soluble in acidic solutions. Conversely, in basic solutions, iron ions will form insoluble oxides and precipitate from the formulation, unless a chelating agent, such as EDTA is present.

[0009] Soluble ferric pyrophosphate (SFP) is a complex iron salt that has a molecular mass of about 1000 Da and is highly soluble in aqueous solutions, allowing its infusion via aqueous solutions, e.g., dialysate. The administration of SFP overcomes both absolute and functional iron deficiencies in patients, including hemodialysis-dependent CKD (HDD-CKD) patients, and could significantly reduce the amount of erythropoiesis-stimulating agents needed to treat these patients.

[0010] U.S. Patent Nos. 6,689,275; 6,779,468; and 7,857,977; incorporated herein by reference, disclose the addition of SFP to liquid bicarbonate solutions for hemodialysis. However, conventional SFP compositions, such as food grade SFP (FCC-SFP), can dissolve incompletely in aqueous solutions and are not suitable for pharmaceutical applications.

SUMMARY

[0010a] In one aspect of the present disclosure, there is provided a solid particulate formulation of soluble ferric pyrophosphate comprising milled soluble ferric pyrophosphate having a particle size less than 5 μm, optionally less than 4 μm, wherein 90% of the particles have a particle size between 1 μm and 50 μm, wherein the soluble ferric pyrophosphate dissolves in aqueous solution in less than 1 minute.

[0010b] In another aspect of the present disclosure, there is provided a sachet comprising the solid particulate formulation as defined herein.

[0010c] In yet another aspect of the present disclosure, there is provided a use of soluble ferric pyrophosphate disclosed herein for the preparation of a medicament for administering a dialysate to a subject in need thereof, wherein a solid particulate formulation of soluble ferric pyrophosphate is mixed with a hemodialysis solution to form said dialysate.

[0010d] In a further aspect of the present disclosure, there is provided a soluble ferric pyrophosphate disclosed herein for use in administering a dialysate, wherein a solid particulate formulation of soluble ferric pyrophosphate is mixed with a hemodialysis solution to form the dialysate.

[0010e] In another aspect of the present disclosure, there is provided a kit comprising the solid particulate formulation of soluble ferric pyrophosphate or sachet as defined herein and a dialysis concentrate formulation in a solid or liquid form.

WHAT IS CLAIMED:

1. A solid particulate formulation of soluble ferric pyrophosphate comprising milled soluble ferric pyrophosphate having a particle size less than 5 μm, optionally less than 4 μm, wherein 90% of the particles have a particle size between 1 μm and 50 μm, wherein the soluble ferric pyrophosphate dissolves in aqueous solution in less than 1 minute.

2. The solid particulate formulation of claim 1, wherein 90% of the particles have a particle size between 5 μm and 50 μm.

3. The solid particulate formulation of claim 1, wherein 90% of the particles have a particle size between 3 μm and 40 μm.

4. The solid particulate formulation of claim 1, wherein 90% of the particles have a particle size between 10 μm and 30 μm.

5. The solid particulate formulation of claim 1, wherein 90% of the particles have a particle size between 1 μm and 25 μm.

6. The solid particulate formulation of claim 1, wherein the solubility of the soluble ferric pyrophosphate in aqueous solution is greater than 1 gram per mL.

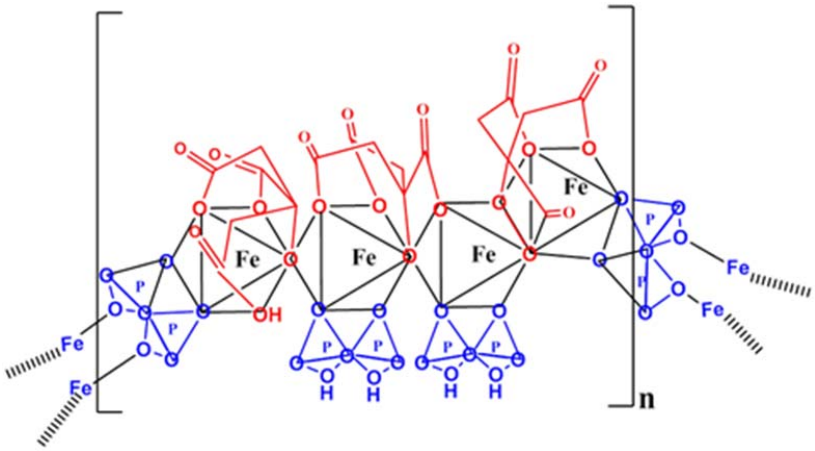
7. The solid particulate formulation of any of claims 1-6, wherein the soluble ferric pyrophosphate has an angle of repose less than 45 degrees, optionally less than 42 degrees.

8. The solid particulate formulation of any one of claims 1-7 that is stable in aqueous solution at ambient temperature for at least 24 months.

9. The solid particulate formulation of any one of claims 1-8, wherein the soluble ferric pyrophosphate comprises

a) iron in an amount of 7% to 11% by weight, citrate in an amount of at least 14%, and pyrophosphate in an amount of at least 10%,
b) iron in an amount from 7.5-9.0% by weight, citrate in an amount from 15-22% by weight, pyrophosphate in an amount from 15-22% by weight, phosphate in an amount less than 2%, sodium in an amount from 18-25% by weight, and sulfate in an amount from 20-35% by weight, or
c) iron in an amount from 9-14% by weight, citrate in an amount from 30-60% by weight, pyrophosphate in an amount from 5-20% by weight, sodium in an amount from 1-15% by weight, and no sulfate.

10. The solid particulate formulation of any one of claims 1-9, comprising a compound having structure (I):



(I).

11. A sachet comprising the solid particulate formulation of any one of claims 1-10.

12. The sachet of claim 11, comprising a dose of soluble ferric pyrophosphate that will result in a final iron concentration of 110 μg/L or 2 μM in a dialysate to be administered to a patient receiving hemodialysis.

13. Use of soluble ferric pyrophosphate according to any of claims 1-5 for the preparation of a medicament for administering a dialysate to a subject in need thereof, wherein a solid particulate formulation of soluble ferric pyrophosphate is mixed with a hemodialysis solution to form said dialysate.

14. A soluble ferric pyrophosphate according to any of claims 1-5 for use in administering a dialysate, wherein a solid particulate formulation of soluble ferric pyrophosphate is mixed with a hemodialysis solution to form the dialysate.

15. The soluble ferric pyrophosphate or use of claim 13 or 14, wherein the dialysis solution is an acid solution or a base solution.

16. The soluble ferric pyrophosphate or use of claim 15, wherein the acid solution comprises water, sodium chloride, potassium chloride, calcium chloride, magnesium chloride, dextrose, and citric or acetic acid or a citrate or acetate salt.

17. The soluble ferric pyrophosphate or use of claim 15 or 16, wherein the solubility of the solid particulate formulation in the acid solution is greater than 1 gram per mL.

18. The soluble ferric pyrophosphate or use of claim 15, wherein the base solution comprises sodium bicarbonate or a combination of sodium bicarbonate and sodium chloride.

19. The soluble ferric pyrophosphate or use of claim 15 or 18, wherein the solubility of the solid particulate formulation in the base solution is greater than 1 gram per mL.

20. The soluble ferric pyrophosphate or use of any one of claims 13-19, wherein the mixing of soluble ferric pyrophosphate results in a final iron concentration of about 100 µg/L to about 150 µg/L in the dialysate.

21. The soluble ferric pyrophosphate or use of any one of claims 13-20, wherein the soluble ferric pyrophosphate comprises

a) iron chelated with citrate and pyrophosphate,

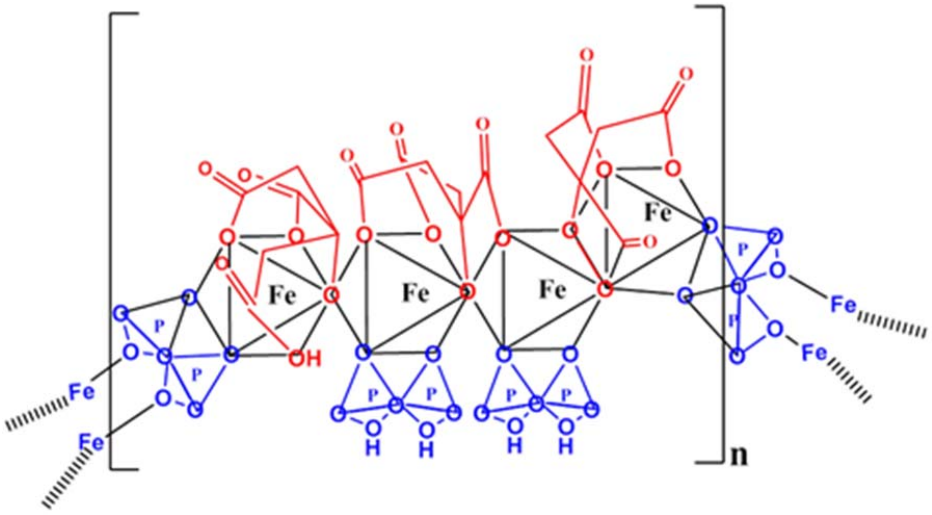
b) iron in an amount of 7% to 11% by weight, citrate in an amount of at least 14%, and pyrophosphate in an amount of at least 10%,

c) iron in an amount from 7.5-9.0% by weight, citrate in an amount from 15-22% by weight, pyrophosphate in an amount from 15-22% by weight, phosphate in an amount less than 2%, sodium in an amount from 18-25% by weight, and sulfate in an amount from 20-35% by weight,

d) iron in an amount from 9-14% by weight, citrate in an amount from 30-60% by weight, pyrophosphate in an amount from 5-20% by weight, sodium in an amount from 1-15% by weight, and no sulfate, or

e) iron chelated with citrate and pyrophosphate having at least one of: a Fe-O distance of 2.00 angstroms in the primary coordination shell, a Fe-C distance of 2.98 angstroms, and a Fe-P distance of 3.20 angstroms in the second coordination sphere of Fe.

22. The soluble ferric pyrophosphate or use of any one of claims 13-21, wherein the solid particulate formulation comprises a compound having structure (I):



(I).

23. A kit comprising the solid particulate formulation of soluble ferric pyrophosphate or sachet of any one of claims 1-12 and a dialysis concentrate formulation in a solid or liquid form.

24. The kit of claim 23, wherein the dialysis concentrate formulation is a solid form.

25. The kit of claim 23, wherein the dialysis concentrate formulation is a liquid form.

26. The kit of any of claims 23-25, wherein the dialysis concentrate formulation is an acid.

27. The kit of any of claims 23-25, wherein the dialysis concentrate formulation is a base.