CLAIMS

~~What is claimed:~~

1. A pharmaceutical composition in the form of an orally disintegrating tablet for oral administration comprising:

a. a topically acting corticosteroid or pharmaceutically acceptable salt, ester, or polymorph in an amount of about 5% less by weight in the composition;

b. a pharmaceutically acceptable carrier for adsorption of the corticosteroid drug particles;

c. rapidly dispersing microgranules.

2. The pharmaceutical composition of claim 1, wherein the orally disintegrating tablet disintegrates within 30 seconds when tested using the USP <701> method for disintegration time.

3. The pharmaceutical composition of claim 1, wherein the orally disintegrating tablet disintegrates within 60 seconds on contact with saliva in the oral cavity of a patient in need thereof.

4. The pharmaceutical composition of claims 1, 2, or 3, wherein the pharmaceutically acceptable carrier for adsorption of the corticosteroid drug particles is chosen from the group consisting of microcrystalline cellulose, silicified microcrystalline cellulose, pregelatinized starch, corn starch, colloidal silica, or amorphous magnesium aluminum silicate.

5. The pharmaceutical composition of claim 4, wherein the carrier is silicified microcrystalline cellulose.

6. The pharmaceutical composition of claims 1, 2, 3, 4, or 5, wherein the rapidly dispersing microgranules comprise a sugar alcohol, or a saccharide, or a mixture thereof and at least one disintegrant.

7. The pharmaceutical composition of claim 6, wherein the sugar alcohol or saccharide and the disintegrant are present in a ratio of sugar alcohol or saccharide to disintegrant from 90:1 0 to 99:1.

8. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, or 7, ~~or 8,~~ wherein said corticosteroid is selected from the group consisting of budesonide, fluticasone, flunisolide, ciclesonide, mometasone, beclomethasone, and salts, solvates, esters, and mixtures thereof.

9. The pharmaceutical composition of claim 8, wherein said corticosteroid is fluticasone.

10. The pharmaceutical composition of claim 9, wherein said corticosteroid is fluticasone propionate.

11. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, wherein the topically acting corticosteroid is in an amount of about 3% or less by weight in the composition.

12. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, wherein the topically acting corticosteroid is in an amount of about 1.5% or less by weight in the composition.

13. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, wherein the topically acting corticosteroid is in an amount of about 1% or less by weight in the composition.

14. The pharmaceutical composition of claims l, 2, 3, 4, 5, 6, 7, 8, 9, or 10, wherein the topically acting corticosteroid is in an amount of about 0.5% or less by weight in the composition.

15. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, wherein the topically acting corticosteroid is in an amount of about 4.5 mg in the composition.

16. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, or 8, wherein the topically acting corticosteroid is in an amount of about 3 mg in the composition.

17. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, or 8, wherein the topically acting corticosteroid is in an amount of about 1.5 mg in the composition.

18. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, wherein the topically acting corticosteroid is in an amount of about 6 mg in the composition.

19. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, or 8, wherein the topically acting corticosteroid is fluticasone propionate in the range of 0.05 to about 15 mg in the composition at a drug content of from about 0.16% to 5% by weight of the composition.

20. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, or 8, wherein the topically acting corticosteroid is fluticasone propionate in the range of 0.75 to about 4.5 mg in the composition at a drug content of from about 0.25% to 1.5% by weight in the composition.

21. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, or 8, wherein the topically acting corticosteroid is fluticasone propionate in the range of 0.05 to about 18 mg in the composition at a drug content of from about 0.125% to 5% by weight in the composition.

22. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 21, wherein the corticosteroid is micronized with a particle size of not more than 50 microns.

23. The pharmaceutical composition of claim 22, wherein the corticosteroid has a mean particle size of not more than 10 microns.

24. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, or 23, wherein the composition further comprises~~ing~~ an adhesive agent.

25. The pharmaceutical composition of claim 24, wherein the adhesive agent is selected from the group consisting of sucrose aluminum sulfate complex, chitosan and derivatives thereof, polyvinylpyrrolidone, methylcellulose, hydroxypropyl cellulose,

hydroxypropyl methylcellulose, hydroxyethyl ethylcellulose, sodium carboxymethylcellulose, cross-linked polyacrylic acid, cross-linked polyacrylates, aminoalkyl methacrylate copolymers, carbopol polymers, hydrophilic polysaccharide gums, maltodextrins, pectins, xanthan gums, alginic acid, modified alginic acids, and combinations thereof.

26. The pharmaceutical composition of claims 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 wherein the disintegrant is selected from the group consisting of crospovidone, sodium starch glycolate, crosslinked carboxymethyl cellulose, and low substituted hydroxylpropylcellulose.

27. The pharmaceutical composition of claims 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, or 26, wherein the sugar alcohol or saccharide is selected from the group consisting of sucralose, lactose, sucrose, maltose, mannitol, sorbitol, xylitol, maltitol, and mixtures thereof.

28. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, or 27, further comprising a free flowing sugar alcohol or saccharide selected from the group consisting of spray-dried mannitol, spray-dried lactose, and combinations thereof.

29. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, or 28, further comprising a lubricant selected from the group consisting of magnesium stearate, stearic acid, sodium stearyl fumarate, glyceryl behenate, and a mixture thereof.

30. The ~~solid~~ pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, or 29, further comprising at least one antifungal agent.

31. The pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, or 29, further comprising at least one antiviral agent.

32. The pharmaceutical composition of claims 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, or 31, wherein the rapidly dispersing microgranules further compris~~eing~~ an additive with a dual function and wherein the ratio of sugar alcohol or saccharide to disintegrant to the dual-function additive is from 88:10:2 to 98.5:1:0.5.

33. The pharmaceutical composition of claim 32, wherein the dual-function additive is selected from the group consisting of pregelatinized starch, hydroxypropylcellulose and the alike.

34. The pharmaceutical composition of claims 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, or 33, wherein the corticosteroid has an average particle size of less than about 10 μm, the rapidly dispersing microgranules have an average particle size of less than about 300 μm, and the sugar alcohol and/or saccharide has an average particle size of less than about 30 μm.

35. The pharmaceutical composition of claim 34, wherein the corticosteroid is fluticasone propionate with a particle size of less than 5 microns, the carrier is silicified microcrystalline cellulose, the rapidly dispersing microgranules consist of mannitol and crospovidone, the free-flowing sugar alcohol is spray-dried mannitol, and the lubricant is sodium stearyl fumarate.

36. The pharmaceutical composition according to any one of claims 1 to 35 for use in medicine.

3~~6~~7. The pharmaceutical composition according to any one of claims 1 to 35 for use in a~~A~~ method for treating an inflammatory condition of the gastrointestinal tract, wherein the pharmaceutical composition is for ~~comprising~~ administering to an individual in need thereof ~~a pharmaceutical composition according to claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 13, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35~~.

3~~7~~8. The pharmaceutical composition for the use ~~method~~ of claim 3~~6~~7, wherein said condition of the gastrointestinal tract comprises inflammation of the esophagus.

3~~8~~9. The pharmaceutical composition for the use~~method~~ of claim 3~~7~~8, wherein said condition is eosinophilic esophagitis.

~~39~~40. The pharmaceutical composition for the use~~method~~ of claim 3~~8~~9, wherein said condition comprises inflammation of the glottis, epiglottis, tonsils, or oropharynx.

~~40~~1. The pharmaceutical composition for the use~~method~~ of claim 3~~2~~7, wherein said condition is viral or bacterial pharyngitis, gastroesophageal reflux disease (GERD), nonerosive reflux disease (NERD) or erosive esophagitis.

42. Use of: a. a topically acting corticosteroid or pharmaceutically acceptable salt, ester or polymorph in an amount of 5% or less by weight in the composition;

b. a pharmaceutically acceptable carrier for adsorption of the corticosteroid drug particles; and

c. rapidly dispersing microgranules; in the preparation of a pharmaceutical composition in the form of an orally disintegrating tablet for oral administration for treating an inflammatory condition of the gastrointestinal tract.

43. Use according to claim 42, wherein the orally disintegrating tablet disintegrates within 30 seconds when tested using the USP <701> method for disintegration time.

44. Use according to claim 42, wherein the orally disintegrating tablet disintegrates within 60 seconds in contact with saliva in the oral cavity of a patient in need thereof.

45. Use according to any one of claims 42 to 44, wherein the pharmaceutically acceptable carrier for adsorption of the corticosteroid drug particles is chosen from the group consisting of microcrystalline cellulose, silicified microcrystalline cellulose, pregelatinized starch, corn starch, colloidal silica, or amorphous magenisum aluminum silicate.

46. Use according to claim 45, wherein the carrier is silicified microcrystalline cellulose.

47. Use according to any one of claims 42 to 46, wherein the rapidly dispersing microgranules comprise a sugar alcohol, or a saccharide, or a mixture thereof and at least one disintegrant.

48. Use according to claim 47, wherein the sugar alcohol or saccharide and the disintegrant are present in a ratio of sugar alcohol or saccharide to disintegrant from 90:1 0 to 99:1.

49. Use according to any one of claims 42 to 48, wherein said corticosteroid is selected from the group consisting of budesonide, fluticasone, flunisolide, ciclesonide, mometasone, beclomethasone, and salts, solvates, esters, and mixtures thereof.

50. Use according to claim 49, wherein said corticosteroid is fluticasone.

51. Use according to claim 50, wherein said corticosteroid is fluticasone propionate.

52. Use according to any one of claims 42 to 51 , wherein the topically acting corticosteroid is in an amount of about 3% or less by weight in the composition.

53. Use according to any one of claims 42 to 51, wherein the topically acting corticosteroid is in an amount of about 1.5% or less by weight in the composition.

54. Use according to any one of claims 42 to 51, wherein the topically acting corticosteroid is in an amount of about 1% or less by weight in the composition.

55. Use according to any one of claims 42 to 51, wherein the topically acting corticosteroid is in an amount of about 0.5% or less by weight in the composition.

56. Use according to any one of claims 42 to 51, wherein the topically acting corticosteroid is in an amount of about 4.5 mg in the composition.

57. Use according to any one of claims 42 to 49, wherein the topically acting corticosteroid is in an amount of about 3 mg in the composition.

58. Use according to any one of claims 42 to 49, wherein the topically acting corticosteroid is in an amount of about 1.5 mg in the composition.

59. Use according to any one of claims 42 to 51, wherein the topically acting corticosteroid is in an amount of about 6 mg in the composition.

60. Use according to any one of claims 42 to 49, wherein the topically acting corticosteroid is fluticasone propionate in the range of 0.05 to about 15 mg in the composition at a drug content of from about 0.16% to 5% by weight of the composition.

61. Use according to any one of claims 42 to 49, wherein the topically acting corticosteroid is fluticasone propionate in the range of 0.75 to about 4.5 mg in the composition at a drug content of from about 0.25% to 1.5% by weight in the composition.

62. Use according to any one of claims 42 to 49, wherein the topically acting corticosteroid is fluticasone propionate in the range of 0.05 to about 18 mg in the composition at a drug content of from about 0.125% to 5% by weight in the composition.

63. Use according to any one of claims 42 to 62, wherein the corticosteroid is micronized with a particle size of not more than 50 microns.

64. Use according to claim 63, wherein the corticosteroid has a mean particle size of not more than 10 microns.

65. Use according to any one of claims 42 to 64, wherein the composition further comprises an adhesive agent.

66. Use according to claim 65, wherein the adhesive agent is selected from the group consisting of sucrose aluminum sulfate complex, chitosan and derivatives thereof, polyvinylpyrrolidone, methylcellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, hydroxyethyl ethylcellulose, sodium carboxymethylcellulose, cross-linked polyacrylic acid, cross-linked polyacrylates, aminoalkyl methacrylate copolymers, carbopol polymers, hydrophilic polysaccharide gums, maltodextrins, pectins, xanthan gums, alginic acid, modified alginic acids, and combinations thereof.

67. Use according to any one of claims 47 to 66 wherein the disintegrant is selected from the group consisting of crospovidone, sodium starch glycolate, crosslinked carboxymethyl cellulose, and low substituted hydroxylpropylcellulose.

68. Use according to any one of claims 47 to 67, wherein the sugar alcohol or saccharide is selected from the group consisting of sucralose, lactose, sucrose, maltose, mannitol, sorbitol, xylitol, maltitol, and mixtures thereof.

69. Use according to any one of claims 42 to 68, wherein the pharmaceutical composition further comprising a free flowing sugar alcohol or saccharide selected from the group consisting of spray-dried mannitol, spray-dried lactose, and combinations thereof.

70. Use according to any one of claims 42 to 69, wherein the pharmaceutical composition further comprising a lubricant selected from the group consisting of magnesium stearate, stearic acid, sodium stearyl fumarate, glyceryl behenate, and a mixture thereof.

71. Use according to any one of claims 42 to 70, wherein the pharmaceutical composition further comprising at least one antifungal agent.

72. Use according to any one of claims 42 to 70, wherein the pharmaceutical composition further comprising at least one antiviral agent.

73. Use according to any one of claims 47 to 72, wherein the rapidly dispersing microgranules further comprise an additive with a dual function and wherein the ratio of sugar alcohol or saccharide to disintegrant to dual function additive is from 88:10:2 to 98.5:1:0.5.

74. Use according to claim 73, wherein the dual- function additive is selected from the group consisting of pregelatinized starch, hydroxypropylcellulose and the alike.

75. Use according to any one of claims 47 to 74, wherein the corticosteroid has an average particle size of less than about 10 μm, the rapidly dispersing microgranules have an average particle size of less than about 300 μm, and the sugar alcohol and/or saccharide has an average particle size of less than about 30 μm.

76. Use according to claim 75, wherein the corticosteroid is fluticasone propionate with a particle size of less than 5 microns, the carrier is silicified microcrystalline cellulose, the rapidly dispersing microgranules consist of mannitol and crospovidone, the free-flowing sugar alcohol is spray-dried mannitol, and the lubricant is sodium stearyl fumarate.

~~41~~77. A method of preparing the pharmaceutical composition of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35 comprising the steps of:

a) preparing the rapidly dispersing microgranules;

b) preparing a preblend 1 by blending the pharmaceutically acceptable carrier, corticosteroid, and glidant;

c) preparing the preblend 2 by blending filler, the preblend 1 of step b~~a~~, disintegrant, and sweeteners;

d) preparing the final compressible blend, by blending the rapidly dispersing granules of step a, lubricant, the preblend 2 of step c, filler;

e) preparing the tablet by compressing the blend of step d.

4278. The method of claim 4177 comprising the steps of:

a) preparing the rapidly dispersing microgranules;

b) preparing a preblend 1 by blending the silicified microcrystalline cellulose, micronized fluticasone propionate and colloidal silicon dioxide;

c) preparing the preblend 2 by blending mannitol, the preblend 1 of step ba, crospovidone, and sucralose powder;

d) preparing the final compressible blend, by blending the rapidly dispersing granules of step a, sodium stearyl fumarate, the preblend 2 of step c, sugar alcohol, or rinsed mannitol;

e) preparing the tablet by compressing the blend of step d.

4379. The method of claim 4177 comprising the steps of:

a) preparing the rapidly dispersing microgranules;

b) preparing the preblend 1 comprising charging a blender with one quarter of the carrier, corticosteroid, glidant, and another quarter of the carrier and blending the contents;

c) preparing the preblend 2 comprising charging a high shear granulator with a free flowing filler, preblend 1, remaining half of the carrier, disintegrant, and sweetener and blending the contents;

d) preparing the final compressible blend comprising charging a blender with one half of the rapidly dispersing granules of step a, lubricant, the preblend 2 of step c, and remaining half of the rapidly dispersing granules of step a and blending;

e) preparing the orally disintegrating tablets by compressing the compressible blend of step d.

4480. The method of claim 4379 comprising the step of:

a) preparing the rapidly dispersing microgranules;

b) preparing the preblend 1 comprising charging a blender with one quarter of silicified microcrystalline cellulose (SMCC), micronized fluticasone propionate, colloidal silicon dioxide and another quarter of (SMCC) and blending;

c) preparing the preblend 2 comprising charging a high shear granulator with spray-dried mannitol, preblend 1, remaining half of SMCC, crospovidone, and sucralose powder and blending;

d) preparing the final compressible blend comprising charging a V-blender with one half of the rapidly dispersing granules of step a, sodium stearyl fumarate, the preblend 2 of step c, and remaining half of rapidly dispersing granules of step a and blending;

e) preparing the orally disintegrating tablets by compressing the compressible blend of step d.

45~~81~~. The method of claim 41~~77~~ comprising the steps of:

a) preparing the rapidly dispersing microgranules or granulate with an average particle size of not more than about 400 μm by granulating one or more sugar alcohols and/or saccharides, each having an average particle diameter of not more than about 30 μm, with a disintegrant in the presence of water or an alcohol-water mixture and then drying the granulate;

b) preparing a milled preblend 1 by blending the pharmaceutically acceptable carrier-, corticosteroid and glidant in a blender and then milling through a comminuting mill equipped with an screen with a 30 Mesh opening;

c) preparing the milled preblend 2 by blending half of free flowing mannitol, preblend 1 from step b, disintegrant, and sweetener in a blender and then milling through a comminuting mill equipped with a screen with a 30 Mesh opening, and rinsing the mill with remaining half of free flowing mannitol;

d) preparing the compressible blend by blending the rapidly dispersing granules of step a, lubricant, the milled preblend 2 of step c, rinsed with free flowing mannitol;

e) preparing the orally disintegrating tablets by compressing the compressible blend of step d.

46~~82~~. The method of claim 45~~81~~ comprising the steps of:

a)_____preparing the rapidly dispersing microgranules or granulate with an average particle size of not more than about 400 μm by granulating one or more sugar alcohols and/or saccharides, each having an average particle diameter of not more than about 30 μm, with crospovidone in presence of water or an alcohol-water mixture and then drying the granulate;

~~f~~b) preparing a milled preblend 1 by blending silicified microcrystalline cellulose, micronized fluticasone proprionate and colloidal silicon dioxide in a blender and then milling through a comminuting mill equipped with an screen with a 30 Mesh opening;

c~~g~~) preparing the milled preblend 2 by blending half of free flowing mannitol, preblend 1 from step b, crospovidone, and sucralose powder in a blender and then milling through a comminuting mill equipped with a screen with a 30 Mesh opening, and rinsing the mill with remaining half of free flowing mannitol;

d~~h~~) preparing the compressible blend by blending the rapidly dispersing granules of step a, sodium stearyl fumarate, the milled preblend 2 of step c, rinsed with free flowing mannitol;

~~i~~e) preparing the orally disintegrating tablets by compressing the compressible blend of step d.