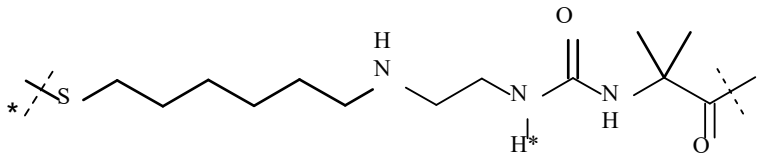
Claims

1. A liquid pharmaceutical formulation, wherein the pharmaceutical formulation comprises a PTH conjugate of formula (IIf-i)

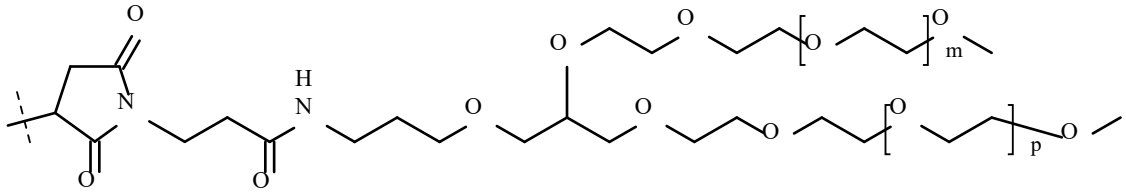


(IIf-i),

wherein

the unmarked dashed line indicates the attachment to a nitrogen of -D which is a PTH moiety by forming an amide bond; and

the dashed line marked with the asterisk indicates attachment to a moiety



wherein

m and p are independently an integer ranging from and including 400 to 500; and wherein the liquid formulation comprises

PTH conjugate, of which PTH moiety	0.25 - 0.35 mg/ml
succinic acid	1.0 - 1.4 mg/ml
D-mannitol	36 - 48 mg/ml
m-cresol	2.0 - 3.0 mg/ml

and wherein the pH ranges from 3.5 to 5.0.

2. The liquid pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation further comprises a pH-adjusting agent, which is a base.

3. The liquid pharmaceutical formulation of claim 2, wherein the pH-adjusting agent is selected from the group consisting of Tris (tris(hydroxymethyl)aminomethane), potassium hydroxide, lysine, sodium hydroxide and mixtures thereof.

4. The liquid pharmaceutical formulation of claim 2 or 3, wherein the pH-adjusting agent is sodium hydroxide.

5. The liquid pharmaceutical formulation of any one of claims 1 to 4, wherein the liquid pharmaceutical formulation comprises

PTH conjugate, of which PTH moiety	0.25 - 0.35 mg/ml
succinic acid	1.0 - 1.4 mg/ml
D-mannitol	36 - 48 mg/ml
m-cresol	2.0 - 3.0 mg/ml

and wherein the pH ranges from 3.7 to 4.3.

6. The liquid pharmaceutical composition of any one of claims 1 to 5, wherein the liquid pharmaceutical composition comprises 0.3 mg/ml PTH moiety, 1.18 mg/ml succinic acid, 41.7 mg/ml D-mannitol, 2.5 mg/ml m-cresol and wherein the pH is 4.0.

7. The liquid pharmaceutical formulation of any one of claims 1 to 6, -D has the sequence SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114 or SEQ ID NO:115.

8. The liquid pharmaceutical formulation of any one of claims 1 to 7, wherein -D has the sequence of SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:110, SEQ ID NO:111 or SEQ ID NO:112.

9. The liquid pharmaceutical formulation of any one of claims 1 to 8, wherein the PTH moiety has the sequence SEQ ID NO:51.

10. The liquid pharmaceutical formulation of any one of claims 14 to 18, wherein the unmarked dashed line in formula (IIf-i) indicates the attachment to the N-terminal amine functional group of -D.

11. Method of manufacturing the liquid pharmaceutical formulation of any one of claims 6 to 10, wherein the method comprises the steps of

(i) admixing the PTH conjugate with at least succinic acid, mannitol, m-cresol and optionally an antioxidant to yield a formulation comprising

PTH conjugate, of which PTH moiety	0.30 mg/ml
succinic acid	1.18 mg/ml
D-mannitol	41.7 mg/ml
m-cresol	2.5 mg/ml

(ii) adjusting the pH of the admixture of step (i) to a pH of about 4 with NaOH and HCl;

(iii) optionally, filtering the admixture from step (ii);

(iv) transferring amounts of the admixture from step (ii) or (iii) equivalent to the desired number of dosages into a container;

(v) sealing the container; and

wherein the order of steps (ii) and (iii) may optionally be reversed.

12. The method of manufacturing of claim 11, wherein steps (ii) and (iii) are not reversed.

13. The liquid pharmaceutical formulation of any one of claims 1 to 10 for use as a medicament.

14. Use of the liquid pharmaceutical formulation of any one of claims 1 to 10 for the manufacture of a medicament for the treatment, control, delay or prevention of one or more diseases selected from the group consisting of hypoparathyroidism, osteoporosis, fracture repair, osteomalacia, osteomalacia and osteoporosis in patients with hypophasphatasia, steroid-induced osteoporosis, male osteoporosis, arthritis, osteoarthritis, osteogenenesis imperfecta, fibrous dysplasia, rheumatoid arthritis, osteopenia, periodontal disease, bone fracture, alopecia, chemotherapy-induced alopecia and thrombocytopenia, chronic periodontitis, osteonecrosis of jaw and poorly healing fractures due to ALPL gene mutations.

15. The use of claim 14, wherein the disease is hypoparathyroidism.