CLAIMS

1. A pharmaceutical composition for pulmonary delivery, the composition comprising a dry powder comprising a plurality of small porous carrier particles having a MMD of about 1-10 microns and a plurality of active agent particles having a MMD of less than about 4 microns and wherein the small porous carrier particles and the active agent particles form an ordered mixture of respirable agglomerates.

2. The pharmaceutical composition of claim 1 wherein the plurality of active agent particles comprise two different actives.

3. The pharmaceutical composition of claim 1 wherein the plurality of active agent particles comprise three different actives.

4. The pharmaceutical composition of claim 3 wherein the three different actives comprise beta-adrenoceptor agonist, anticholinergic, and corticosteroid.

5. The pharmaceutical composition of claim 1 wherein the dry powder is characterized by a tap density of 0.03 to 0.5 g/cm^3, the small porous carrier particles comprise an MMD of about 1 - 5 microns, and the active agent particles comprise an MMD of less than about 3 microns.

6. The pharmaceutical composition of claim 1 wherein the dry powder is characterized by a fine particle fraction, expressed as a percentage of the nominal dose < 3.3µm (FPF<3.3µm) of greater than about 40%.

7. The pharmaceutical composition of claim 1 wherein the dry powder is characterized by a fine particle fraction, expressed as a percentage of the nominal dose less than 4.7 µm (i.e. FPF< 4.7 µm) of greater than about 50%.

8. The pharmaceutical composition of claim 1 wherein the dry powder is characterized by a lung deposition of at least 40% of a nominal dose.

9. The pharmaceutical composition of claim 1 wherein the dry powder is characterized by delivery from a passive dry powder inhaler substantially independently of a peak inspiratory flow rate.

10. The pharmaceutical composition of claim 1 wherein:

the plurality of small porous carrier particles have a geometric diameter of 2-3 microns, and consist essentially of distearoylphosphatidylcholine and calcium chloride; at least 50% of the

active agent particles have a geometric diameter of less than 3 microns; and the dry powders characterized by one or more of a tapped density of 0.03 to 0.5 g/cm3, a MMAD of about 1 to 5 microns, and a FPF< 4.7 µm of at least 50%.

11. The dry powder pharmaceutical composition of claim 1 characterized by particles comprising:

a porous carrier particle comprising a MMD of 1 to 5 microns;

a first species of active agent particles comprising glycopyrrolate, including any pharmaceutically acceptable salts, esters, isomers or solvates thereof, wherein at least 50% of the first active agent particles have a geometric diameter of 0.01 – 3 microns;

a second species of active agent particles comprising indacaterol, including any pharmaceutically acceptable salts, esters, isomers or solvates thereof, wherein at least 50% of the first active agent particles have a geometric diameter of 0.01 – 3 microns;

a third species of active agent particles comprising mometasone including any pharmaceutically acceptable salts, esters, isomers or solvates thereof, wherein at least 50% of the first active agent particles have a geometric diameter of 0.01 – 3 microns;

wherein each of the first, second and third active agent particles adhere to the carrier particle to form an ordered mixture of respirable agglomerate particles, and wherein the composition is characterized by a tapped density of 0.03 to 0.5 g/cm3, and a FPF< 4.7 µm of at least about 50%.

12. The dry powder formulation of claim 11 wherein the respirable agglomerates comprise

(i) about 91-99% small porous carrier particles comprising a 2:1 molar ratio of DSPC:CaCl2; ; and

(ii) the active species comprise about 0.5-3% w/w indacaterol acetate, about 0.5-3% w/w mometasone furoate, and about 0.5-3% w/w glycopyrronium bromide.

13. An inhalation unit dosage form comprising

a receptacle; and

a dry powder composition contained within the receptacle, the dry powder composition deliverable from a passive dry powder inhaler, the dry powder composition comprising particles comprising:

a small porous carrier particle comprising a MMD of about 1 to 5 microns and a tapped density of less than about 0.5 g/cm3;

a first species of active agent particles comprising glycopyrrolate, including any pharmaceutically acceptable salts, esters, isomers or solvates thereof, wherein at least 50% of the first active agent particles have a geometric diameter of less than 3 microns;

a second species of active agent particles comprising indacaterol, including any pharmaceutically acceptable salts, esters, isomers or solvates thereof, wherein at least 50% of the first active agent particles have a geometric diameter of less than 3 microns;

a third species of active agent particles comprising mometasone including any pharmaceutically acceptable salts, esters, isomers or solvates thereof; wherein at least 50% of the first active agent particles have a geometric diameter of less than 3 microns;

wherein each of the first, second and third active agent particles and the small porous carrier particles form an ordered mixture of respirable agglomerates, and wherein the composition is characterized by a tapped density of 0.03 to 0.5 g/cm3 and an FPF< 4.7 µm of at least about 50%.

CLAIMS

1. A pharmaceutical composition for pulmonary delivery via a dry powder inhaler, the composition comprising a dry powder comprising a plurality of small porous carrier particles having a mass median diameter (MMD) of about 1-10 microns and a plurality of active agent particles having a MMD of less than about 4 microns wherein the plurality of active agent particles are selected from the group consisting of particles of indacaterol or a pharmaceutically acceptable salt or ester thereof, particles of glycopyrronium or a pharmaceutically acceptable salt or ester thereof, and particles of mometasone or a pharmaceutically acceptable salt or ester thereof and wherein the small porous carrier particles and the active agent particles form an ordered mixture of respirable agglomerates.

2. The pharmaceutical composition of claim 1 wherein the plurality of active agent particles comprise two different actives selected from the group consisting of particles of indacaterol or a pharmaceutically acceptable salt or ester thereof, particles of glycopyrronium or a pharmaceutically acceptable salt or ester thereof, and particles of mometasone or a pharmaceutically acceptable salt or ester thereof.

3. The pharmaceutical composition of claim 1 wherein the plurality of active agent particles comprise all three of: (i) active agent particles of indacaterol or a pharmaceutically acceptable salt or ester thereof; and (ii) active agent particles of glycopyrronium or a pharmaceutically acceptable salt or ester thereof; and (ii) active agent particles of mometasone or a pharmaceutically acceptable salt or ester thereof.

4. The pharmaceutical composition of claim 1 wherein the dry powder is characterized by a tap density of 0.03 to 0.5 g/cm^3, the small porous carrier particles comprise an MMD of about 1 - 5 microns, and the active agent particles comprise an MMD of less than about 3 microns.

5. The pharmaceutical composition of claim 1 wherein the dry powder is characterized by a fine particle fraction (FPF), expressed as a percentage of the nominal dose < 3.3 μm (FPF<3.3 μm) of greater than about 40%.

6. The pharmaceutical composition of claim 1 wherein the dry powder is characterized by a fine particle fraction (FPF), expressed as a percentage of the nominal dose less than 4. 7 μm (FPF< 4.7 μm) of greater than about 50%.

7. The pharmaceutical composition of claim 1 wherein the dry powder is characterized by a lung deposition of at least 40% of a nominal dose.

8. The pharmaceutical composition of claim 1 wherein the dry powder is characterized by delivery from a passive dry powder inhaler substantially independently of a peak inspiratory flow rate.

9. The pharmaceutical composition of claim 1 wherein:

the plurality of small porous carrier particles have a geometric diameter of 2-3 microns, and consist essentially of distearoylphosphatidylcholine and calcium chloride; at least 50% of the active agent particles have a geometric diameter of less than 3 microns; and

the dry powder is characterized by one or more of a tapped density of 0.03 to 0.5 g/cm^3, a mass median aerodynamic diameter (MMAD) of about 1 to 5 microns, and a FPF< 4.7 μm of at least 50%.

10. The dry powder pharmaceutical composition of claim 2 wherein:

the porous carrier particles have a MMD of 1 to 5 microns;

at least 50% of the active agent particles comprising glycopyrronium or a pharmaceutically acceptable salt or ester thereof have a geometric diameter of 0.01 - 3 microns;

at least 50% of the active agent particles comprising indacaterol or a pharmaceutically acceptable salt or ester thereof have a geometric diameter of 0.01 - 3 microns;

at least 50% of the active agent particles comprising mometasone or a pharmaceutically acceptable salt or ester thereof have a geometric diameter of 0.01 - 3 microns;

wherein the active agent particles adhere to the carrier particle to form an ordered mixture of respirable agglomerate particles, and wherein the composition is characterized by a tapped density of 0.03 to 0.5 g/cm^3, and a FPF< 4.7 μm of at least about 50%.

11. The dry powder formulation of claim 10 wherein:

(i) the small porous carrier particles comprise a 2:1 molar ratio of distearoyl-phosphatidylcholine (DSPC) to $CaCl_2$ and are present in an amount of about 91-99%; and

(ii) wherein the particles of indacaterol or a pharmaceutically acceptable salt or ester thereof comprise indacaterol acetate, and wherein said particles are present in an amount of about 0.5-3% w/w; and

(iii) wherein the particles of glycopyrronium or a pharmaceutically acceptable salt or ester thereof comprise glycopyrronium bromide, and wherein said particles are present in an amount of about 0.5-3% w/w; and (iv) wherein the particles of mometasone or a pharmaceutically acceptable salt or ester thereof comprise mometasone furoate, and wherein said particles are present in an amount of about 0.5-3% w/w.

12. An inhalation unit dosage form comprising

a receptacle; and

the dry powder composition of claim 10 contained within the receptacle.

13. A process for making the dry powder formulation of respirable agglomerate particles of claim 1, the process comprising the steps of: (a) preparing a first feedstock comprising a hydrophobic excipient dispersed in an aqueous liquid phase and spray-drying said first feedstock to provide a bulk powder composition comprising a plurality of small porous powder carrier particles; (b) providing active agent particles of at least one of: (i) particles of indacaterol or a pharmaceutically acceptable salt or ester thereof; (ii) particles of glycopyrronium or a pharmaceutically acceptable salt or ester thereof; and (iii) particles of mometasone or a pharmaceutically acceptable salt or ester thereof wherein at least 50% of the active agent particles have a geometric diameter of less than 3 microns; (c) preparing a second feedstock comprising a suspension of the carrier particles of step (a) and the drug particles of step (b) in a non-aqueous anti-solvent; and (d) subjecting the second feedstock to a solvent removal process to yield a bulk powder formulation comprising an ordered mixture of respirable aggregate particles comprising small porous carrier particles and micronized drug particles, wherein the respirable agglomerate particles are characterized by a tapped density of 0.03 to 0.5 g/cm^3, and a FPF<4.7 μm of at least about 50%.

14. The process of claim 13 wherein the hydrophobic excipient comprises DSPC and calcium chloride.

15. The process of claim 14 wherein the step of providing active agent particles comprises providing at least two of: (i) particles of indacaterol or a pharmaceutically acceptable salt or ester thereof; (ii) particles of glycopyrronium or a pharmaceutically acceptable salt or ester thereof; and (iii) particles of mometasone or a pharmaceutically acceptable salt or ester thereof.

16. The process of claim 14, wherein the step of providing active agent particles comprises providing all three of: (i) particles of indacaterol or a pharmaceutically acceptable salt or ester thereof; (ii) particles of glycopyrronium or a pharmaceutically acceptable salt or ester thereof; and (iii) particles of mometasone or a pharmaceutically acceptable salt or ester thereof.

17. The process of claim 16, wherein: (i) the indacaterol or pharmaceutically acceptable salt or ester thereof is indacaterol acetate; (ii) the glycopyrronium or pharmaceutically acceptable salt or ester thereof is glycopyrronium bromide; and (iii) the mometasone or pharmaceutically acceptable salt or ester thereof is mometasone furoate.