

Patent Number: 0410348

Title: Topical [spironolactone](#) composition

Title: Composition de [spironolactone](#) à usage topique

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Claims

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- Claims:**
1. A topical composition comprising:
 - o (a) from about 1.0 to about 12.0 weight percent of [spironolactone](#);
 - o (b) from about 2.5 to about 18.5 weight percent of emulsifying agents;
 - o (c) from about 0.5 to about 6.0 weight percent of solvent;
 - o (d) buffering agents sufficient to maintain a pH of from about 4.0 to about 6.0; and
 - o (e) from about 50 to about 80 weight percent water.
 2. A composition according to Claim 1 comprising:
 - o (a) from about 1.0 to about 12.0 weight percent of [spironolactone](#);
 - o (b) from about 2.5 to about 18.5 weight percent of a mixed cetearyl alcohol and [sodium lauryl sulfate](#) and a mixed [glycerol monostearate](#) and [polyoxyethylene stearate](#);
 - o (c) from about 0.5 to about 6.0 weight percent of solvent selected from the group consisting of [diisopropyl adipate](#) and C8-C10 ethoxylated [glyceride](#);
 - o (d) from about 0.2 to about 2.3 weight percent of buffering agents; and
 - o (e) from about 50 to about 80 weight percent of water.
 3. A composition according to Claim 1 comprising:
 - o (a) from about 1.0 to about 12.0 weight percent of [spironolactone](#);
 - o (b) from about 1.5 to about 12.0 weight percent of a mixture of cetearyl alcohol and [sodium lauryl sulfate](#);
 - o (c) from about 1.0 to about 6.5 weight percent of a mixture of [glycerol monostearate](#) and [polyoxyethylene stearate](#);
 - o (d) from about 0.5 to about 6.0 weight percent of [diisopropyl adipate](#);
 - o (e) from about 0.13 to about 1.3 weight percent of a weak acid salt;
 - o (f) from about 0.1 to about 1.0 weight percent of a weak acid; and
 - o (g) from about 50 to about 80 weight percent of water.
 4. A composition according to Claim 1 further containing a preservative selected from the group consisting of [methyl-p-hydroxybenzoate](#), [ethyl-p-hydroxybenzoate](#), [propyl-p-hydroxybenzoate](#), [butyl-p-hydroxybenzoate](#), [benzoic acid](#), and [imidazolidinyl urea](#).
 5. A composition according to Claim 4 further containing:
 - o (a) from about 1.0 to about 12.0 weight percent of a noncomedogenic liquid carrier; and
 - o (b) from about 1.0 to about 15.0 weight percent of an ointment base.
 6. A composition according to Claim 5 wherein the noncomedogenic liquid carrier is mineral oil and the ointment base is petrolatum.
 7. A topical composition comprising:
 - o (a) from about 1.0 to about 12.0 weight percent of [spironolactone](#);
 - o (b) from about 1.5 to about 12.0 weight percent of a mixture of cetearyl alcohol and [sodium lauryl sulfate](#);
 - o (c) from about 1.0 to about 6.5 weight percent of a mixture of [glycerol monostearate](#) and [polyoxyethylene stearate](#);
 - o (d) from about 1.0 to about 12.0 weight percent of mineral oil;
 - o (e) from about 0.5 to about 6.0 weight percent of solvent selected from the group consisting of [diisopropyl adipate](#) and C8-C10 ethoxylated [glyceride](#);
 - o (f) from about 1.0 to about 15.0 weight percent of petrolatum;
 - o (g) from about 0.02 to about 0.3 weight percent of [propyl-p-hydroxybenzoate](#);
 - o (h) from about 0.02 to about 0.3 weight percent of [methyl-p-hydroxybenzoate](#);
 - o (i) from about 0.13 to about 1.3 weight percent of a weak acid salt;
 - o (j) from about 0.1 to about 1.0 weight percent of a weak acid; and
 - o (k) from about 50 to about 80 weight percent of water.
 8. A topical composition according to Claim 7 comprising:
 - o (a) from about 1.0 to about 12.0 weight percent of [spironolactone](#);
 - o (b) from about 7.2 to about 10.8 weight percent of a mixture of cetearyl alcohol and [sodium lauryl sulfate](#);
 - o (c) from about 4.0 to about 6.0 weight percent of a mixture of [glycerol monostearate](#) and [polyoxyethylene stearate](#);
 - o (d) from about 4.8 to about 7.2 weight percent of light mineral oil;
 - o (e) from about 3.6 to about 5.4 weight percent of [diisopropyl adipate](#);
 - o (f) from about 8.4 to about 12.6 weight percent of white petrolatum;
 - o (g) from about 0.04 to about 0.06 weight percent of [propyl-p-hydroxybenzoate](#);
 - o (h) from about 0.12 to about 0.18 weight percent of [methyl-p-hydroxybenzoate](#);

- (i) from about 0.53 to about 0.78 weight percent of sodium citrate dihydrate;
 - (j) from about 0.4 to about 0.6 weight percent of citric acid monohydrate; and
 - (k) from about 55 to about 70 weight percent of water.
- 9. A topical composition according to Claim 8 comprising:
 - (a) from about 1.0 to about 5.0 weight percent of spironolactone;
 - (b) about 9.0 weight percent of a mixture of cetearyl alcohol and sodium lauryl sulfate;
 - (c) about 5.0 weight percent of a mixture of glycerol monostearate and polyoxyethylene stearate;
 - (d) about 6.0 weight percent of light mineral oil;
 - (e) about 4.5 weight percent of diisopropyl adipate;
 - (f) about 10.5 weight percent of white petrolatum;
 - (g) about 0.05 weight percent of propyl-p-hydroxybenzoate;
 - (h) about 0.15 weight percent of methyl-p-hydroxybenzoate;
 - (i) about 0.65 weight percent of sodium citrate dihydrate;
 - (j) about 0.5 weight percent of citric acid monohydrate; and
 - (k) from about 62.65 to about 58.65 weight percent of water.
- 10. A topical composition according to Claim 8 comprising:
 - (a) about 5.0 weight percent of spironolactone;
 - (b) about 9.0 weight percent of a mixture of cetearyl alcohol and sodium lauryl sulfate;
 - (c) about 5.0 weight percent of a mixture of glycerol monostearate and polyoxyethylene stearate;
 - (d) about 6.0 weight percent of light mineral oil;
 - (e) about 4.5 weight percent of diisopropyl adipate;
 - (f) about 10.5 weight percent of white petrolatum;
 - (g) about 0.05 weight percent of propyl-p-hydroxybenzoate;
 - (h) about 0.15 weight percent of methyl-p-hydroxybenzoate;
 - (i) about 0.65 weight percent of sodium citrate dihydrate;
 - (j) about 0.5 weight percent of citric acid monohydrate; and
 - (k) about 58.65 weight percent of water.
- 11. A topical composition according to Claim 8 comprising:
 - (a) about 3.0 weight percent of spironolactone;
 - (b) about 9.0 weight percent of a mixture of cetearyl alcohol and sodium lauryl sulfate;
 - (c) about 5.0 weight percent of a mixture of glycerol monostearate and polyoxyethylene stearate;
 - (d) about 6.0 weight percent of light mineral oil;
 - (e) about 4.5 weight percent of diisopropyl adipate;
 - (f) about 10.5 weight percent of white petrolatum;
 - (g) about 0.05 weight percent of propyl-p-hydroxybenzoate;
 - (h) about 0.15 weight percent of methyl-p-hydroxybenzoate;
 - (i) about 0.65 weight percent of sodium citrate dihydrate;
 - (j) about 0.5 weight percent of citric acid monohydrate; and
 - (k) about 60.65 weight percent of water.
- 12. A topical composition according to Claim 8 comprising:
 - (a) about 1.0 weight percent of spironolactone;
 - (b) about 9.0 weight percent of a mixture of cetearyl alcohol and sodium lauryl sulfate;
 - (c) about 5.0 weight percent of a mixture of glycerol monostearate and polyoxyethylene stearate;
 - (d) about 6.0 weight percent of light mineral oil;
 - (e) about 4.5 weight percent of diisopropyl adipate;
 - (f) about 10.5 weight percent of white petrolatum;
 - (g) about 0.05 weight percent of propyl-p-hydroxybenzoate;
 - (h) about 0.15 weight percent of methyl-p-hydroxybenzoate;
 - (i) about 0.65 weight percent of sodium citrate dihydrate;
 - (j) about 0.5 weight percent of citric acid monohydrate; and
 - (k) about 62.65 weight percent of water.
- 13. A topical composition according to Claim 8 wherein the mixture of cetearyl alcohol and sodium lauryl sulfate is about 90% cetearyl alcohol and about 10% sodium lauryl sulfate, and the mixture of glycerol monostearate and polyoxyethylene stearate is about 50% glycerol monostearate and about 50% polyoxyethylene stearate.
- 14. A topical composition according to Claim 9 wherein the mixture of cetearyl alcohol and sodium lauryl sulfate is about 90% cetearyl alcohol and about 10% sodium lauryl sulfate, and the mixture of glycerol monostearate and polyoxyethylene stearate is about 50% glycerol monostearate and 50% polyoxyethylene stearate.
- 15. A topical composition according to Claim 10 wherein the mixture of cetearyl alcohol and sodium lauryl sulfate is about 90% cetearyl alcohol and about 10% sodium lauryl sulfate, and the mixture of glycerol monostearate and polyoxyethylene stearate is about 50% glycerol monostearate and 50% polyoxyethylene stearate.
- 16. A topical composition according to Claim 11 wherein the mixture of cetearyl alcohol and sodium lauryl sulfate is about 90% cetearyl alcohol and about 10% sodium lauryl sulfate, and the mixture of glycerol monostearate and polyoxyethylene stearate is about 50% glycerol monostearate and 50%

polyoxyethylene stearate.

- o 17. A topical composition according to Claim 12 wherein the mixture of cetearyl alcohol and sodium lauryl sulfate is about 90% cetearyl alcohol and about 10% sodium lauryl sulfate, and the mixture of glycerol monostearate and polyoxyethylene stearate is about 50% glycerol monostearate and 50% polyoxyethylene stearate.
- o 18. A process for preparing a topical spironolactone composition comprising:
 - o (a) forming an oil phase by heating a mixture of a mixed cetearyl alcohol and sodium lauryl sulfate, a mixed glycerol monostearate and polyoxyethylene stearate, mineral oil, diisopropyl adipate and petrolatum until melted;
 - o (b) forming an aqueous phase by mixing together and heating an acid component, an acid salt component, a preservative component and water;
 - o (c) adding spironolactone and a preservative component to the oil phase and homogenizing the ingredients;
 - o (d) emulsifying the homogeneous oil phase with the aqueous phase under vacuum using homogenizer and agitator speeds suitable to provide the desired emulsification; and
 - o (e) cooling and blending the emulsified mixture with agitation to produce the product.
- o 19. A process according to Claim 18 for preparing a topical spironolactone cream which comprises:
 - o (a) forming an oil phase by heating until melted a mixture of white petrolatum, mineral oil, diisopropyl adipate, a cetearyl alcohol and sodium lauryl sulfate mixture, and a glycerol monostearate and polyoxyethylene stearate mixture;
 - o (b) forming an aqueous phase by heating a mixture of methyl paraben, sodium citrate, citric acid and water;
 - o (c) adding propyl paraben and spironolactone to the oil phase and homogenizing the oil phase;
 - o (d) emulsifying the homogeneous oil phase with the aqueous phase by adding the oil phase to the aqueous phase under a vacuum with simultaneous homogenization and agitation at speeds suitable for producing the desired emulsification while maintaining a temperature sufficient to keep the oil phase ingredients in a melted form;
 - o (e) cooling the emulsion gradually to about 25°C while blending the mixture by gradually reducing the agitation to produce the product.
- o 20. Use of 1 to 12 weight percent of spironolactone, 0.5 to 6 weight percent of a solvent selected from the group of diisopropyl adipate and C8-C10 ethoxylated glyceride as well as suitable carriers such as emulsifying and buffering agents and water for preparing a medicament for treating a skin site having excess androgenic activity.
- o 21. Use according to Claim 20 wherein the excess androgenic activity is acne.
- o 22. Use according to Claim 20 wherein the excess androgenic activity is hirsutism.
- o 23. Use according to Claim 20 wherein the excess androgenic activity is seborrhea.
- o 24. Use according to Claim 20 wherein the excess androgenic activity is alopecia.

Claims for the following Contracting States: ES, GR

- o 1. A process for preparing a topical spironolactone composition comprising:
 - o (a) forming an oil phase by heating a mixture of a mixed cetearyl alcohol and sodium lauryl sulfate, a mixed glycerol monostearate and polyoxyethylene stearate, mineral oil, diisopropyl adipate and petrolatum until melted;
 - o (b) forming an aqueous phase by mixing together and heating an acid component, an acid salt component, a preservative component and water;
 - o (c) adding spironolactone and a preservative component to the oil phase and homogenizing the ingredients;
 - o (d) emulsifying the homogeneous oil phase with the aqueous phase under vacuum using homogenizer and agitator speeds suitable to provide the desired emulsification; and
 - o (e) cooling and blending the emulsified mixture with agitation to produce the product.
- o 2. A process according to Claim 1 for preparing a topical spironolactone cream which comprises:
 - o (a) forming an oil phase by heating until melted a mixture of white petrolatum, mineral oil, diisopropyl adipate, a cetearyl alcohol and sodium lauryl sulfate mixture, and a glycerol monostearate and polyoxyethylene stearate mixture;
 - o (b) forming an aqueous phase by heating a mixture of methyl paraben, sodium citrate, citric acid and water;
 - o (c) adding propyl paraben and spironolactone to the oil phase and homogenizing the oil phase;
 - o (d) emulsifying the homogeneous oil phase with the aqueous phase by adding the oil phase to the aqueous phase under a vacuum with simultaneous homogenization and agitation at speeds suitable for producing the desired emulsification while maintaining a temperature

- sufficient to keep the oil phase ingredients in a melted form;
- o (e) cooling the emulsion gradually to about 25°C while blending the mixture by gradually reducing the agitation to produce the product.
3. Process according to Claim 1 wherein the composition prepared comprises:
 - o (a) from about 1.0 to about 12.0 weight percent of spironolactone;
 - o (b) from about 2.5 to about 18.5 weight percent of emulsifying agents;
 - o (c) from about 0.5 to about 6.0 weight percent of solvent;
 - o (d) buffering agents sufficient to maintain a pH of from about 4.0 to about 6.0; and
 - o (e) from about 50 to about 80 weight percent water.
 4. Process according to Claim 1 wherein the composition prepared comprises:
 - o (a) from about 1.0 to about 12.0 weight percent of spironolactone;
 - o (b) from about 2.5 to about 18.5 weight percent of a mixed cetearyl alcohol and sodium lauryl sulfate and a mixed glycerol monostearate and polyoxyethylene stearate;
 - o (c) from about 0.5 to about 6.0 weight percent of solvent selected from the group consisting of diisopropyl adipate and C8-C10 ethoxylated glyceride;
 - o (d) from about 0.2 to about 2.3 weight percent of buffering agents; and
 - o (e) from about 50 to about 80 weight percent of water.
 5. Process according to Claim 1 wherein the composition prepared comprises:
 - o (a) from about 1.0 to about 12.0 weight percent of spironolactone;
 - o (b) from about 1.5 to about 12.0 weight percent of a mixture of cetearyl alcohol and sodium lauryl sulfate;
 - o (c) from about 1.0 to about 6.5 weight percent of a mixture of glycerol monostearate and polyoxyethylene stearate;
 - o (d) from about 0.5 to about 6.0 weight percent of diisopropyl adipate;
 - o (e) from about 0.13 to about 1.3 weight percent of a weak acid salt;
 - o (f) from about 0.1 to about 1.0 weight percent of a weak acid; and
 - o (g) from about 50 to about 80 weight percent of water.
 6. Process according to Claim 1 wherein the composition further comprises a preservative selected from the group consisting of methyl-p-hydroxybenzoate, ethyl-p-hydroxybenzoate, propyl-p-hydroxybenzoate, butyl-p-hydroxybenzoate, benzoic acid, and imidazolidinyl urea.
 7. Process according to Claim 6 wherein the composition further comprises:
 - o (a) from about 1.0 to about 12.0 weight percent of a noncomedogenic liquid carrier; and
 - o (b) from about 1.0 to about 15.0 weight percent of an ointment base.
 8. Process according to Claim 7 wherein the noncomedogenic liquid carrier is mineral oil and the ointment base is petrolatum.
 9. Process according to Claim 1 wherein the composition prepared comprises:
 - o (a) from about 1.0 to about 12.0 weight percent of spironolactone;
 - o (b) from about 1.5 to about 12.0 weight percent of a mixture of cetearyl alcohol and sodium lauryl sulfate;
 - o (c) from about 1.0 to about 6.5 weight percent of a mixture of glycerol monostearate and polyoxyethylene stearate;
 - o (d) from about 1.0 to about 12.0 weight percent of mineral oil;
 - o (e) from about 0.5 to about 6.0 weight percent of solvent selected from the group consisting of diisopropyl adipate and C8-C10 ethoxylated glyceride;
 - o (f) from about 1.0 to about 15.0 weight percent of petrolatum;
 - o (g) from about 0.02 to about 0.3 weight percent of propyl-p-hydroxybenzoate;
 - o (h) from about 0.02 to about 0.3 weight percent of methyl-p-hydroxybenzoate;
 - o (i) from about 0.13 to about 1.3 weight percent of a weak acid salt;
 - o (j) from about 0.1 to about 1.0 weight percent of a weak acid; and
 - o (k) from about 50 to about 80 weight percent of water.
 10. Process according to Claim 9 wherein the composition prepared comprises:
 - o (a) from about 1.0 to about 12.0 weight percent of spironolactone;
 - o (b) from about 7.2 to about 10.8 weight percent of a mixture of cetearyl alcohol and sodium lauryl sulfate;
 - o (c) from about 4.0 to about 6.0 weight percent of a mixture of glycerol monostearate and polyoxyethylene stearate;
 - o (d) from about 4.8 to about 7.2 weight percent of light mineral oil;
 - o (e) from about 3.6 to about 5.4 weight percent of diisopropyl adipate;
 - o (f) from about 8.4 to about 12.6 weight percent of white petrolatum;
 - o (g) from about 0.04 to about 0.06 weight percent of propyl-p-hydroxybenzoate;
 - o (h) from about 0.12 to about 0.18 weight percent of methyl-p-hydroxybenzoate;
 - o (i) from about 0.53 to about 0.78 weight percent of sodium citrate dihydrate;
 - o (j) from about 0.4 to about 0.6 weight percent of citric acid monohydrate; and
 - o (k) from about 55 to about 70 weight percent of water.

- o 11. Process according to Claim 10 wherein the composition prepared comprises:
 - o (a) from about 1.0 to about 5.0 weight percent of spironolactone;
 - o (b) about 9.0 weight percent of a mixture of cetearyl alcohol and sodium lauryl sulfate;
 - o (c) about 5.0 weight percent of a mixture of glycerol monostearate and polyoxyethylene stearate;
 - o (d) about 6.0 weight percent of light mineral oil;
 - o (e) about 4.5 weight percent of diisopropyl adipate;
 - o (f) about 10.5 weight percent of white petrolatum;
 - o (g) about 0.05 weight percent of propyl-p-hydroxybenzoate;
 - o (h) about 0.15 weight percent of methyl-p-hydroxybenzoate;
 - o (i) about 0.65 weight percent of sodium citrate dihydrate;
 - o (j) about 0.5 weight percent of citric acid monohydrate; and
 - o (k) from about 62.65 to about 58.65 weight percent of water.
- o 12. Process according to Claim 10 wherein the composition prepared comprises:
 - o (a) about 5.0 weight percent of spironolactone;
 - o (b) about 9.0 weight percent of a mixture of cetearyl alcohol and sodium lauryl sulfate;
 - o (c) about 5.0 weight percent of a mixture of glycerol monostearate and polyoxyethylene stearate;
 - o (d) about 6.0 weight percent of light mineral oil;
 - o (e) about 4.5 weight percent of diisopropyl adipate;
 - o (f) about 10.5 weight percent of white petrolatum;
 - o (g) about 0.05 weight percent of propyl-p-hydroxybenzoate;
 - o (h) about 0.15 weight percent of methyl-p-hydroxybenzoate;
 - o (i) about 0.65 weight percent of sodium citrate dihydrate;
 - o (j) about 0.5 weight percent of citric acid monohydrate; and
 - o (k) about 58.65 weight percent of water.
- o 13. Process according to Claim 10 wherein the composition prepared comprises:
 - o (a) about 3.0 weight percent of spironolactone;
 - o (b) about 9.0 weight percent of a mixture of cetearyl alcohol and sodium lauryl sulfate;
 - o (c) about 5.0 weight percent of a mixture of glycerol monostearate and polyoxyethylene stearate;
 - o (d) about 6.0 weight percent of light mineral oil;
 - o (e) about 4.5 weight percent of diisopropyl adipate;
 - o (f) about 10.5 weight percent of white petrolatum;
 - o (g) about 0.05 weight percent of propyl-p-hydroxybenzoate;
 - o (h) about 0.15 weight percent of methyl-p-hydroxybenzoate;
 - o (i) about 0.65 weight percent of sodium citrate dihydrate;
 - o (j) about 0.5 weight percent of citric acid monohydrate; and
 - o (k) about 60.65 weight percent of water.
- o 14. Process according to Claim 10 wherein the compositions prepared comprises:
 - o (a) about 1.0 weight percent of spironolactone;
 - o (b) about 9.0 weight percent of a mixture of cetearyl alcohol and sodium lauryl sulfate;
 - o (c) about 5.0 weight percent of a mixture of glycerol monostearate and polyoxyethylene stearate;
 - o (d) about 6.0 weight percent of light mineral oil;
 - o (e) about 4.5 weight percent of diisopropyl adipate;
 - o (f) about 10.5 weight percent of white petrolatum;
 - o (g) about 0.05 weight percent of propyl-p-hydroxybenzoate;
 - o (h) about 0.15 weight percent of methyl-p-hydroxybenzoate;
 - o (i) about 0.65 weight percent of sodium citrate dihydrate;
 - o (j) about 0.5 weight percent of citric acid monohydrate; and
 - o (k) about 62.65 weight percent of water.
- o 15. Process according to Claim 10 wherein the mixture of cetearyl alcohol and sodium lauryl sulfate is about 90% cetearyl alcohol and about 10% sodium lauryl sulfate, and the mixture of glycerol monostearate and polyoxyethylene stearate is about 50% glycerol monostearate and about 50% polyoxyethylene stearate.
- o 16. Process according to Claim 11 wherein the mixture of cetearyl alcohol and sodium lauryl sulfate is about 90% cetearyl alcohol and about 10% sodium lauryl sulfate, and the mixture of glycerol monostearate and polyoxyethylene stearate is about 50% glycerol monostearate and 50% polyoxyethylene stearate.
- o 17. Process according to Claim 12 wherein the mixture of cetearyl alcohol and sodium lauryl sulfate is about 90% cetearyl alcohol and about 10% sodium lauryl sulfate, and the mixture of glycerol monostearate and polyoxyethylene stearate is about 50% glycerol monostearate and 50% polyoxyethylene stearate.
- o 18. Process according to Claim 13 wherein the mixture of cetearyl alcohol and sodium lauryl sulfate is about 90% cetearyl alcohol and about 10% sodium lauryl sulfate, and the mixture of glycerol monostearate and polyoxyethylene stearate is about 50% glycerol monostearate and 50% polyoxyethylene stearate.

- o 19. Process according to Claim 14 wherein the mixture of cetearyl alcohol and sodium lauryl sulfate is about 90% cetearyl alcohol and about 10% sodium lauryl sulfate, and the mixture of glycerol monostearate and polyoxyethylene stearate is about 50% glycerol monostearate and 50% polyoxyethylene stearate.
- o 20. Use of 1 to 12 weight percent of spironolactone, 0.5 to 6 weight percent of a solvent selected from the group of diisopropyl adipate and C8-C10 ethoxylated glyceride as well as suitable carriers such as emulsifying and buffering agents and water for preparing a medicament for treating a skin site having excess androgenic activity.
- o 21. Use according to Claim 20 wherein the excess androgenic activity is acne.
- o 22. Use according to Claim 20 wherein the excess androgenic activity is hirsutism.
- o 23. Use according to Claim 20 wherein the excess androgenic activity is seborrhea.
- o 24. Use according to Claim 20 wherein the excess androgenic activity is alopecia.