CLAIMS

1. A topical suspension formulation comprising:

a tetracycline, or a pharmaceutically acceptable salt, hydrate, or polymorph thereof in a suspended form within the formulation;

a liquid medium that does not dissolve or substantially minimally dissolves the tetracycline; and

a polymeric hydrocarbon gelling agent,

wherein the particle size of the tetracycline has a D90 value of from 2 micrometres to 10 micrometres.

2. A topical suspension formulation according to claim 1 wherein the formulation is free of hydrophobic, non-hygroscopic silicone thickening agents.

3. The topical suspension formulation of claim 1 or 2, wherein the tetracycline has a D90 particle size that has a value that is from 3 micrometres to 8 micrometres.

4. The topical suspension formulation of claim 1, wherein the tetracycline has a D90 particle size that has a value that is from 4 micrometres to about 10 micrometres and a D50 particle size that has a value that is from 1 micrometre to about 5 micrometres.

5. The topical suspension formulation of claim 1, wherein the tetracycline has a D90 particle size that has a value that is from 4 micrometres to 10 micrometres , a D50 particle size that has a value that is from about 1 micrometre to about 5 micrometres , and a D10 particle size that has a value that is from 0.5 micrometres to about 1.5 micrometres.

6. A topical suspension formulation according to any preceding claim wherein the tetracycline is minocycline or doxycycline, or a pharmaceutically acceptable salt, hydrates or polymorph thereof.

7. A topical suspension formulation according to claim 6 wherein the concentration of minocycline is from 0.05% to about 10%.

8. A topical suspension formulation according to any preceding claim and comprising minocycline, wherein the concentration of 4-epi minocycline is not more than 4% after storage for 6 months at real-time (25°C /60% relative humidity (RH)) and at accelerated (40°C/75% RH) stability conditions, as determined by HPLC analysis.

9. A topical suspension formulation according to any preceding claim and comprising minocycline wherein the concentration of 4-epi minocycline in the minocycline suspension formulation when stored at 40°C /75%RH for one month results in less than 3% of 4-epi-minocycline, as determined by HPLC analysis.

10. A topical suspension formulation according to any preceding claim and comprising minocycline wherein the concentration of 4-epi minocycline in the minocycline suspension formulation when stored at 40°C /75%RH for three months results in less than 4% of 4-epi-minocycline, as determined by HPLC analysis.

11. A topical suspension formulation according to any preceding claim and comprising minocycline wherein the concentration of 4-epi minocycline is no more than 4% after storage for 12 months at real-time (25°C /60% RH) stability conditions, as determined by HPLC analysis.

12. A topical suspension formulation according to any preceding claim , wherein the liquid medium is a non-comedogenic liquid medium .

13. A topical suspension formulation according to claim 12, wherein the non-comedogenic liquid medium is one or more of a mineral oil, a light mineral oil, a minimally comedogenic oil and an additional non-comedogenic oil.

14. A topical suspension formulation according to claim 12, wherein the non-comedogenic liquid medium is mineral oil.

15. A topical suspension formulation according to any preceding claim , wherein the non-comedogenic liquid medium is characterized as (a) resulting in less than 5% of the tetracycline active ingredient being dissolved in the medium at room temperature after 2 hours, as measured by HPLC and/or (b) resulting in less than 4% of 4-epi-minocycline, if minocycline is used as the active ingredient, when stored for 1 month at room temperature, as measured by HPLC.

16. A topical suspension formulation according to any preceding claim, wherein the mineral oil constitutes at least about 70% of the suspension formulation.

17. A topical suspension formulation according to any preceding claim wherein the polymeric hydrocarbon gelling agent is a mixture of a mineral oil and one or more copolymers based on one or more monomers selected from alkene monomers, particularly C_1–C_{10}, or C_1 to C_6, or C_2 to C_4 alkene monomers, and phenylalkene monomers, particularly C_1–C_{10}, or C_1 to C_6, or C_2 to C_4phenylalkene monomers, or is a gel comprising an oil and one or more gelling polymers.

18. A topical suspension formulation according to claim 17 wherein the one or more copolymers comprises an ethylene/propylene/styrene copolymer.

19. A topical suspension formulation according to claim 17 or 18 wherein the one or more copolymers comprises a butylene/ethylene/styrene copolymer.

20. A topical suspension formulation according to claim 17, 18 or 19 wherein the suspension further comprises an anti-oxidant, particularly butylatedhydroxytoluene.

21. A topical suspension formulation according to claim 17 wherein the polymeric gelling agent comprises ethylene/propylene/styrene copolymer and butylene/ethylene/styrene copolymer and butylatedhydroxytoluene as an optional anti-oxidant.

22. A topical suspension formulation according to any preceding claim, wherein the formulation is free of a skin penetration enhancing agent or an excipient that functions primarily or solely as a skin penetration enhancer.

23. A topical suspension formulation according to any preceding claim, wherein the formulation is free of a compound that results in dissolution of the tetracycline active ingredient.

24. A topical suspension formulation according to claim 21, wherein the compound that results in dissolution of the tetracycline active ingredient comprises one or more of water, hydrophilic solvents and emollient esters.

25. A topical suspension formulation according to any preceding claim, wherein the liquid medium comprises a mixture of a non-comedogenic medium and a comedogenic medium and the non-comedogenic medium is present in a greater amount than the comedogenic medium.

26. A topical suspension formulation according to any preceding claim, wherein the composition consists essentially of the pharmaceutically effective amount of minocycline, a non-comedogenic liquid medium that does not dissolve or minimally dissolves tetracycline, and the polymeric hydrocarbon gelling agent to thicken the composition and optionally one or more of 4-epi minocycline, colorants, dyes, fragrances and a sunscreen material.

27. A topical suspension formulation according to any preceding claim, wherein the composition consists of the pharmaceutically effective amount of minocycline, a non-comedogenic liquid medium that does not dissolve or minimally dissolves tetracycline, and the polymeric hydrocarbon gelling agent to thicken the composition.

28. A topical suspension formulation according to any preceding claim, wherein the composition consists of a pharmaceutically effective amount of minocycline, a non-comedogenic liquid medium that does not dissolve or minimally dissolves tetracycline, and a gelling agent to thicken the composition and 4-epi minocycline, and optionally one or more of a comedogenic liquid medium present at an amount less than the non-comedogenic liquid medium, colorants, dyes, fragrances and sunscreen materials.

29. A topical suspension formulation according to any preceding claim, wherein the composition is nonfoamable and is free of a foaming adjuvant.

30. A method of treating an infection or inflammation of the skin, the method comprising topically administering to a subject in need of such treatment a suspension formulation according to any preceding claim.

31. A method of treating an infection or inflammation of the skin according to claim 30 wherein the disease is characterized as acne or rosacea.

32. A method of treating an ophthalmic disease or condition, the method comprising topically administering to a surface of the eye of a subject in need of such treatment a suspension formulation according to any one of claims 1 to 29.

33. A topical suspension formulation according to any one of claims 1 to 29, wherein the tetracycline is crystalline minocycline free base.

34. A topical suspension composition according to any one of claims 1 to 29 or 33, further comprising one or more of a sunscreen agent, a fragrance and a colorant or dye.

35. A topical minocycline suspension formulation for treating an individual afflicted with acne vulgaris, the composition consisting essentially of a pharmaceutically effective amount of minocycline, a hydrophobic liquid medium that does not dissolve or minimally dissolves tetracycline, and a polymeric hydrocarbon gelling agent to thicken the composition, wherein:

the hydrophobic liquid medium is characterized as (a) resulting in less than 5% of the tetracycline active ingredient being dissolved in the medium at room temperature after 2 hours as determined by HPLC, and/or (b) results in less than 4% of 4-epi-minocycline (when minocycline is used as the active ingredient) when stored for 1 month at room temperature, as determined by HPLC.

36. A topical suspension formulation comprising:

a tetracycline or its pharmaceutically acceptable salts, hydrates, or morphs in a suspended form within the formulation;

a non-comedogenic, hydrophobic liquid medium that does not dissolve or substantially minimally dissolves the tetracycline; and

a polymeric hydrocarbon gelling agent to thicken the suspension.

37. A formulation according to claim 35 or 36 wherein the formulation is as further defined in any one of claims 1 to 29 or 33 to 34.

38. A formulation according to any one of claims 1 to 29, or 33 to 37, for use as a medicament.

39. A formulation according to claim 38 for use in treating infection or inflammation of the skin.

40. A formulation according to claim 39 for use in treating acne or rosacea.

41. A formulation according to claim 38 for use in treating an ophthalmic disease or condition.

42. A formulation according to any one of claims 1 to 29 or 33 to 37, or a formulation for use according to any one of claims 38 to 41, further comprising another anti-acne agent.

43. A formulation, or formulation for use, according to claim 42 wherein the anti-acne agent is a retinoid, such as tretinoin, adapalene, or tazarotene.

CLAIMS

1. A topical suspension formulation comprising:

a tetracycline, or a pharmaceutically acceptable salt, hydrate, or polymorph thereof in a suspended form within the formulation;

a liquid medium that does not dissolve or substantially minimally dissolves the tetracycline; and

a polymeric hydrocarbon gelling agent,

wherein the particle size of the tetracycline has a D90 value of from 2 micrometres to 10 micrometres.

2. A topical suspension formulation according to claim 1 wherein the formulation is free of hydrophobic, non-hygroscopic silicone thickening agents.

3. The topical suspension formulation of claim 1 or 2, wherein the tetracycline has a D90 particle size that has a value that is from 3 micrometres to 8 micrometres.

4. The topical suspension formulation of claim 1, wherein the tetracycline has a D90 particle size that has a value that is from 4 micrometres to about 10 micrometres and a D50 particle size that has a value that is from 1 micrometre to about 5 micrometres.

5. The topical suspension formulation of claim 1, wherein the tetracycline has a D90 particle size that has a value that is from 4 micrometres to 10 micrometres , a D50 particle size that has a value that is from about 1 micrometre to about 5 micrometres , and a D10 particle size that has a value that is from 0.5 micrometres to about 1.5 micrometres.

6. A topical suspension formulation according to any preceding claim wherein the tetracycline is minocycline or doxycycline, or a pharmaceutically acceptable salt, hydrates or polymorph thereof.

7. A topical suspension formulation according to claim 6 wherein the concentration of minocycline is from 0.05% to about 10% (w/w).

8. A topical suspension formulation according to any preceding claim and comprising minocycline, wherein the concentration of 4-epi minocycline is not more than 4% (w/w) after storage for 6 months at real-time (25°C /60% relative humidity (RH)) and at accelerated (40°C/75% RH) stability conditions, as determined by HPLC analysis.

9. A topical suspension formulation according to any preceding claim and comprising minocycline wherein the concentration of 4-epi minocycline in the minocycline suspension formulation when stored at 40°C /75%RH for one month results in less than 3% (w/w) of 4-epi-minocycline, as determined by HPLC analysis.

10. A topical suspension formulation according to any preceding claim and comprising minocycline wherein the concentration of 4-epi minocycline in the minocycline suspension formulation when stored at 40°C /75%RH for three months results in less than 4% (w/w) of 4-epi-minocycline, as determined by HPLC analysis.

11. A topical suspension formulation according to any preceding claim and comprising minocycline wherein the concentration of 4-epi minocycline is no more than 4% (w/w) after storage for 12 months at real-time (25°C /60% RH) stability conditions, as determined by HPLC analysis.

12. A topical suspension formulation according to any preceding claim , wherein the liquid medium is a non-comedogenic liquid medium .

13. A topical suspension formulation according to claim 12, wherein the non-comedogenic liquid medium is one or more of a mineral oil, a light mineral oil, a minimally comedogenic oil and an additional non-comedogenic oil.

14. A topical suspension formulation according to claim 12, wherein the non-comedogenic liquid medium is mineral oil.

15. A topical suspension formulation according to any preceding claim , wherein the non-comedogenic liquid medium is characterized as (a) resulting in less than 5% (w/w) of the tetracycline active ingredient being dissolved in the medium at room temperature after 2 hours, as measured by HPLC and/or (b) resulting in less than 4% (w/w) of 4-epi-minocycline, if minocycline is used as the active ingredient, when stored for 1 month at room temperature, as measured by HPLC.

16. A topical suspension formulation according to any preceding claim, wherein the mineral oil constitutes at least about 70% (w/w) of the suspension formulation.

17. A topical suspension formulation according to any preceding claim wherein the polymeric hydrocarbon gelling agent is a mixture of a mineral oil and one or more copolymers based on one or more monomers selected from alkene monomers, particularly C_1 –C_{10}, or C_1 to C_6, or C_2 to C_4 alkene monomers, and phenylalkene monomers, particularly C_1 –C_{10}, or C_1 to C_6, or C_2 to C_4phenylalkene monomers, or is a gel comprising an oil and one or more gelling polymers.

18. A topical suspension formulation according to claim 17 wherein the one or more copolymers comprises an ethylene/propylene/styrene copolymer.

19. A topical suspension formulation according to claim 17 or 18 wherein the one or more copolymers comprise a butylene/ethylene/styrene copolymer.

20. A topical suspension formulation according to claim 17, 18 or 19 wherein the suspension further comprises an anti-oxidant, particularly butylatedhydroxytoluene.

21. A topical suspension formulation according to claim 17 wherein the polymeric gelling agent comprises ethylene/propylene/styrene copolymer and butylene/ethylene/styrene copolymer and butylatedhydroxytoluene as an optional anti-oxidant.

22. A topical suspension formulation according to any preceding claim, wherein the formulation is free of a skin penetration enhancing agent or an excipient that functions primarily or solely as a skin penetration enhancer.

23. A topical suspension formulation according to any preceding claim, wherein the formulation is free of a compound that results in dissolution of the tetracycline active ingredient.

24. A topical suspension formulation according to claim 23, wherein the compound that results in dissolution of the tetracycline active ingredient comprises one or more of water, hydrophilic solvents and emollient esters.

25. A topical suspension formulation according to any preceding claim, wherein the liquid medium comprises a mixture of a non-comedogenic medium and a comedogenic medium and the non-comedogenic medium is present in a greater amount than the comedogenic medium.

26. A topical suspension formulation according to any preceding claim, wherein the composition consists essentially of the pharmaceutically effective amount of minocycline, a non-comedogenic liquid medium that does not dissolve or minimally dissolves tetracycline, and the polymeric hydrocarbon gelling agent to thicken the composition and optionally one or more of 4-epi minocycline, colorants, dyes, fragrances and a sunscreen material.

27. A topical suspension formulation according to any preceding claim, wherein the composition consists of the pharmaceutically effective amount of minocycline, a non-comedogenic liquid medium that does not dissolve or minimally dissolves tetracycline, and the polymeric hydrocarbon gelling agent to thicken the composition.

28. A topical suspension formulation according to any preceding claim, wherein the composition consists of a pharmaceutically effective amount of minocycline, a non-comedogenic liquid medium that does not dissolve or minimally dissolves tetracycline, and a gelling agent to thicken the composition and 4-epi minocycline, and optionally one or more of a comedogenic liquid medium present at an amount less than the non-comedogenic liquid medium, colorants, dyes, fragrances and sunscreen materials.

29. A topical suspension formulation according to any preceding claim, wherein the composition is nonfoamable and is free of a foaming adjuvant.

30. A suspension formulation according to any preceding claim for use in the treatment of an infection or inflammation of the skin.

31. A suspension treatment for use according to claim 30, wherein the infection or inflammation is characterized as acne or rosacea.

32. A suspension formulation according to any one of claims 1 to 29, for use in treatment of an ophthalmic disease.

33. A topical suspension formulation according to any one of claims 1 to 29, wherein the tetracycline is crystalline minocycline free base.

34. A topical suspension composition according to any one of claims 1 to 29 or 33, further comprising one or more of a sunscreen agent, a fragrance and a colorant or dye.

35. A topical minocycline suspension formulation for treating an individual afflicted with acne vulgaris, the composition consisting essentially of a pharmaceutically effective amount of minocycline, a hydrophobic liquid medium that does not dissolve or minimally dissolves tetracycline, and a polymeric hydrocarbon gelling agent to thicken the composition, wherein:

the hydrophobic liquid medium is characterized as (a) resulting in less than 5% (w/w) of the tetracycline active ingredient being dissolved in the medium at room temperature after 2 hours as determined by HPLC, and/or (b) results in less than 4% (w/w) of 4-epi-minocycline (when minocycline is used as the active ingredient) when stored for 1 month at room temperature, as determined by HPLC.

36. A topical suspension formulation comprising:

a tetracycline, or its pharmaceutically acceptable salts, hydrates, or morphs in a suspended form within the formulation;

a non-comedogenic, hydrophobic liquid medium that does not dissolve or substantially minimally dissolves the tetracycline; and

a polymeric hydrocarbon gelling agent to thicken the suspension.

37. A formulation according to claim 35 or 36 wherein the formulation is as further defined in any one of claims 1 to 29 or 33 to 34.

38. A formulation according to any one of claims 1 to 29, or 33 to 37, for use as a medicament.

39. A formulation according to claim 38 for use in treating infection or inflammation of the skin.

40. A formulation according to claim 39 for use in treating acne or rosacea.

41. A formulation according to claim 38 for use in treating an ophthalmic disease or condition.

42. A formulation according to any one of claims 1 to 29 or 33 to 37, or a formulation for use according to any one of claims 38 to 41, further comprising another anti-acne agent.

43. A formulation, or formulation for use, according to claim 42 wherein the anti-acne agent is a retinoid, such as tretinoin, adapalene, or tazarotene.