CLAIMS

1. A pharmaceutical composition for pulmonary delivery, the composition comprising a dry powder comprising a plurality of porous carrier particles and a plurality of active agent particles and wherein the porous carrier particles and the active agent particles form an ordered mixture of respirable agglomerates.

2. A pharmaceutical composition according to claim 1 wherein the plurality of active agent particles comprise a single active.

3. A pharmaceutical composition according to claim 1 wherein the plurality of active agent particles comprise two different actives.

4. A pharmaceutical composition according to claim 1 wherein the plurality of active agent particles comprise three different actives.

5. A pharmaceutical composition according to claim 4 wherein the three different actives comprise a beta-adrenoceptor agonist, an anticholinergic, and a corticosteroid.

6. A pharmaceutical composition according to claim 5 wherein the three different actives comprise:
(i) indacaterol acetate, glycopyrronium bromide and mometasone furoate;
(ii) indacaterol acetate, tiotropium bromide and mometasone furoate;
(iii) indacaterol acetate, tiotropium bromide and budesonide; or
(iv) indacaterol acetate, tiotropium bromide and budesonide.

7. A pharmaceutical composition according to claim 1 wherein the dry powder is characterized by a tap density of 0.03 to 0.5 $g.cm^3$, the 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.

8. A pharmaceutical composition according to claim 1 wherein the dry powder is characterized by either:

(i) a fine particle fraction, expressed as a percentage of the nominal dose < 3.3µm ($FPF_{<3.3\mu m}$) of greater than about 40%;
(ii) a fine particle fraction, expressed as a percentage of the nominal dose less than 4.7 µm (i.e. $FPF_{<4.7\mu m}$) of greater than about 50%; or
(iii) a fine particle fraction, expressed as a percentage of the nominal dose on stage 4 to filter ($FPF_{S4\text{-}F}$) of at least 40% of a nominal dose.

9. A pharmaceutical composition according to any one of the preceding claims wherein the plurality of 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 MMAD of about 1 to 5 microns, and a $FPF_{<4.7\mu m}$ of at least 50%.

10. A pharmaceutical composition according to claim 1 that is deliverable from a dry powder inhaler, the composition comprising particles comprising:

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

a first species of active agent particles comprising glycopyrronium bromide, 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/cm^3, and a $FPF_{<4.7\mu m}$ of at least about 50%.

11. A pharmaceutical composition according to claim 10 that is dry powder formulation wherein the respirable agglomerates comprise:

(i) about 91-99% porous carrier particles comprising a 2:1 molar ratio of DSPC:$CaCl_2$; 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.

12. A process for making a dry powder formulation of respirable agglomerate particles, 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 porous powder carrier particles;

(b) providing at least a first active drug ingredient to having a size of at least 50% having 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 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 $FPF_{< 4.7\ \mu m}$ of at least about 50%.

13. A process according to claim 12 wherein the first active drug ingredient is a beta adrenoreceptor agonist and a second active drug ingredient is provided which is an anti-inflammatory.

14. A process according to claim 13 wherein the beta adrenoreceptor agonist is indacaterol or a salt thereof and the second active drug ingredient is mometasone furoate.

15. A process according to any one of claims 12 to 14 wherein a third active drug ingredient is provided which is glycopyrronium bromide.

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 powder is 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%.