenocysteine; X_{B22} = Tyr, Phe or His; X_{B23} = Glu, Arg, Ser, Gly or is absent; X_{B24} = Arg, Asp, Val or is absent; X_{B25} = Gly, Leu, Val or is absent; X_{B26} = Phe, Val, Ile or is absent; X_{B27} = Phe, Asn, Pro, Glu or is absent; X_{B28} = Tyr, Cys, His or is absent; X_{B29} = Thr, His, Leu, Tyr or is absent; X_{B30} = Pro, Glu, Leu, Ile, Arg or is absent; X_{B31} = Ile, Lys or is absent; X_{B32} = Thr, Lys, Leu, Gln or is absent; X_{B33} = Cys or is absent; X_{B34} = Glu, Pro, Val or is absent; X_{B35} = Glu, Gly or is absent; X_{B36} = Glu, Gly or is absent; X_{B37} = Glu, Val or is absent; X_{B38} = Ala, Asp or is absent; and X_{B39} = Ala or is absent (SEQ ID NO: 6).

12. The insulin analog of claim 7, wherein the B-chain peptide comprises the sequence X_{B1}-X_{B2}-X_{B3}-X_{B4}-X_{B5}-X_{B6}-X_{B7}-X_{B8}-Cys_{B9}-Gly-Ser-X_{B12}-X_{B13}-X_{B14}-X_{B15}-X_{B16}-X_{B17}-X_{B18}-X_{B19}-X_{B20}-Cys_{B21}-X_{B22}-X_{B23}, wherein X_{B1} = Thr, Asn or is absent; X_{B2} = Phe, Ser or is absent; X_{B3} = Phe or Asp; X_{B4} = Thr or Val; X_{B5} = Pro, Asn or hydroxyproline; X_{B6} = Lys, Asn or Gln; X_{B7} = His or Tyr; X_{B8} = Arg, Ile or Leu; Cys_{B9} = Cys or selenocysteine; X_{B12} = His, Asp, Glu or gamma carboxyglutamate; X_{B13} = Val, Ile or Leu; X_{B14} = Thr, Ala, Pro, or Val; X_{B15} = Glu, Val, Asn or Asp; X_{B16} = Ser, Gln, Tyr or Ala; X_{B17} = Tyr or Leu; X_{B18} = Tyr, Asp, Met or Val; X_{B19} = Leu, Asp, Gln or Lys; X_{B20} = Leu or Val; Cys_{B21} = Cys, amidated Cys, selenocysteine or amidated selenocysteine; X_{B22} = Tyr or Gly; and X_{B23} = Glu, Arg, Gly or is absent (SE ID NO: 7).

13. The insulin analog of claim 12, wherein the B-chain peptide comprises the sequence X_{B1}-X_{B2}-X_{B3}-X_{B4}-X_{B5}-X_{B6}-His-X_{B8}-Cys_{B9}-Gly-Ser-X_{B12}-X_{B13}-X_{B14}-X_{B15}-X_{B16}-X_{B17}-X_{B18}-X_{B19}-X_{B20}-$CysB_{21}$-X_{B22}-X_{B23}, wherein X_{B1} = Thr or is absent; X_{B2} = Phe or is absent; X_{B3} = Phe or Asp; X_{B4} = Thr or Val; X_{B5} = Pro, Asn or hydroxyproline; X_{B6} = Lys or Gln; X_{B8} = Arg or Leu; X_{B12} = His, Glu or gamma carboxyglutamate; X_{B13} = Ile or Leu; X_{B14} = Thr, or

Val; X_{B15} = Glu, or Asn; X_{B16} = Ser or Ala; X_{B17} = Tyr or Leu, X_{B18} = Tyr or Met; X_{B19} = Leu or Asp, X_{B20} = Leu or Val; X_{B22} = Tyr; and X_{B23} = Glu or Arg (SEQ ID NO: 8).

14. The insulin analog according to any one of claims 7 to 12, wherein X_{B22} is Tyr.

15. The insulin analog according to any one of claims 1 to 14, wherein the A chain peptide comprises the sequence Gly-X_{A2}-X_{A3}-X_{A4}-X_{A5}-Cys_{A6}-Cys_{A7}-X_{A8}-X_{A9}-X_{A10}-Cys_{A11}-X_{A12}-X_{A13}-X_{A14}-X_{A15}-Phe-X_{A17}-X_{A18}-X_{A19}-Cys_{A20}-X_{A21}-X_{A22}-X_{A23}-X_{A24}-X_{A25}-X_{A26}-X_{A27}-X_{A28}-X_{A29}-X_{A30}-X_{A31}-X_{A32}-X_{A33}-X_{A34},

wherein X_{A2} = Val or Ile; X_{A3} = Val or Ala; X_{A4} = Glu, gamma carboxyglutamate or Cys; X_{A5} = Gln, Glu, gamma carboxyglutamate, His or Val; Cys_{A6}, Cys_{A7}, and Cys_{A11} are independently Cys or selenocysteine; X_{A8} = Thr, His, Asp, Gln, Tyr, Lys or Val; X_{A9} = Ser, Arg, Asn, His or Lys; X_{A10} = Ile, Pro, Tyr, Ala, Ser, Phe, His or Thr; X_{A12} = Ser or Thr; X_{A13} = Leu, Asn, Val or Asp; X_{A14} = Tyr, Ala, Gln, Asp or Glu; X_{A15} = Gln, Glu or Thr; or Ala; X_{A17} = Glu, Lys, Arg, Ile, Met, Thr or Ser; X_{A18} = Lys, Thr, Asn, Gln or Glu; X_{A19} = Tyr or Phe; Cys_{A20} = Cys, selenocysteine, amidated Cys, or amidated selenocysteine; X_{A21} = Asn, Pro, His, Ser, Gly, Ala, or is absent; X_{A22} = Pro, Asn, Thr, Leu, Ser or is absent; X_{A23} = Thr, Leu, Val, Ser or is absent; X_{A24} = Arg, Thr, Met, Gln, Leu or is absent; X_{A25} = Glu, Gly or is absent; from X_{A26} = Ser, Leu or is absent; X_{A27} to X_{A31} are independently Ser or are absent; X_{A32} = Ala, Ser or is absent; X_{A33} = Ala, Val or is absent; and X_{A34} = Ala or is absent (SEQ ID NO: 9).

16. The insulin analog according to any one of claims 1 to 6, comprising:

an A chain peptide comprising a sequence Gly-X_{A2}-Val-X_{A4}-X_{A5}-CysA6-CysA7-X_{A8}-X_{A9}-X_{A10}-Cys_{A11}-Ser-X_{A13}-X_{A14}-X_{A15}-X_{A16}-X_{A17}-X_{A18}-Tyr-Cys_{A20}-X_{A21}, wherein X_{A2} is Val or Ile, X_{A4} is Glu or gamma carboxyglutamate, X_{A5} is His or Gln, X_{A8} is His or Thr, X_{A9} is Arg or Ser, X_{A10} is Pro or Ile, X_{A13} is Asn or Leu, X_{A14} is Ala or Tyr, X_{A15} is Glu or Gln, X_{A16} is Phe or Leu, X_{A17} is Lys or Glu, X_{A18} is Lys or Asn and X_{A21} is Asn or absent (SEQ ID NO: 10); and

an B chain peptide comprising the sequence X_{B1}-X_{B2}-X_{B3}-X_{B4}-X_{B5}-X_{B6}-His-X_{B8}-Cys_{B9}-Gly-Ser-X_{B12}-X_{B13}-X_{B14}-X_{B15}-X_{B16}-X_{B17}-X_{B18}-X_{B19}-X_{B20}-Cys_{B21}-X_{B22}-X_{B23}, wherein X_{B1} = Thr or is absent; X_{B2} = Phe or is absent; X_{B3} = Phe or Asp; X_{B4} = Thr or Val; X_{B5} = Pro, Asn or hydroxyproline; X_{B6} = Lys or Gln; X_{B8} = Arg or Leu; X_{B12} = His, Glu or gamma

carboxyglutamate; X_{B13} = Ile or Leu; X_{B14} = Thr, or Val; X_{B15} = Glu, or Asn; X_{B16} = Ser or Ala; X_{B17} = Tyr or Leu; X_{B18} = Tyr or Met; X_{B19} = Leu or Asp, X_{B20} = Leu or Val; X_{B22} = Gly or Tyr; and X_{B23} = Glu or Arg (SEQ ID NO: 11).

17. The insulin analog of claim 15 or claim 16, comprising:

an A chain peptide comprising a sequence

Gly-X_{A2}-Val-X_{A4}-X_{A5}-Cys_{A6}-Cys_{A7}-X_{A8}-X_{A9}-X_{A10}-Cys_{A11}-Ser-X_{A13}-X_{A14}-X_{A15}-Phe-X_{A17}-X_{A18}-Tyr-Cys_{A20}-X_{A21}, wherein X_{A2} is Val or Ile, X_{A4} is Glu or gamma carboxyglutamate, X_{A5} is His or Gln, X_{A8} is His or Thr, X_{A9} is Arg or Ser, X_{A10} is Pro or Ile, X_{A13} is Asn or Leu, X_{A14} is Ala or Tyr, X_{A15} is Glu or Gln, X_{A17} is Lys or Glu, X_{A18} is Lys or Asn and X_{A21} is Asn or absent (SEQ ID NO: 12); and

an B chain peptide comprising the sequence X_{B1}-X_{B2}-X_{B3}-X_{B4}-X_{B5}-X_{B6}-His-X_{B8}-Cys_{B9}-Gly-Ser-X_{B12}-X_{B13}-X_{B14}-X_{B15}-X_{B16}-X_{B17}-X_{B18}-X_{B19}-X_{B20}-Cys_{B21}-Tyr-X_{B23}, wherein X_{B1} = Thr or is absent; X_{B2} = Phe or is absent; X_{B3} = Phe or Asp; X_{B4} = Thr or Val; X_{B5} = Pro, Asn or hydroxyproline; X_{B6} = Lys or Gln; X_{B8} = Arg or Leu; X_{B12} = His, Glu or gamma carboxyglutamate; X_{B13} = Ile or Leu; X_{B14} = Thr, or Val; X_{B15} = Glu, or Asn; X_{B16} = Ser or Ala; X_{B17} = Tyr or Leu; X_{B18} = Tyr or Met; X_{B19} = Leu or Asp, X_{B20} = Leu or Val; and X_{B23} = Glu or Arg (SEQ ID NO: 13).

18. The insulin analog according to any one of claims 15 to 17, comprising:

an A chain peptide comprising a sequence

Gly-Val-Val-X_{A4}-X_{A5}-Cys_{A6}-Cys_{A7}-X_{A8}-X_{A9}-X_{A10}-Cys_{A11}-Ser-X_{A13}-X_{A14}-X_{A15}-Phe-X_{A17}-X_{A18}-Tyr-Cys_{A20}-X_{A21}, wherein X_{A4} is Glu or gamma carboxyglutamate, X_{A5} is His or Gln, X_{A8} is His or Thr, X_{A9} is Arg or Ser, X_{A10} is Pro or Ile, X_{A13} is Asn or Leu, X_{A14} is Ala or Tyr, X_{A15} is Glu or Gln, X_{A17} is Lys or Glu, X_{A18} is Lys or Asn and X_{A21} is Asn or absent (SEQ ID NO: 14); and

an B chain peptide comprising the sequence X_{B1}-X_{B2}-X_{B3}-X_{B4}-X_{B5}-X_{B6}-His-Arg-Cys_{B9}-Gly-Ser-X_{B12}-Ile-X_{B14}-X_{B15}-X_{B16}-X_{B17}-X_{B18}-X_{B19}-Leu-Cys_{B21}-Tyr-X_{B23}, wherein X_{B1} = Thr or is absent; X_{B2} = Phe or is absent; X_{B3} = Phe or Asp; X_{B4} = Thr or Val; X_{B5} = Pro, Asn or hydroxyproline; X_{B6} = Lys or Gln; X_{B12} = His, Glu or gamma carboxyglutamate; X_{B14} = Thr, or Val; X_{B15} = Glu, or Asn; X_{B16} = Ser or Ala; X_{B17} = Tyr or Leu; X_{B18} = Tyr or Met; X_{B19} = Leu or Asp, and X_{B23} = Glu or Arg (SEQ ID NO: 15).

~~19. The insulin analog according to any one of claims 1 to 18, wherein one or more or all of the following apply;~~

~~i) X_{A4} is gamma carboxyglutamate,~~

~~ii) X_{B5} is hydroxyproline; and~~

~~iii) X_{B12} is gamma carboxyglutamate.~~

~~20. The insulin analog according to any one of claims 1 to 19, comprising:~~

~~an A chain peptide comprising the sequence Gly Ile Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn (SEQ ID NO: 16); and~~

~~a B chain peptide comprising the sequence Phe Val Asn Gln His Leu Cys Gly Ser His Leu Val Glu Ala Xaa Tyr Leu Val Cys Gly Glu, where Xaa is an aromatic residue or large aliphatic residue (SEQ ID NO: 17).~~

~~21. The insulin analog according to any one of claims 1 to 19, comprising:~~

~~an A chain peptide comprising the sequence Gly Ile Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn (SEQ ID NO: 18); and~~

~~a B chain peptide comprising the sequence Phe Val Asn Gln His Leu Cys Gly Ser His Leu Val Glu Ala Leu Tyr Leu Val Cys Xaa Glu, where Xaa is an aromatic residue or large aliphatic residue (SEQ ID NO: 19).~~

~~22. The insulin analog according to any one of claims 1 to 21, wherein Cys_{B9} of the B chain peptide is bonded to Cys_{A6} of the A chain peptide.~~

~~23. The insulin analog according to any one of claims 1 to 22, wherein Cys_{B21} of the B chain peptide is bonded to Cys_{A20} of the A chain peptide.~~

~~24. The insulin analog according to any one of claims 1 to 23, wherein Cys_{A7} is bonded to Cys_{A11}.~~

~~25. The insulin analog according to any one of claims 1 to 24, wherein the A chain peptide and the B chain peptide are linked together at one pair of their respective terminal ends.~~

~~26. The insulin analog according to any one of claims 1 to 25, wherein the A chain peptide and the B chain peptide are linked together at both terminal ends.~~

~~27. The insulin analog according to any one of claims 1 to 26 which has an IC_{50} against the human IR-B receptor of less than 10^{-6} M.~~

~~28. The insulin analog according to any one of claims 1 to 27, wherein in solution at least 75% of the analog is monomeric in solution.~~

~~29. The insulin analog according to any one of claims 1 to 28 which has increased bioavailability when administered to a human when compared human insulin.~~

~~30. The insulin analog of claim 29 which has a peak bioavailability within 0.5 to 3 hours of administration to a human.~~

~~31. The insulin analog of claim 29 or claim 30 which has an onset of activity within 10 minutes of administration.~~

~~32. The insulin analog of any one of claims 1 to 31, wherein the analog does not bind human IGF-IR or binds human IGF-IR weakly.~~

~~33. The insulin analog of claim 32, wherein the analog has an affinity (K_d) for human IGF-IR of weaker than 100 nM.~~

~~32. A pharmaceutical composition, comprising the insulin analog of any one of claims 1 to 31 or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable carriers.~~

~~33. A method for treating and/or preventing an insulin related condition, comprising administering a therapeutically effective amount of the insulin analog of any one of claims 1 to 32 to a subject in need thereof.~~

~~34. The method of claim 33, wherein the insulin related condition is hyperglycemia, insulin resistance, type 1 diabetes, gestational diabetes or type 2 diabetes.~~

~~35. A method for decreasing blood glucose levels, comprising administering a therapeutically effective amount of the insulin analog of any one of claims 1 to 32 to a subject in need thereof.~~

~~36. Use of the insulin analog of any one of claims 1 to 32 in the manufacture of a medicament for treating and/or preventing an insulin related condition in a subject.~~

~~37. Use of the insulin analog of any one of claims 1 to 32 in the manufacture of a medicament for decreasing blood glucose levels in a subject.~~

~~38. An insulin analog of any one of claims 1 to 32 for use in treating and/or preventing an insulin related condition in a subject.~~

~~39. An insulin analog of any one of claims 1 to 32 for use in decreasing blood glucose levels in a subject.~~

~~40. A method of redesigning or modifying a polypeptide which is known to bind to an insulin receptor (IR) comprising performing structure based evaluation of a structure defined by the atomic coordinates of Appendix I or a subset thereof and redesigning or chemically modifying the polypeptide as a result of the evaluation.~~

~~41. The method of claim 40, wherein structure based evaluation comprises comparison of the structure defined by the atomic coordinates of Appendix I or a subset thereof, with the atomic coordinates of insulin or a subset thereof.~~

~~42. The method of claim 40 or claim 41, wherein structure based evaluation further comprises molecular modelling of a complex formed between the structure defined by the atomic coordinates of Appendix I or a subset thereof with the atomic coordinates of an insulin receptor or a subset thereof.~~

43. The method of claim any one of claims 40 to 42, further comprising synthesising or obtaining the redesigned or chemically modified polypeptide and testing for its ability to bind IR.

44. The method according to any one of claims 40 to 42, further comprising synthesising or obtaining the redesigned or chemically modified polypeptide and determining the ability of the redesigned or chemically modified polypeptide to modulate IR activation.

45. The method according to any one of claims 40 to 42, further comprising synthesising or obtaining the redesigned or chemically modified polypeptide and determining the ability of the redesigned or chemically modified polypeptide to lower blood glucose levels.

46. The method of any one of claims 40 to 45, wherein the polypeptide which is known to bind to IR is insulin.

47. The method of claim 46, wherein the insulin is human insulin.

48. A polypeptide which has been redesigned or modified by the method of any one of claims 40 to 47.

49. The polypeptide of claim 48, which is monomeric.

50. An isolated molecule which is an IR agonist, wherein the molecule is identified and/or designed based on the 3D structure of Con-Ins G1 defined by the atomic coordinates of Appendix I or a subset thereof.

51. The molecule of claim 50, wherein the molecule is a peptide, polypeptide or peptidomimetic.

52. The molecule of claim 50 or claim 51 which is monomeric.

53. The molecule according to any one of claims 50 to 52, which has an IC_{50} against the human IR-B receptor of less than 10^{-6} M.

54. A method of identifying a compound which binds IR, the method comprising:

i) generating a three-dimensional structure model of a polypeptide having

a) a structure defined by the atomic coordinates of Appendix I or a subset thereof, or

b) a structure having a root mean square deviation less than about 2.0Å when superimposed on the corresponding backbone atoms of a), and

ii) designing or screening for a compound which potentially binds the IR.

55. The method of claim 54, wherein generating a three dimensional structure model comprises generating a model of the polypeptide bound to IR or regions thereof.

56. The method of claim 54 or claim 55, further comprising synthesising the compound which potentially binds the IR.

57. The method according to any one of claims 54 to 56, wherein the compound modulates at least one biological activity of IR.

58. The method according to any one of claims 54 to 57, wherein the compound is monomeric.

59. The method of any one of claims 54 to 58 which further comprises testing the compound designed or screened for in ii) for its ability to modulate blood glucose levels.

60. The method according to any one of claims 54 to 59, wherein i) and ii) are performed *in silico*.

61. A computer based method of identifying a compound which mimics insulin activity, the method comprising

i) generating a three-dimensional structure model of a polypeptide having

a) a structure defined by the atomic coordinates of Appendix I or a subset thereof, or

b) a structure having a root mean square deviation less than about 2.0 Å when superimposed on the corresponding backbone atoms of a), and

ii) designing or screening for a compound which mimics insulin activity.

62. The method of claim 61, wherein generating a three dimensional structure model comprises generating a model of the polypeptide bound to IR or regions thereof.

63. The method of claim 61 or claim 62, further comprising synthesising the compound which potentially binds the IR.

64. The method according to any one of claims 61 to 63, wherein the compound modulates at least one biological activity of IR.

65. The method according to any one of claims 61 to 64, wherein the compound is monomeric.

66. The method according to any one of claims 61 to 65, the method further comprising testing the compound designed or screened for in ii) for its ability to modulate blood glucose levels.

67. The method according to any one of claims 61 to 66, wherein i) and ii) are performed *in silico*.

68. A compound identified using a method according to any one of claims 54 to 67.

69. A crystal of Con Ins G1 polypeptide having a space group P432 with unit cell dimensions of a = b= c = 74.91 Å with up to about 2 % variation in any cell dimension.

70. The structure of Con Ins G1 polypeptide as defined by the atomic coordinates of Appendix I.

71. The use of the structure of claim 70 as a structural model.

~~72. The use of the structural model according to claim 71 for identification of insulin analogs.~~

~~73. An insulin analog identified by the use of claim 72.~~

~~74. A pharmaceutical composition comprising the polypeptide of claim 48 or claim 49, the molecule according to any one of claims 50 to 53, the compound of claim 68, or the insulin analog of claim 72.~~

~~75.~~1. A peptide comprising an ~~insulin~~ A chain ~~peptide~~ and ~~an insulin~~a B chain ~~peptide~~, ~~wherein the B chain peptide comprises a substitution at amino acid 10 and amino acid 20~~wherein the A chain comprises a sequence set forth in SEQ ID NO:1, wherein the B chain comprises a sequence set forth in SEQ ID NO:30, and wherein:

X_{A2} = Ile; X_{A3} = Val; X_{A4} = Glu; X_{A5} = Gln; X_{A6} = Cys, X_{A7} = Cys; X_{A8} = His; X_{A9} = Arg;

X_{A10} = Ile; X_{A11} = Cys; X_{A12} = Ser, X_{A13} = Leu; X_{A14} = Tyr; X_{A15} = Gln; X_{A16} = Leu; X_{A17} = Glu;

X_{A18} = Asn; X_{A19} = Tyr; X_{A20} = Cys, X_{A21} = Asn, Pro, His, Ser, Gly, Ala, or is absent; and X_{A22} to X_{A34} = absent.

2. The peptide of claim 1, wherein the A chain has the sequence GIVEQCCHRICSLYQLENYCG (SEQ ID NO:58).

3. The peptide of claim 1, wherein the A chain has the sequence GIVEQCCHRICSLYQLENYCG (SEQ ID NO: 58) and the B chain has the sequence FVNQHLCGSELVEALYLVCYER (SEQ ID NO:30).

~~76. The peptide of claim 75, wherein the substitution at amino acid 20 is G20Y, G20F, or G20P.~~

~~77. The peptide of claim 76, wherein the substitution at amino acid 20 is G20P and the peptide further comprises a substitution at amino acid 21, wherein the substitution at amino acid 21 is G21H.~~

~~78. The peptide of any one of claims 75 to 77, wherein the substitution at amino acid 10 is H10E, H10D or H10Q.~~

~~79 The peptide of any one of claims 75 to 78, further comprising at least one substitution in the A chain peptide.~~

~~80. The peptide of claim 79, wherein the at least one substitution in the A chain peptide is T8H, T8Y, T8K, or S9R.~~

~~81. The peptide of claim 80, further comprising at least two substitutions in the A chain peptide.~~

~~82. The peptide of claim 79, wherein the at least two substitutions in the A chain peptide are two of the substitutions selected from: T8H, T8Y, T8K, and S9R.~~

~~83. The peptide of any one of claims 75 to 82, wherein the peptide is a des octapeptide insulin.~~

~~84. The peptide of any one of claims 75 to 83, wherein the B chain peptide comprises the sequence of FVNQHLCGSELVEALYLVCYER (SEQ ID NO: 30).~~

~~85. The peptide of any one of claims 75 to 84, wherein the A chain comprises the sequence of GIVEQCCHRICSLYQLENYCN (SEQ ID NO: 39).~~

~~86.~~4. The peptide of ~~any one of claims 75 to 85~~claim 3, wherein the A chain ~~peptide~~ and B chain ~~peptide~~ are bonded via at least one disulfide bond.

5. The peptide of claim 4, wherein the A chain and B chain are bonded via at least 2 disulfide bonds.

6. The peptide of claim 5, wherein the A chain and B chain are bonded via at least 3 disulfide bonds.

7. The peptide of claim 6, wherein the at least 2 disulfide bonds are between the first Cys and the third Cys in the A chain, or between the second Cys in the A chain and the first Cys in the B chain, or between the fourth Cys in the A chain and the second Cys in the B chain.

8. The peptide of claim 7, wherein there are disulfide bonds between the first Cys and the third Cys in the A chain, between the second Cys in the A chain and the first Cys in the B chain, and between the fourth Cys in the A chain and the second Cys in the B chain.

~~87.~~9. The peptide of ~~any one of claims 75 to 86~~claim 8, wherein the peptide is a monomer.

10. The peptide of claim 1, wherein the peptide is a des-octapeptide insulin.

11. The peptide of claim 1, wherein:

(a) the peptide has an IC_{50} against the human IR-B receptor of less than 10^{-6} M; and/or

(b) at least 75% of the peptide is monomeric in solution; and/or

(c) the peptide has increased bioavailability when administered to a human when compared to human insulin; and/or

(d) the peptide has a peak bioavailability within 0.5 to 3 hours of administration to a human; and/or

(e) the peptide has an onset of activity within 10 minutes of administration; and/or

(f) the peptide does not bind human IGF-IR or binds human IGF-IR weakly; and/or

(g) the peptide has an affinity (Kct) for human IGF-IR of weaker than 100 nM.

~~88. The peptide of any one of claims 75 to 87, wherein the insulin A chain peptide is at least 70% identical to wild type human insulin A chain peptide.~~

~~89.~~12. A pharmaceutical composition comprising the peptide of ~~any one of claims 75 to 88~~claim 1 and a pharmaceutically acceptable carrier.

~~90. A method of increasing insulin receptor activation in a subject comprising administering a therapeutically effective amount of any one of the peptides of any one of claims 75 to 88 to a subject in need thereof.~~

~~91. A method of lowering the blood sugar in a subject comprising administering a therapeutically effective amount of any one of the peptides of any one of claims 75 to 88 to a subject in need thereof.~~

~~92. A method of treating type 1 diabetes in a subject comprising administering a therapeutically effective amount of any one of the peptides of any one of claims 75 to 88 to a subject in need thereof.~~

~~93. The method of claim 92, wherein the subject has been diagnosed with type 1 diabetes prior to administering the peptide.~~

~~94. A therapeutic protein having an A chain peptide bonded to a B chain peptide via at least one disulfide bond, wherein the A chain comprises the sequence of GIVEQCCHRICSLYQLENYCN (SEQ ID NO: 39), and wherein the B chain peptide comprises the sequence of FVNQHLCGSELVEALYLVCYER (SEQ ID NO: 30).~~