We claim:

1. A particle encapsulating conjugate comprising an active agent coupled to a targeting moiety by a linker.

2. The particle of claim 1, wherein the conjugate comprises a formula selected from the group X-Y-Z, X-Y-Z-Y-X, X-$(Y-Z)_n$, $(X-Y)_n$-Z, X-Y-Z_n, and $(X-Y-Z-Y)_n$-Z;

wherein X is a targeting moiety,

Y is a linker,

Z is an active agent, and

n is an integer between 2 and 1,000.

3. The particle of claim 1, wherein the conjugate comprises the formula X-Y-Z;

wherein X is a targeting moiety,

Y is a linker, and

Z is an active agent.

4. The particle of any one of claims 1-3, wherein each linker is independently selected from the group consisting of substituted and unsubstituted C_1-C_{30} alkyl, substituted and unsubstituted C_2-C_{30} alkenyl, substituted and unsubstituted C_2-C_{30} alkynyl, substituted and unsubstituted C_3-C_{30} cycloalkyl, substituted and unsubstituted C_1-C_{30} heterocycloalkyl, substituted and unsubstituted C_3-C_{30} cycloalkenyl, substituted and unsubstituted C_1-C_{30} heterocycloalkenyl, substituted and unsubstituted aryl, and substituted and unsubstituted heteroaryl.

5. The particle of claim 4, wherein each linker is independently selected from the group consisting of C_2-C_{30} carboxylic acids, C_2-C_{30} di-carboxylic acids, and derivatives thereof.

6. The particle of claim 5, wherein the linker is a derivative of a C_2-C_{30} carboxylic acids or a C_2-C_{30} di-carboxylic acid comprising an atom or group of atoms selected from the group consisting of–O-, -C(=O)-, -NR, -O-C(=O)-NR-, -S-, and -S-S-, wherein R is a linear or branched alkyl or heteroalkyl group.

7. The particle of claim 4, wherein the linker is selected from the group consisting of C_2-C_{30} carboxylic acids and di-carboxylic acids containing a dithio (-S-S-) group in the backbone.

8. The particle of claim 4, wherein the linker is not polymeric.

9. The particle of any one of claims 1-3, wherein the active agent is selected from the group consisting of therapeutic, prophylactic, nutraceutical, and diagnostic agents.

10. The particle of claim 9 wherein the active agent is selected from chemotherapeutic agents, anti-infective agents, and combinations thereof.

11. The particle of claim 9 wherein the active agent is a protein, peptide, lipid, carbohydrate, sugar, nucleic acid, or combination thereof.

12. The particle of claim 9, wherein the active agent is an organometallic compound.

13. The particle of claim 12, wherein the active agent is a platinum compound.

14. The particle of claim 13, wherein the active agent is cabazitaxel.

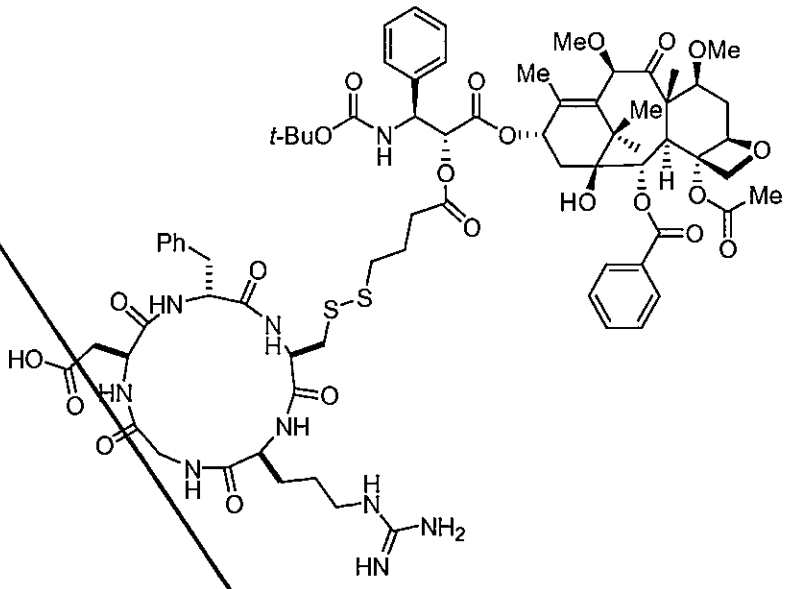
15. The particle of any one of claims 1-14, wherein the targeting moiety is selected from the group consisting of peptides and polypeptides, antibody mimetics, nucleic acids, glycoproteins, small molecules, carbohydrate, and lipids.

16. The particle of claim 15, wherein the targeting moiety targets cancer cells.

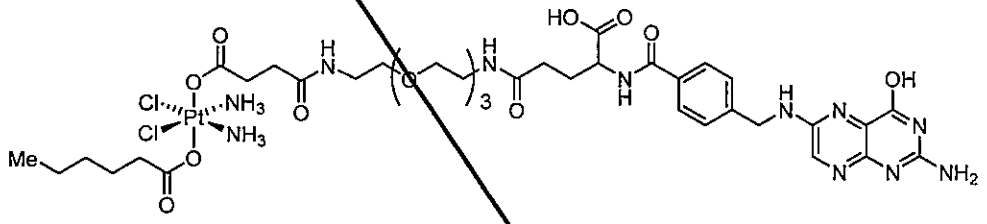
17. The particle of claim 15, wherein the targeting moiety targets a marker selected from the group consisting of CD19, CD70, CD56, PSMA, alpha integrin, CD22, CD138, EGFR, EphA2, AGS-5, Nectin-4, HER2, GPMNB, CD74, and Le.

18. The particle of claim 15, wherein the targeting moiety is selected from the group consisting of RGD, Cy5.5, and PSMA.

19. The particle of claim 3, wherein the particle comprises a conjugate having the formula

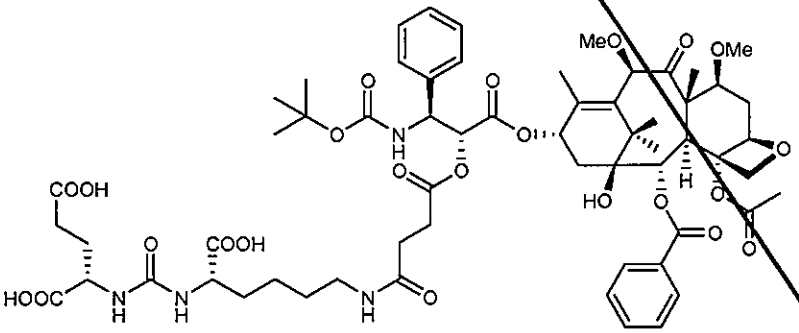


20. The particle of claim 3, wherein the particle comprises a conjugate having the formula

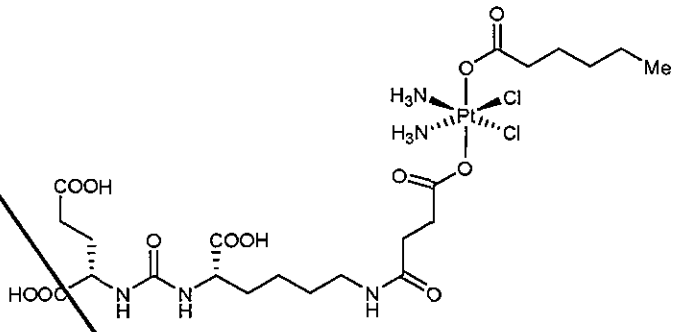


.

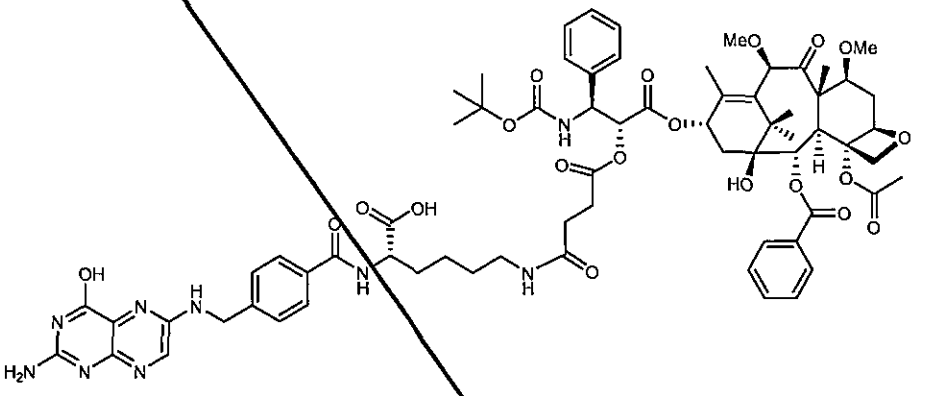
21. The particle of claim 3, wherein the particle comprises a conjugate having the formula



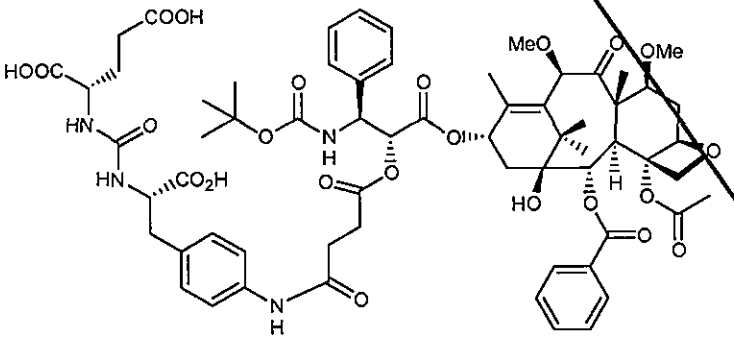
22. The particle of claim 3, wherein the particle comprises a conjugate having the formula



23. The particle of claim 3, wherein the particle comprises a conjugate having the formula

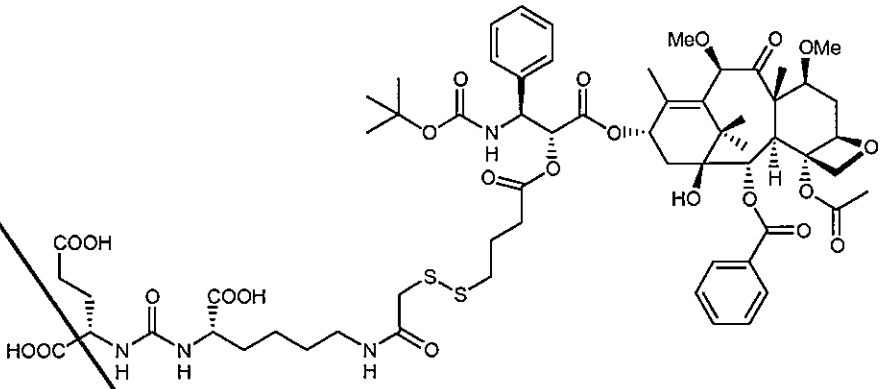


24. The particle of claim 3, wherein the particle comprises a conjugate having the formula



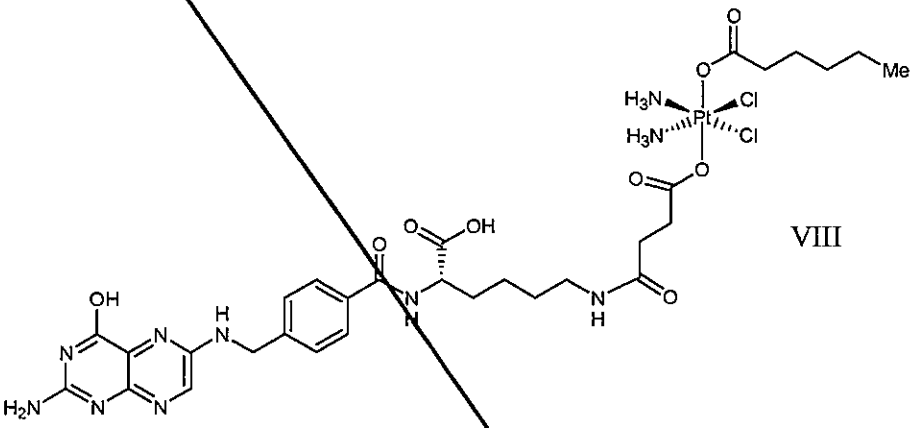
VI

25. The particle of claim 3, wherein the particle comprises a conjugate having the formula



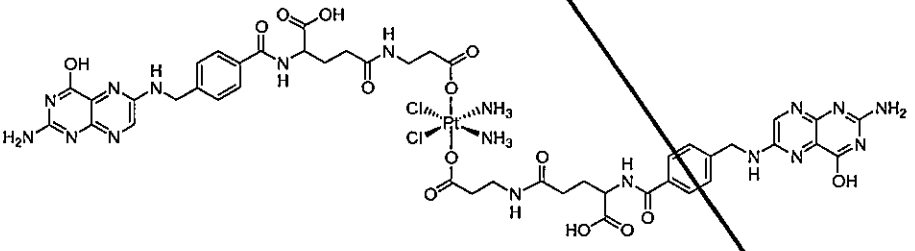
VII

26. The particle of claim 3, wherein the particle comprises a conjugate having the formula



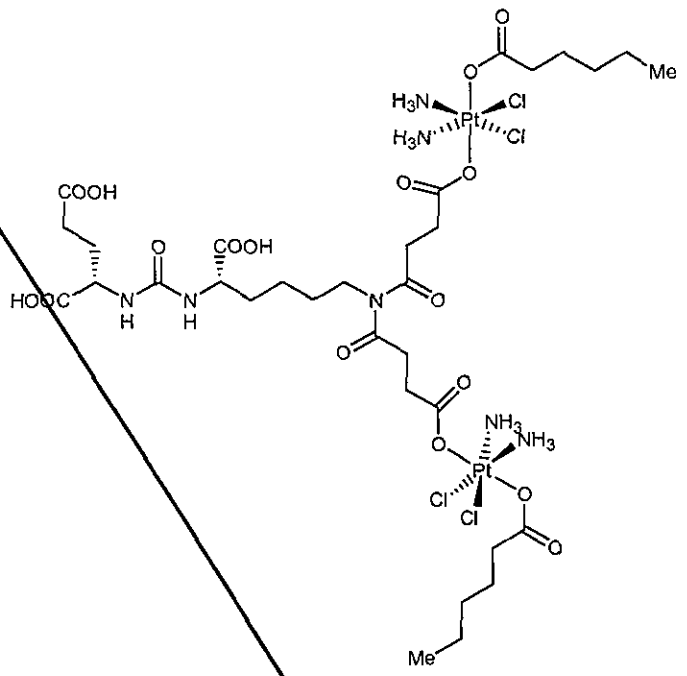
VIII

27. The particle of claim 3, wherein the particle comprises a conjugate having the formula



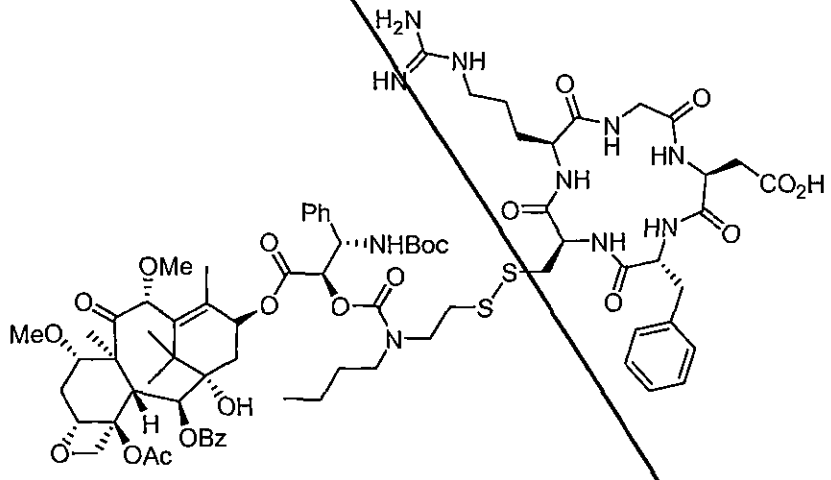
IX

28. The particle of claim 3, wherein the particle comprises a conjugate having the formula



X

29. The particle of claim 3, wherein the particle comprises a conjugate having the formula



30. The particle of any one of claims 1-3 and 19-29, wherein the polymeric matrix comprises one or more polymers selected from the group consisting of hydrophobic polymers, hydrophilic polymers, and copolymers thereof.

31. The particle of claim 19, wherein the hydrophobic polymers are selected from the group consisting of polyhydroxyacids, polyhydroxyalkanoates, olycaprolactones, = poly(orthoesters),

polyanhydrides, poly(phosphazenes), poly(lactide-co-caprolactones), polycarbonates, polyesteramides, polyesters, and copolymers thereof.

32. The particle of claim 19, wherein the hydrophilic polymers are selected from the group consisting of polyalkylene glycols, polyalkylene oxides, poly(oxyethylated polyol), poly(olefinic alcohol), polyvinylpyrrolidone), poly(hydroxyalkylmethacrylamide), poly(hydroxyalkylmethacrylate), poly(saccharides), poly(hydroxy acids), poly(vinyl alcohol), and copolymers thereof.

33. The particle of any one of claims 1-3 and 19-29, wherein the polymeric matrix comprises one or more polymers selected from the group consisting of poly(lactic acid), poly(glycolic acid), poly(lactic-co-glycolic acid), poly(ethylene oxide), poly(ethylene glycol), poly(propylene glycol), and copolymers thereof.

34. The particle of any one of claims 1-3 and 19-29, wherein the particle has a diameter between 10 nm and 300 nm or 50 and 120 nm.

35. The particle of any one of claims 1-3 and 19-29, wherein the particle has a diameter between 500 nm and 1.5 microns or 300 and 500 nm.

36. The particle of any one of claims 1-3 and 19-29, wherein the polymeric matrix comprises two or more different polymers.

37. The particle of any one of claims 1-3 and 19-29, wherein the conjugate is present in an amount between 0.1% and 10 % (w/w) based upon the weight of the particle.

38. A pharmaceutical formulation comprising the particle of any one of claims 1-3 and 19-29 and a pharmaceutically acceptable excipient.

39. A method of making the particle of any one of claims 1-3 and 19-29 comprising the steps of

forming a conjugate comprising an active agent connected to a targeting moiety by a linker , and

forming a particle comprising a polymeric matrix encapsulating the conjugate.

40. The method of claim 39, wherein the conjugate is formed from a linker precursor selected from the group consisting of C_2-C_{30} carboxylic

acids and substituted carboxylic acids, C_2-C_{30} di-carboxylic acids and substituted di-carboxylic acids, and acid anhydrides, acid esters, and acid halides thereof.

41. A method of treating a subject in need thereof comprising administering a therapeutically effective amount of the formulation of claim 38.

Claims

1. A solid polymeric controlled release nanoparticle comprising a solid polymeric matrix encapsulating a conjugate comprising an active agent coupled to a targeting moiety by a linker,

wherein the active agent is selected from the group consisting of proteins, peptides, lipids, carbohydrates, sugars, small molecules that are non-polymeric and/or non-oligomeric, and combinations thereof.

2. The solid polymeric nanoparticle of claim 1, wherein the conjugate comprises a formula selected from the group X-Y-Z, X-Y-Z-Y-X, X-$(Y-Z)_n$, $(X-Y)_n$-Z, X-Y-Z_n, and $(X-Y-Z-Y)_n$-Z;

wherein X is a targeting moiety,

Y is a linker,

Z is an active agent, and

n is an integer between 2 and 1,000.

3. The solid polymeric nanoparticle of claim 1, wherein the conjugate comprises the formula X-Y-Z;

wherein X is a targeting moiety,

Y is a linker, and

Z is an active agent.

4. The solid polymeric nanoparticle of any one of claims 1-3, wherein each linker is independently selected from the group consisting of substituted and unsubstituted C_1-C_{30} alkyl, substituted and unsubstituted C_2-C_{30} alkenyl, substituted and unsubstituted C_2-C_{30} alkynyl, substituted and unsubstituted C_3-C_{30} cycloalkyl, substituted and unsubstituted C_1-C_{30} heterocycloalkyl, substituted and unsubstituted C_3-C_{30} cycloalkenyl, substituted and unsubstituted C_1-C_{30} heterocycloalkenyl, substituted and unsubstituted aryl, and substituted and unsubstituted heteroaryl.

5. The solid polymeric nanoparticle of claim 4, wherein each linker is independently selected from the group consisting of C_2-C_{30} carboxylic acids, C_2-C_{30} di-carboxylic acids, and derivatives thereof.

6. The solid polymeric nanoparticle of claim 5, wherein the linker is a derivative of a C_2-C_{30} carboxylic acids or a C_2-C_{30} di-carboxylic acid comprising an atom or group of atoms selected

from the group consisting of–O-, -C(=O)-, -NR, -O-C(=O)-NR-, -S-, and -S-S-, wherein R is a linear or branched alkyl or heteroalkyl group.

7. The solid polymeric nanoparticle of claim 4, wherein the linker is selected from the group consisting of C_2-C_{30} carboxylic acids and di-carboxylic acids containing a dithio (-S-S-) group in the backbone.

8. The solid polymeric nanoparticle of claim 4, wherein the linker is not polymeric.

9. The solid polymeric nanoparticle of any one of claims 1-3, wherein the active agent is selected from the group consisting of therapeutic, prophylactic, nutraceutical, and diagnostic agents.

10. The solid polymeric nanoparticle of claim 9 wherein the active agent is selected from chemotherapeutic agents, anti-infective agents, and combinations thereof.

11. The solid polymeric nanoparticle of claim 9, wherein the active agent is an organometallic compound.

12. The solid polymeric nanoparticle of claim 11, wherein the active agent is a platinum compound.

13. The solid polymeric nanoparticle of claim 12, wherein the active agent is cabazitaxel.

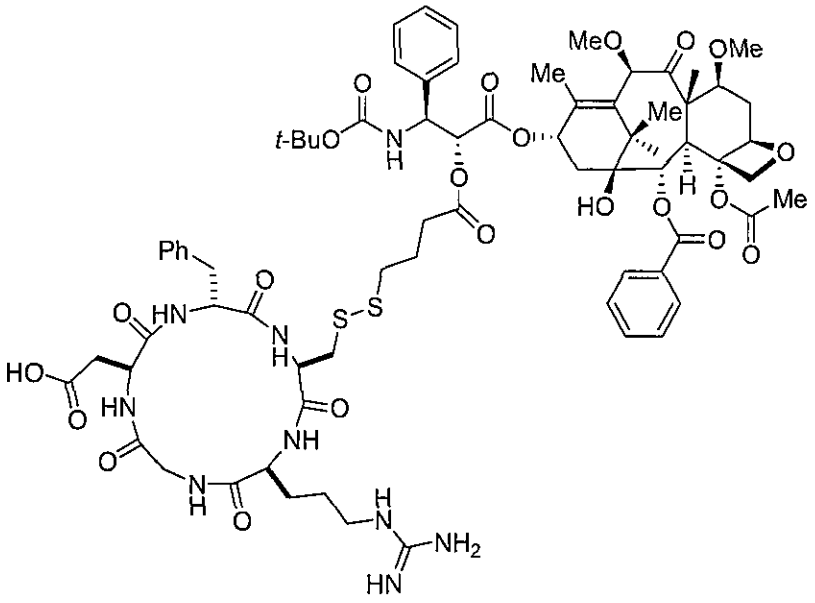
14. The solid polymeric nanoparticle of any one of claims 1-13, wherein the targeting moiety is selected from the group consisting of peptides and polypeptides, antibody mimetics, nucleic acids, glycoproteins, small molecules, carbohydrate, and lipids.

15. The solid polymeric nanoparticle of claim 14, wherein the targeting moiety targets cancer cells.

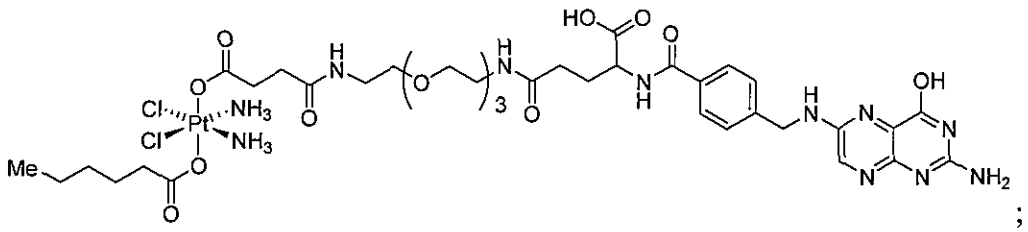
16. The solid polymeric nanoparticle of claim 14, wherein the targeting moiety targets a marker selected from the group consisting of CD19, CD70, CD56, PSMA, alpha integrin, CD22, CD138, EGFR, EphA2, AGS-5, Nectin-4, HER2, GPMNB, CD74, and Le.

17. The solid polymeric nanoparticle of claim 14, wherein the targeting moiety is selected from the group consisting of RGD, Cy5.5, and PSMA.

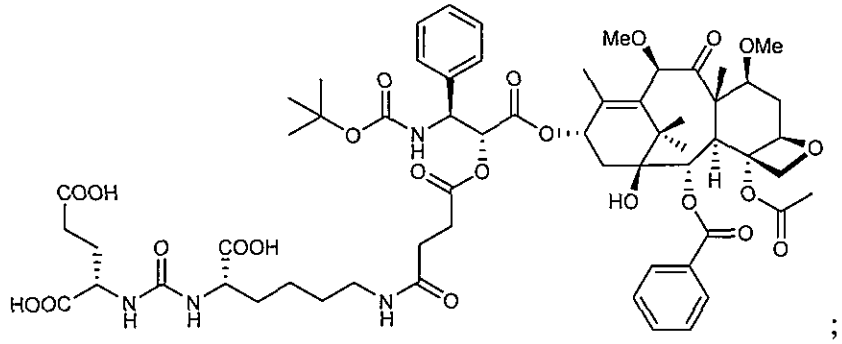
18. The solid polymeric nanoparticle of claim 3, wherein the conjugate comprises a formula selected from the group consisting of:



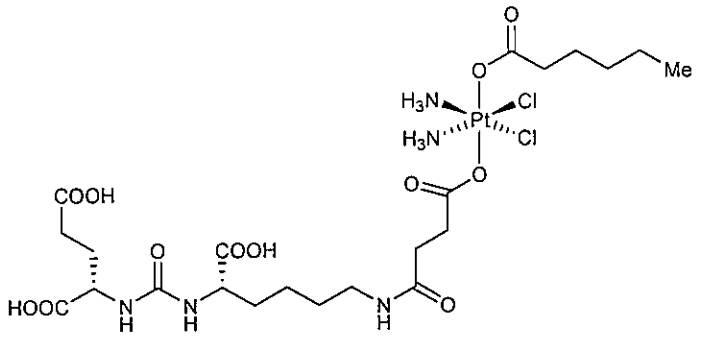
;



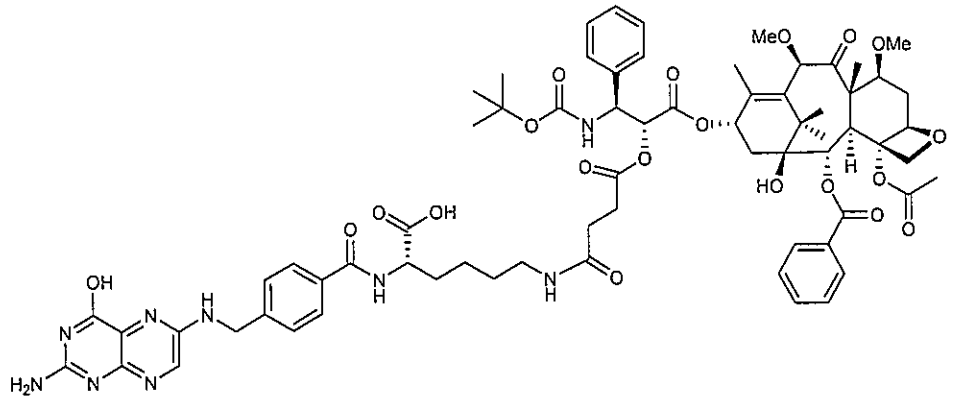
;



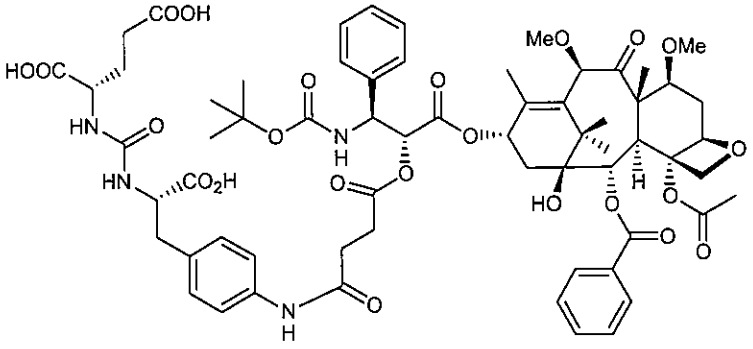
;



;

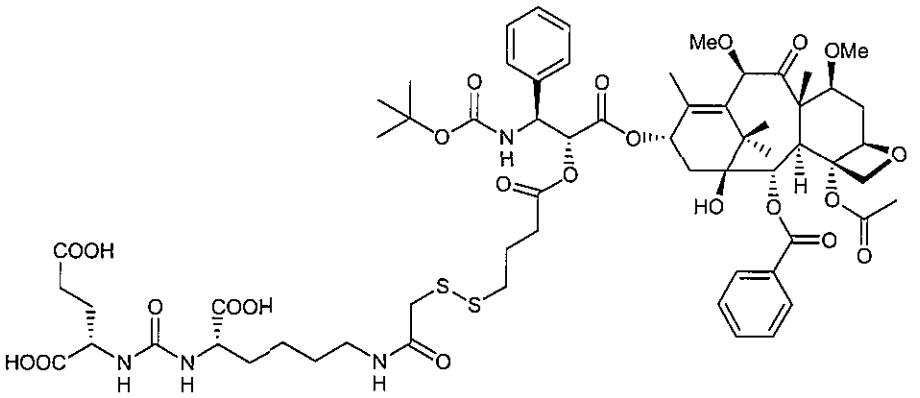


;



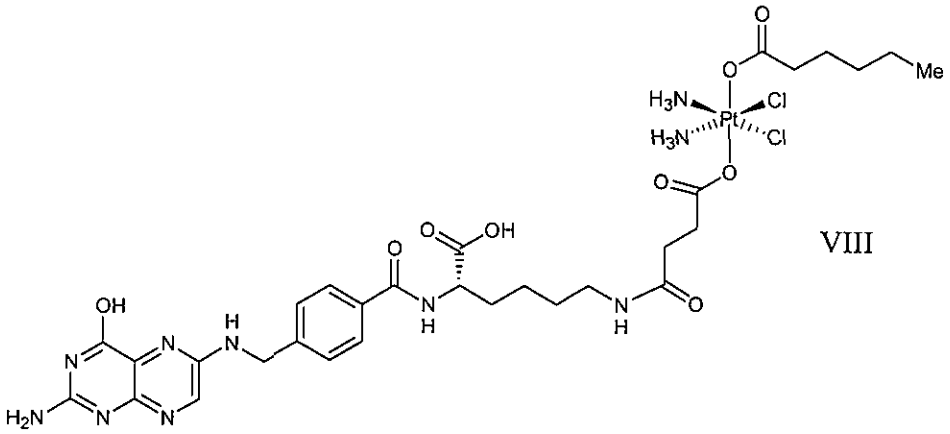
VI

;



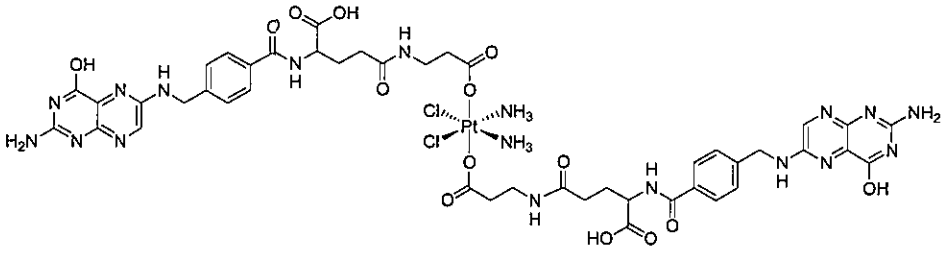
VII

;



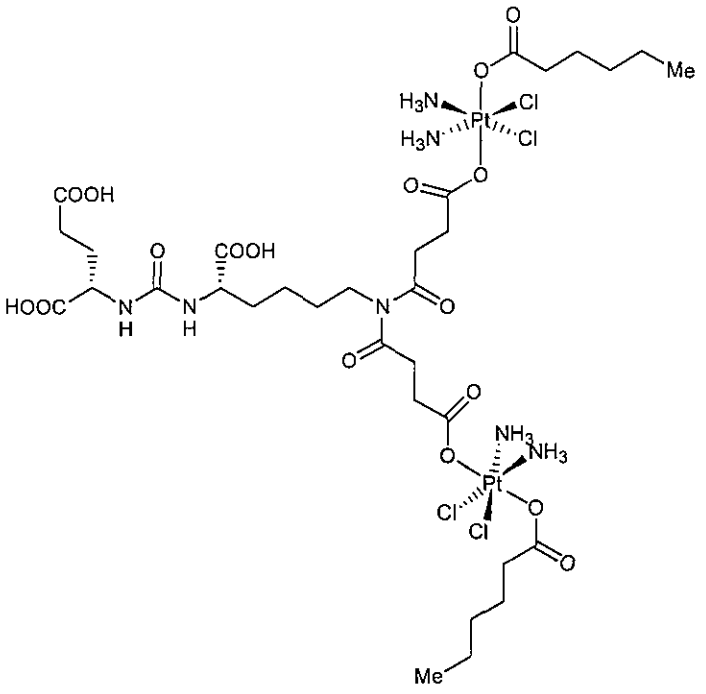
VIII

;



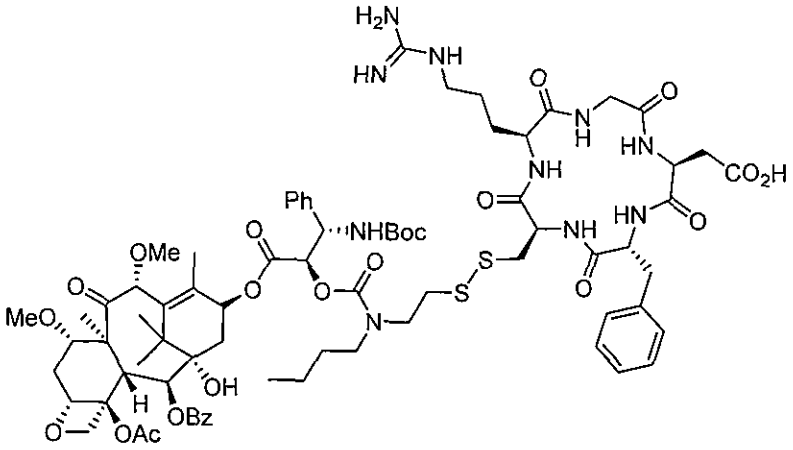
IX

;



X

; and



19. The solid polymeric nanoparticle of any one of claims 1-18, wherein the solid polymeric matrix comprises one or more polymers selected from the group consisting of hydrophobic polymers, hydrophilic polymers, and copolymers thereof.

20. The solid polymeric nanoparticle of claim 19, wherein the hydrophobic polymers are selected from the group consisting of polyhydroxyacids, polyhydroxyalkanoates, polycaprolactones, poly(orthoesters), polyanhydrides, poly(phosphazenes), poly(lactide-co-caprolactones), polycarbonates, polyesteramides, polyesters, and copolymers thereof.

21. The solid polymeric nanoparticle of claim 19, wherein the hydrophilic polymers are

selected from the group consisting of polyalkylene glycols, polyalkylene oxides, poly(oxyethylated polyol), poly(olefinic alcohol), polyvinylpyrrolidone, poly(hydroxyalkylmethacrylamide), poly(hydroxyalkylmethacrylate), poly(saccharides), poly(hydroxy acids), poly(vinyl alcohol), and copolymers thereof.

22. The solid polymeric nanoparticle of any one of claims 1-18, wherein the solid polymeric matrix comprises one or more polymers selected from the group consisting of poly(lactic acid), poly(glycolic acid), poly(lactic-co-glycolic acid), poly(ethylene oxide), poly(ethylene glycol), poly(propylene glycol), and copolymers thereof.

23. The solid polymeric nanoparticle of any one of claims 1-22, wherein the particle has a diameter between 10 nm and 500 nm.

24. The solid polymeric nanoparticle of any one of claims 1-23, wherein the solid polymeric matrix comprises two or more different polymers.

25. The solid polymeric nanoparticle of any one of claims 1-24, wherein the conjugate is present in an amount between 0.1% and 10 % (w/w) based upon the weight of the particle.

26. A pharmaceutical formulation comprising the solid polymeric nanoparticle of any one of claims 1-25 and a pharmaceutically acceptable excipient.

27. A method of making the solid polymeric controlled release nanoparticle of any one of claims 1-25 comprising the steps of

forming a conjugate comprising an active agent connected to a targeting moiety by a linker, and

forming a particle comprising a solid polymeric matrix encapsulating the conjugate.

28. The method of claim 27, wherein the conjugate is formed from a linker precursor selected from the group consisting of C_2-C_{30} carboxylic acids and substituted carboxylic acids, C_2-C_{30} di-carboxylic acids and substituted di-carboxylic acids, and acid anhydrides, acid esters, and acid halides thereof.