SUMMARY OF THE INVENTION

[0005] The pharmaceutical described herein is a liquid oral pharmaceutical composition comprising phenylephrine and substantially aldehyde-free polyethylene glycol.

[0006] The composition may further comprise one or more second active agents selected from analgesics, decongestants, expectorants, anti-tussives, antipyretics, anti-inflammatory agents, cough suppressants and antihistamines.

[0007] The composition may be a solution or a suspension. Suspension embodiments may further comprise viscosity modifying agents. In some embodiments the composition may be filled into capsules.

SUMMARY OF THE INVENTION

[0005] The pharmaceutical described herein is a liquid oral pharmaceutical composition comprising phenylephrine and substantially aldehyde-free polyethylene glycol.

[0006] The composition may further comprise one or more second active agents selected from analgesics, decongestants, expectorants, anti-tussives, antipyretics, anti-inflammatory agents, cough suppressants and antihistamines.

[0007] The composition may be a solution or a suspension. Suspension embodiments may further comprise viscosity modifying agents. In some embodiments the composition may be filled into capsules.

BRIEF DESCRIPTION OF THE FIGURES

FIGURE 1

[0008] Figure 1 is a plot showing degradation of phenylephrine in a polyethylene glycol composition as a function of total aldehyde concentration in the polyethylene glycol.

DETAILED DESCRIPTION OF THE INVENTION

[0009] The invention provides an oral, liquid pharmaceutical composition comprising the pharmaceutical active phenylephrine. The composition is palatable and has improved phenylephrine stability. The composition of the invention may be a solution or a suspension or alternatively filled into capsules. In solution and suspension embodiments, the composition comprises phenylephrine, an artificial sweetener, and substantially aldehyde-free polyethylene glycol. Optionally, the composition may comprise one or more other active agents.

The present invention also provides any one of the embodiments disclosed below and indicated with the numbers 1 to 39.

1. An oral liquid pharmaceutical composition comprising:

   (a) phenylephrine or a pharmaceutically acceptable salt thereof; and

   (b) substantially aldehyde-free polyethylene glycol, wherein the substantially aldehyde-free polyethylene glycol has less than 20 ppm total aldehyde content and maintains said level of aldehyde content for at least six months.

2. The composition of claim 1, wherein the substantially aldehyde-free polyethylene glycol has less than 10 ppm total aldehyde content and maintains said level of aldehyde content for at least one year.

3. The composition of claim 1 or claim 2, further comprising at least one second active agent selected from the group consisting of analgesics, decongestants, expectorants, anti-tussives, antipyretics, anti-inflammatory agents, cough suppressants and antihistamines.

4. The composition of claim 3, wherein the second active agent is selected from the group consisting of non-steroidal anti-inflammatory drugs (NSAIDS), propionic acid derivatives, ibuprofen, naproxen, ketoprofen, flurbiprofen, zomepirac, sulindac fenoprofen, suprofen, fluprofen, fenbufen; acetic acid derivatives, tolmetin sodium,, indomethacin, fenamic acid derivatives, mefenamic acid meclofenamate sodium, biphenyl carboxylic acid derivatives, diflunisal, flufenisal, oxicams, piroxicam, sudoxicam, isoxicam, chlorpheniramine, brompheniramine; dexchlorpheniramine, dexbrompheniramine, triprolidine, chlorcyclizine, diphenhydramine, doxylamine, tripelenamine, cyproheptatine, bromodiphenhydramine, phenindamine, pyrilamine, azatadine, acrivastine, astemizole, azelastine, cetirizine, ebastine, fexofenadine, ketotifen, carbinoxamine, desloratadine, loratadine, pheniramine, thonzylamine, mizolastine, terfenadine, chlophendianol, caramiphen, dextromethorphan, diphenhydramine, codeine, hydrocodone, pseudoephedrine, ephedrine, phenylephrine, phenylpropenolamine, terpin hydrate, guaifenesin, potassium, potassium guaicolsulfonate, Cox 2 inhibitors, Celecoxib, Rofecoxib, Valdecoxib, aspirin, acetaminophen, phenacetin, salicylate salts and combination thereof.

5. The composition of claim 4, wherein the at least one second active agent is selected from the group consisting of chlorpheniramine, dextromethorphan, guaifenesin, acetaminophen, chlophendianol, diphenhydramine, brompheniramine, loratadine, aspirin and doxylamine succinate.

6. The composition of any one of claims 1 to 5, further comprising a flavor system.

7. The composition of claim 6, wherein the flavor system includes non-aldehyde flavorants.

8. The composition of any one of claims 1 to 7, wherein the composition is an aqueous based solution, aqueous based suspension, or liquid fill for a capsule.

9. The composition of any one of claims 1 to 8, further comprising an antioxidant.

10. The composition of claim 9, wherein the antioxidant is propyl gallate.

11. A method of treating a mammal in need of treatment comprising providing an effective amount of oral liquid pharmaceutical composition of any one of claims 1 to 10.

12. An aqueous oral pharmaceutical composition comprising

(a) phenylephrine or a pharmaceutically acceptable salt thereof;

(b) substantially aldehyde-free polyethylene glycol, wherein the substantially aldehyde-free polyethylene glycol has less than 20 ppm total aldehyde content and maintains said level of aldehyde content for at least six months;

(c) artificial sweetener;

(d) up to about 45% glycerin; and

(e) up to about 50% sorbitol.

13. The composition of claim 12, wherein the substantially aldehyde-free polyethylene glycol has less than 10 ppm total aldehyde content and maintains said level of aldehyde content for at least one year.

14. The composition of claim 12 or claim 13, wherein the artificial sweetener is selected from the group consisting of sucralose, saccharine salts, cyclamates, acesulfame K, dipeptide based sweeteners, aspartame and mixtures thereof

15. The composition of claim 14, where in the artificial sweetener comprises sucralose.

16. The composition of any one of claims 12 to 15, further comprising a flavor system.

17. The composition of claim 16, wherein the flavor system includes non-aldehyde flavorants.

18. The composition of any one of claims 12 to 17, further comprising at least one second active agent selected from the group consisting of analgesics, decongestants, expectorants, anti-tussives, antipyretics, anti-inflammatory agents, cough suppressants and antihistamines.

19. The composition of claim 18, wherein the second active agent is selected propionic acid derivatives, ibuprofen, naproxen, ketoprofen, flurbiprofen, fenoprofen, from the group consisting of non-steroidal anti-inflammatory drugs (NSAIDS), suprofen, fluprofen, fenbufen; acetic acid derivatives, tolmetin sodium, zomepirac, sulindac, indomethacin, fenamic acid derivatives, mefenamic acid meclofenamate sodium, biphenyl carboxylic acid derivatives, diflunisal, flufenisal, oxicams, piroxicam, sudoxicam, isoxicam, chlorpheniramine, brompheniramine; dexchlorpheniramine, dexbrompheniramine, triprolidine, chlorcyclizine, diphenhydramine, doxylamine, tripelenamine, cyproheptatine, bromodiphenhydramine, phenindamine, pyrilamine, azatadine, acrivastine, astemizole, azelastine, cetirizine, ebastine, fexofenadine, ketotifen, carbinoxamine, desloratadine, loratadine, pheniramine, thonzylamine, mizolastine, terfenadine, chlophendianol, caramiphen, dextromethorphan, diphenhydramine, codeine, hydrocodone, pseudoephedrine, ephedrine, phenylephrine, phenylpropenolamine, terpin hydrate, guaifenesin, potassium, potassium guaicolsulfonate, Cox 2 inhibitors, Celecoxib, Rofecoxib, Valdecoxib, aspirin, acetaminophen, phenacetin, salicylate salts and combination thereof.

20. The composition of claim 19, wherein the at least one second active agent is selected from the group consisting of chlorpheniramine, dextromethorphan, guaifenesin, acetaminophen, chlophendianol, diphenhydramine, brompheniramine, loratadine, aspirin and doxylamine succinate.

21. The composition of any one of claims 12 to 20 wherein the composition is an aqueous based solution.

22. The composition of any one of claims 12 21, further comprising an antioxidant.

23. The composition of claim 22, wherein the antioxidant is propyl gallate.

24. The composition of any one of claims 12 to 23, further comprising a buffering agent.25.

25. The composition of claim 24, wherein the buffering agent maintains a pH below 5.4 in the composition.

26. The composition of claim 25, wherein the buffering agent maintains a pH between about 2 and about 5 in the composition.

27. The composition of any one of claims 12 to 26, further comprising a preservative.

28. The composition of claim 27, wherein the preservative is selected from the group consisting of sodium benzoate, sorbates, parabens, EDTA and combinations thereof.

29. An aqueous oral pharmaceutical composition comprising:

(a) phenylephrine or a pharmaceutically acceptable salt thereof;

(b) substantially aldehyde-free polyethylene glycol, wherein the substantially aldehyde-free polyethylene glycol has less than 20 ppm total aldehyde content and maintains said level of aldehyde content for at least six months;

(c) an artificial sweetener;

(d) a viscosity modifying agent;

(e) up to about 45% glycerin; and

(f) up to about 50% sorbitol.

30. The composition of claim 29, wherein the substantially aldehyde-free polyethylene glycol has less than 10 ppm total aldehyde content and maintains said level of aldehyde content for at least one year.

31. The composition of claim 29 or claim 30, wherein the viscosity modifying agent is selected from the group consisting of chitosen, microcrystalline cellulose, xanthan, HPMC, HPC, HEC, galaotomannons and combinations thereof.

32. The composition of any one of claims 29 to 31, wherein the artificial sweetener is selected from the group consisting of sucralose, saccharine salts, cyclamates, acesulfame K, dipeptide based sweeteners, aspartame and mixtures thereof.

33. The composition of claim 32, wherein the artificial sweetener comprises sucralose.

34. The composition of any one of claims 29 to 33, further comprising an effective amount of at least a second active agent selected from the group consisting of analgesics, decongestants, expectorants, anti-tussives, antipyretics, anti-inflammatory agents, cough suppressants and antihistamines.

35. The composition of claim 34, wherein the second active agent is selected from the group consisting of non-steroidal anti-inflammatory drugs (NSAIDS), propionic acid derivatives, ibuprofen, naproxen, ketoprofen, flurbiprofen, fenoprofen, suprofen, fluprofen, fenbufen; acetic acid derivatives, tolmetin sodium, zomepirac, sulindac, indomethacin, fenamic acid derivatives, diflunisal, flufenisal, oxicams, piroxicam, sudoxicam,isoxicam, chlorpheniramine, brompheniramine; dexchlorpheniramine, dexbrompheniramine, triprolidine, chlorcyclizine, diphenhydramine, doxylamine, tripelenamine, cyproheptatine, bromodiphenhydramine, phenindamine, pyrilamine, azatadine, acrivastine, astemizole, azelastine, cetirizine, ebastine, fexofenadine, ketotifen, carbinoxamine, desloratadine, loratadine, pheniramine, thonzylamine, mizolastine, terfenadine, chlophendianol, caramiphen, dextromethorphan, diphenhydramine, codeine, hydrocodone, pseudoephedrine, ephedrine, phenylephrine, phenylpropenolamine, terpin hydrate, guaifenesin, potassium, potassium guaicolsulfonate, Cox 2 inhibitors, Celecoxib, Rofecoxib, Valdecoxib, aspirin, acetaminophen, phenacetin, salicylate salts and combination thereof.

36. The composition of claim 35, wherein the second active agent is selected from the group consisting of chlorpheniramine, dextromethorphan, guaifenesin, acetaminophen, chlorphendianol, doxylamine succinate and ibuprofen.

37. A method of treating an mammal in need of treatment comprising providing an effective amount of an aqueous oral pharmaceutical composition of any one of claims 12 to 29

38. The method of claim 37, wherein the pharmaceutical composition further comprises at least one second active agent.

39. The method of claim 38, wherein the second active agent is selected from the group consisting of analgesics, decongestants, expectorants, anti-tussives, antipyretics, anti-inflammatory agents, cough suppressants and antihistamines.

BRIEF DESCRIPTION OF THE FIGURES

FIGURE 1

[0008] Figure 1 is a plot showing degradation of phenylephrine in a polyethylene glycol composition as a function of total aldehyde concentration in the polyethylene glycol.

DETAILED DESCRIPTION OF THE INVENTION

[0009] The invention provides an oral, liquid pharmaceutical composition comprising the pharmaceutical active phenylephrine. The composition is palatable and has improved phenylephrine stability. The composition of the invention may be a solution or a suspension or alternatively filled into capsules. In solution and suspension embodiments, the composition comprises phenylephrine, an artificial sweetener, and substantially aldehyde-free polyethylene glycol. Optionally, the composition may comprise one or more other active agents.