What is claimed is :

1. A fumaryl diketopiperazine (FDKP) composition comprising FDKP having a trans isomer content of about 45% to about 65%.

2. Fumaryl diketopiperazine (FDKP) microparticles comprising the FDKP composition of claim 1.

3. The FDKP composition according to claim 1, or the FDKP microparticles according to claim 2, wherein:

i) said trans isomer content is from 50% to 65%; or

ii) said trans isomer content is from 53% to 63%.

4. FDKP microparticles according to claim 2 or claim 3, further comprising:

i) a drug or an active agent;

ii) a drug or an active agent that is a peptide or protein;

iii) an endocrine hormone; and/or

iv) an endocrine hormone that is insulin, parathyroid hormone, calcitonin, glucagon, glucagon-like peptide 1, oxyntomodulin, an analog or active fragment of said endocrine hormone.

5. The FDKP microparticles according to claim 4, wherein the drug or active agent is adsorbed onto the microparticles.

6. The FDKP microparticles according to any one of claims 2 to 5 wherein the microparticles further comprise a surfactant, preferably wherein the surfactant is polysorbate-80.

7. A dry powder comprising the FDKP microparticles of any one of claims 2 to 6.

8. Use of a dry powder formulation in the manufacture of a medicament for treating an endocrine-related disease or disorder, wherein the dry powder formulation comprises fumaryl diketopiperazine (FDKP) microparticles comprising an FDKP trans isomer content of 45% to 65% and an endocrine hormone suitable to treat an endocrine-related disease or disorder.

9. The use as claimed in claim 8, wherein:

i) the endocrine hormone is insulin, parathyroid hormone, calcitonin, glucagon, glucagon-like peptide 1, oxyntomodulin, or an analog of said endocrine hormone; and/or

ii) the endocrine-related disease is diabetes.

10. A method of making microparticles suitable for pulmonary administration as a dry powder comprising:

a) synthesizing an FDKP compound having an FDKP trans isomer content of 45% to 65%;

b) dissolving the FDKP compound in a solution having a basic pH to form an FDK solution;

c) providing a solution of a volatile acid, and

d) mixing the solutions together in a high-shear mixer to produce said microparticles in a suspension.

11. The method according to claim 10 wherein the volatile acid is acetic acid.

12. The method according to claim 10 or claim 11, further comprising:

i) determining the trans isomer content of the FDKP; or

ii) mixing said microparticles with a solution comprising a drug.

13. The method according to claim 12, wherein the step of determining the trans isomer content of the FDKP is performed using high pressure liquid chromatography.

14. The method according to claim 12, wherein the drug is:

i) an endocrine hormone; and/or

ii) insulin, parathyroid hormone, calcitonin, glucagon, glucagon-like peptide 1, oxyntomodulin, or an analog or active fragment of said drug.

15. A method for synthesizing a diketopiperazine having a trans isomer content of 45% to 65% comprising:

a) saponifying an ester of a diketopiperazine in a mixture of water and a water-miscible solvent at a basic pH; and

b) recrystallizing the diketopiperazine in a reaction mixture comprising trifluoroacetic acid and glacial acetic acid at a resultant ratio ranging from 0.4 to 0.7.

16. The method according to claim 15, wherein the water-miscible solvent is:

i) an alcohol, tetrahydrofuran, diozane, and acetonitrile;

ii) methanol, ethanol, or isopropanol; and/or

iii) methanol in a water: methanol ratio ranging from 1:1 to 3:1.

17. The method according to claim 15, wherein:

i) the method further comprises the step of determining the trans isomer content of the diketopiperazine;

ii) the diketopiperazine is of the formula 3,6-bis(N-X-4-aminobutyl)-2,5-diketopiperazine wherein X is selected from the group consisting of fumaryl, succinyl, maleyl, and glutaryl;

iii) the diketopiperazine is 3,6-bis(N-fumaryl-4-aminobutyl)-2,5-diketopiperazine; and/or

iv) the reaction mixture in the recrystallizing step is held for a period of about 4 hours or greater than 4 hours.

18. A dry powder formulation comprising microparticles comprising 3,6-bis(N-fumaryl-4-aminobutyl)-2,5-diketopiperazine and insulin, wherein the trans-FDKP isomer content of the microparticles is from 53 to 63%.

19. The dry powder formulation according to claim 18 wherein the microparticles comprise 10% to 15% insulin by weight.

20. A drug delivery system comprising an inhaler, a unit dose cartridge and a dry powder according to claim 19.

21. The FDKP composition according to claim 1, or the FDKP microparticles according to claim 2, further comprising an active agent comprising at least one of a vasoactive agent, a neuroactive agent, an immunomodulating agent, an anticoagulant, a cytotoxic agent, an antibiotic, an antiviral agent, an antigen, an infectious agent, an inflammatory mediator, a hormone, a cell surface antigen, and analogs thereof.

22. The FDKP composition according to claim 1, or the FDKP microparticles according to claim 2, further comprising an active agent comprising at least one of a small molecule pharmaceutical, a biological, a bioactive agent, a protein, a polypeptide, a peptide, a nucleic acid, an organic macromolecule, a synthetic organic compound, a polysaccharide, a sugar, a fatty acid, a lipid, an antibody or fragment thereof, F(ab), $F(ab)_2$, a single-chain antibody, a single-chain antibody fused to another polypeptide, a therapeutic monoclonal antibody, a diagnostic monoclonal antibody, a cytokines, a lipokine, an enkephalin, an alkyne, a cyclosporin, an anti-IL-8 antibody, an IL-8 antagonist, ABX-IL-8, a prostaglandin, PG-I2, an LTB receptor blocker, LY29311, BIIL 284, CP105696, a triptan, sumatriptan, palmitoleate, insulin, growth hormone, parathyroid hormone (PTH), parathyroid hormone related peptide (PTHrP), ghrelin, obestatin, enterostatin, granulocyte macrophage colony stimulating factor (GM-CSF), amylin, an amylin analog, glucagon-like peptide 1 (GLP-1), clopidogrel, PPACK (D-phenylalanyl-L-prolyl-L-arginine chloromethyl ketone), oxyntomodulin (OXM), peptide YY(3-36) (PYY), adiponectin,

cholecystokinin (CCK), secretin, gastrin, glucagon, motilin, somatostatin, brain natriuretic peptide (BNP), atrial natriuretic peptide (ANP), IGF-1, growth hormone releasing factor (GHRF), integrin beta-4 precursor (ITB4) receptor antagonist, nociceptin, nocistatin, orphanin FQ2, calcitonin, CGRP, angiotensin, substance P, neurokinin A, pancreatic polypeptide, neuropeptide Y, delta-sleep-inducing peptide, vasoactive intestinal peptide, and analogs thereof.

23. The dry powder according to claim 7, comprising an active agent comprising at least one of a vasoactive agent, a neuroactive agent, an immunomodulating agent, an anticoagulant, a cytotoxic agent, an antibiotic, an antiviral agent, an antigen, an infectious agent, an inflammatory mediator, a hormone, a cell surface antigen, and analogs thereof.

24. The dry powder according to claim 7, comprising an active agent comprising at least one of a small molecule pharmaceutical, a biological, a bioactive agent, a protein, a polypeptide, a peptide, a nucleic acid, an organic macromolecule, a synthetic organic compound, a polysaccharide, a sugar, a fatty acid, a lipid, an antibody or fragment thereof, F(ab), $F(ab)_2$, a single-chain antibody, a single-chain antibody fused to another polypeptide, a therapeutic monoclonal antibody, a diagnostic monoclonal antibody, a cytokines, a lipokine, an enkephalin, an alkyne, a cyclosporin, an anti-IL-8 antibody, an IL-8 antagonist, ABX-IL-8, a prostaglandin, PG-I2, an LTB receptor blocker, LY29311, BIIL 284, CP105696, a triptan, sumatriptan, palmitoleate, insulin, growth hormone, parathyroid hormone (PTH), parathyroid hormone related peptide (PTHrP), ghrelin, obestatin, enterostatin, granulocyte macrophage colony stimulating factor (GM-CSF), amylin, an amylin analog, glucagon-like peptide 1 (GLP-1), clopidogrel, PPACK (D-phenylalanyl-L-prolyl-L-arginine chloromethyl ketone), oxyntomodulin (OXM), peptide YY(3-36) (PYY), adiponectin, cholecystokinin (CCK), secretin, gastrin, glucagon, motilin, somatostatin, brain natriuretic peptide (BNP), atrial natriuretic peptide (ANP), IGF-1, growth hormone releasing factor (GHRF), integrin beta-4 precursor (ITB4) receptor antagonist, nociceptin, nocistatin, orphanin FQ2, calcitonin, CGRP, angiotensin, substance P, neurokinin A, pancreatic polypeptide, neuropeptide Y, delta-sleep-inducing peptide, vasoactive intestinal peptide, and analogs thereof.

25. The method according to claim 12, wherein said drug comprises at least one of a vasoactive agent, a neuroactive agent, an immunomodulating agent, an anticoagulant, a cytotoxic agent, an antibiotic, an antiviral agent, an antigen, an infectious agent, an inflammatory mediator, a hormone, a cell surface antigen, and analogs thereof.

26. The method according to claim 12, wherein said drug comprises at least one of a small molecule pharmaceutical, a biological, a bioactive agent, a protein, a polypeptide, a peptide, a nucleic acid, an organic macromolecule, a synthetic organic compound, a polysaccharide, a sugar, a fatty acid, a lipid, an antibody or fragment thereof, F(ab), $F(ab)_2$, a single-chain antibody, a single-chain antibody fused to another polypeptide, a therapeutic monoclonal antibody, a diagnostic monoclonal antibody, a cytokines, a lipokine, an enkephalin, an alkyne, a cyclosporin, an anti-IL-8 antibody, an IL-8 antagonist, ABX-IL-8, a prostaglandin, PG-I2, an LTB receptor blocker, LY29311, BIIL 284, CP105696, a triptan, sumatriptan, palmitoleate, insulin, growth hormone, parathyroid hormone (PTH), parathyroid hormone related peptide (PTHrP), ghrelin, obestatin, enterostatin, granulocyte macrophage colony stimulating factor (GM-CSF), amylin, an amylin analog, glucagon-like peptide 1 (GLP-1), clopidogrel, PPACK (D-phenylalanyl-L-prolyl-L-arginine chloromethyl ketone), oxyntomodulin (OXM), peptide YY(3-36) (PYY), adiponectin, cholecystokinin (CCK), secretin, gastrin, glucagon, motilin, somatostatin, brain natriuretic peptide (BNP), atrial natriuretic peptide (ANP), IGF-1 , growth hormone releasing factor (GHRF), integrin beta-4 precursor (ITB4) receptor antagonist, nociceptin, nocistatin, orphanin FQ2, calcitonin, CGRP, angiotensin, substance P, neurokinin A, pancreatic polypeptide, neuropeptide Y, delta-sleep-inducing peptide, vasoactive intestinal peptide, and analogs thereof.