accommodation of low API loadings, but provide pharmaceutically acceptable content uniformity (as measured by European Pharmacopeia 2.96. or USP <905>).

[0005] The present disclosure relates to pharmaceutical compositions containing psilocybin and methods of preparing the same.

[0005a] In a first aspect of the present disclosure, there is provided a pharmaceutical composition comprising:

a therapeutically effective amount of psilocybin; and

one or more pharmaceutically acceptable excipients,

wherein, after storage of the composition at 40°C and 75% relative humidity for one month, the potency of the psilocybin in the composition decreases by less than 5% and the mass balance of psilocybin and related substances is greater than 97%.

[0005b] In another aspect of the present disclosure, there is provided a method of making a pharmaceutical composition comprising:

a) direct mixing psilocybin and one or more pharmaceutically acceptable excipients to provide a blend, and

b) filling a capsule with the blend to provide the pharmaceutical composition,

wherein the content uniformity of the composition complies with the European Pharmacopeia 2.96. or USP <905>.

[0005c] In yet another aspect of the present disclosure, there is provided a pharmaceutical composition prepared by the process disclosed herein.

[0005d] In a further aspect of the present disclosure, there is provided a use of a composition disclosed herein, in the manufacture of a medicament for treating a mood disorder.

[0005e] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising:

a therapeutically effective amount of psilocybin; and

about 85% to about 99%, by weight, partially pregelatinized starch.

[0005f] In yet another aspect of the present disclosure, there is provided a pharmaceutical composition comprising:

about 1% to about 10%, by weight, psilocybin;
about 85% to about 99%, by weight, partially pregelatinized starch; and
about 0.5% to about 2.0%, by weight, sodium stearyl fumarate.

[0005g] In a further aspect of the present disclosure, there is provided a composition disclosed herein, for use in therapy.

[0006] In one example, the present disclosure provides a pharmaceutical composition comprising: a therapeutically effective amount of psilocybin; and one or more pharmaceutically acceptable excipients, wherein potency of the psilocybin in the composition and the mass balance of psilocybin and related substances in the composition remains at industry and pharmaceutically acceptable levels (e.g., European Pharmacopeia, USP) under industry and pharmaceutically acceptable storage conditions (e.g., European Pharmacopeia, USP) and the psilocybin is provided in pharmaceutically acceptable content uniformity (as measured by European Pharmacopeia 2.96. or USP <905>).

[0007] In one example, the present disclosure provides a pharmaceutical composition comprising: a therapeutically effective amount of psilocybin; and one or more pharmaceutically acceptable excipients, wherein, after storage of the composition at 40°C and 75% relative humidity for one month, the potency of the psilocybin in the composition decreases by less than 5% and the mass balance of psilocybin and related substances is greater than 97%.

[0008] In one example, the present disclosure provides a method of making a pharmaceutical composition comprising: (a) direct mixing psilocybin and one or more pharmaceutically acceptable excipients to provide a blend and (b) filling a capsule with the blend to provide the pharmaceutical composition, wherein the content uniformity of the composition complies with the European Pharmacopeia 2.96. or USP <905>.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] FIG. 1 is a numbered structural formula of psilocybin.

[0010] FIG. 2A is a XRPD diffractogram of Polymorph A

[0011] FIG. 2B is a XRPD diffractogram of Polymorph A'

[0012] FIG. 2C is a XRPD diffractogram of Polymorph B

[0013] FIG. 2D is a XRPD diffractogram of a Hydrate A

CLAIMS

1. A pharmaceutical composition comprising:

   a therapeutically effective amount of psilocybin; and
   one or more pharmaceutically acceptable excipients,

   wherein, after storage of the composition at 40°C and 75% relative humidity for one month, the potency of the psilocybin in the composition decreases by less than 5% and the mass balance of psilocybin and related substances is greater than 97%.

2. The pharmaceutical composition of claim 1, wherein the one or more pharmaceutically acceptable excipients comprises a diluent.

3. The pharmaceutical composition of any one of claims 1-2, wherein the one or more pharmaceutically acceptable excipients comprises a lubricant.

4. The pharmaceutical composition of any one of claims 1-3, wherein the composition comprises:
   a) about 85-99% by weight of a diluent; and
   b) about 0.5-2.0% by weight of a lubricant.

5. The pharmaceutical composition of any one of claims 1-4, wherein the composition comprises about 1%-10% by weight of psilocybin.

6. The pharmaceutical composition of any one of claims 1-4, wherein the composition comprises about 1%-15% by weight of psilocybin.

7. The pharmaceutical composition of any one of claims 1-6, wherein the diluent is pregelatinized starch.

8. The pharmaceutical composition of any one of claims 1-7, wherein the Carr's index of the diluent is about 12% to about 21%.

9. The pharmaceutical composition of any one of claims 1-8, wherein the Carr's index of the diluent is about 21%.

10. The pharmaceutical composition of any one of claims 1-9, wherein the mean average particle size of the diluent is about 60 microns to about 120 microns.

11. The pharmaceutical composition of any one of claims 1-10, wherein the mean average particle size of the diluent is about 90 microns.

12. The pharmaceutical composition of any one of claims 1-11, wherein the flow rate of the diluent is about 2 g/sec to about 10 g/sec, as measured using a Sotax FT300 Flowability Tester (vibration setting at 1.7 g).

13. The pharmaceutical composition of any one of claims 1-12, wherein the lubricant is selected from the group consisting of sodium stearyl fumarate, magnesium stearate, calcium stearate, zinc stearate, glyceryl monostearate, glyceryl behenate, glyceryl palmostearate, magnesium lauryl stearate, stearic acid, talc, and hydrogenated castor oil.

14. The pharmaceutical composition of claim 13, wherein the lubricant is sodium stearyl fumarate.

15. The pharmaceutical composition of any one of claims 1-14, wherein the chemical purity of psilocybin in the composition is greater than 97% as determined by HPLC analysis.

16. The pharmaceutical composition of any one of claims 1-14, wherein the chemical purity of psilocybin in the composition is greater than 97% and contains no single impurity greater than 2% as determined by HPLC analysis.

17. The pharmaceutical composition of any one of claims 1-14, wherein the chemical purity of psilocybin in the composition is greater than 97% and contains no single impurity greater than 1% as determined by HPLC analysis.

18. The pharmaceutical composition of any one of claims 1-17, wherein the composition comprises 1 mg to 40 mg of psilocybin.

19. The pharmaceutical composition of any one of claims 1-17, wherein the composition comprises 1 mg of psilocybin

20. The pharmaceutical composition of any one of claims 1-17, wherein the composition comprises 5 mg of psilocybin.

21. The pharmaceutical composition of any one of claims 1-17, wherein the composition comprises 10 mg of psilocybin.

22. The pharmaceutical composition of any one of claims 1-17, wherein the composition comprises 25 mg of psilocybin.

23. The pharmaceutical composition of any one of claims 1-17, wherein the composition comprises 40 mg of psilocybin.

24. The pharmaceutical composition of any one of claims 1-23, wherein the psilocybin comprises a crystalline psilocybin.

25. The pharmaceutical composition of claim 24, wherein the crystalline psilocybin is crystalline Polymorph A.

26. The pharmaceutical composition of claim 24, wherein the crystalline psilocybin is crystalline Hydrate A.

27. The pharmaceutical composition of claim 24, wherein the crystalline psilocybin is crystalline Polymorph A'.

28. The pharmaceutical composition of claim 24, wherein the crystalline psilocybin is crystalline Polymorph B.

29. The pharmaceutical composition of any one of claims 1-23, wherein the psilocybin comprises amorphous psilocybin.

30. The pharmaceutical composition of any one of claims 1-29, wherein the composition is a capsule.

31. The pharmaceutical composition of claim 30, wherein the capsule material comprises methylcellulose, gellan gum, carrageenan, pectin, glycerin, hydroxypropyl (HP) starch,

plasticizer, buffer (e.g., phosphate buffer), amorphous starch (e.g., amylopectin), a softener or combinations thereof.

32. The pharmaceutical composition of claim 30, wherein the capsule material comprises hydroxypropyl methylcellulose.

33. The pharmaceutical composition of claim 30, the capsule material comprises starch (e.g., hydroxypropyl starch or amylopectin).

34. The pharmaceutical composition of claim 30, the capsule material comprises about 1% to about 7% moisture content.

35. The pharmaceutical composition of claim 30, wherein the capsule material comprises less than about 6% moisture content.

36. The pharmaceutical composition of any one of claims 1-29, wherein the composition is a tablet.

37. The pharmaceutical composition of any one of claims 1-23, wherein the composition is a solution.

38. The pharmaceutical composition of any one of claims 1-36, wherein the content uniformity of the composition complies with the European Pharmacopeia 2.96. or USP <905>.

39. A method of making a pharmaceutical composition comprising:
a) direct mixing psilocybin and one or more pharmaceutically acceptable excipients to provide a blend, and
b) filling a capsule with the blend to provide the pharmaceutical composition,
wherein the content uniformity of the composition complies with the European Pharmacopeia 2.96. or USP <905>.

40. The method of claim 39, wherein the mass balance of psilocybin and related substances in the composition decreases by less than 3% after storage of the composition at 40°C and 75% relative humidity for one month.

41. The method of any one of claims 39-40, wherein the blend comprises about 1% to about 10% by weight of psilocybin.

42. The method of any one of claims 39-41, wherein the capsule contains 1 mg, 5 mg, 10 mg or 25 mg of psilocybin.

43. The method of any one of claims 39-42, wherein the one or more pharmaceutically acceptable excipients comprises a diluent.

44. The method of any one of claims 39-43, wherein the blend further comprises a lubricant.

45. The method of any one of claims 39-44, wherein the blend does not contain a glidant.

46. The method of any one of claims 39-45, wherein the capsule material comprises methylcellulose, gellan gum, carrageenan, pectin, glycerin, hydroxypropyl (HP) starch, plasticizer, buffer (e.g., phosphate buffer), amorphous starch (e.g., amylopectin), a softener or combinations thereof.

47. The method of any one of claims 39-45, wherein the capsule material comprises hydroxypropyl methylcellulose.

48. The method of any one of claims 39-47, wherein the capsule material comprises starch (e.g., hydroxypropyl starch or amylopectin).

49. The method of any one of claims 39-47, wherein the capsule material comprises about 1% to about 7% moisture content.

50. The method of any one of claims 39-47, wherein the capsule material comprises less than about 6% moisture content.

51. A pharmaceutical composition prepared by the process of any one of claims 39-50.

52. Use of a composition of any one of claims 1-38 and 51, in the manufacture of a medicament for treating a mood disorder.

53. A pharmaceutical composition comprising:
a therapeutically effective amount of psilocybin; and

about 85% to about 99%, by weight, partially pregelatinized starch.

54. The pharmaceutical composition of claim 53, further comprising a lubricant.

55. The pharmaceutical composition of claim 54, wherein the composition comprises about 0.5% to about 2.0%, by weight, the lubricant.

56. The pharmaceutical composition of claims 54 or 55, wherein the lubricant is sodium stearyl fumarate.

57. The pharmaceutical composition of any one of claims 53-56, wherein the composition is a capsule.

58. The pharmaceutical composition of any one of claims 53-57, wherein the composition comprises about 1% to about 10%, by weight, psilocybin.

59. The pharmaceutical composition of any one of claims 53-58, wherein the composition does not contain silicified microcrystalline cellulose.

60. The pharmaceutical composition of any one of claims 53-59, wherein the composition comprises 1 mg of psilocybin.

61. The pharmaceutical composition of any one of claims 53-59, wherein the composition comprises 5 mg of psilocybin.

62. The pharmaceutical composition of any one of claims 53-59, wherein the composition comprises 10 mg of psilocybin.

63. The pharmaceutical composition of any one of claims 53-59, wherein the composition comprises 25 mg of psilocybin.

64. The pharmaceutical composition of any one of claims 53-59, wherein the composition comprises 40 mg of psilocybin.

65. A pharmaceutical composition comprising:

about 1% to about 10%, by weight, psilocybin;

about 85% to about 99%, by weight, partially pregelatinized starch; and

about 0.5% to about 2.0%, by weight, sodium stearyl fumarate.

66. The pharmaceutical composition of claim 65, wherein the composition does not contain silicified microcrystalline cellulose.

67. The pharmaceutical composition of claim 65, wherein the composition is a capsule.

68. The pharmaceutical composition of any one of claims 65-67, wherein the composition comprises 1 mg of psilocybin.

69. The pharmaceutical composition of any one of claims 65-67, wherein the composition comprises 5 mg of psilocybin.

70. The pharmaceutical composition of any one of claims 65-67, wherein the composition comprises 10 mg of psilocybin.

71. The pharmaceutical composition of any one of claims 65-67, wherein the composition comprises 25 mg of psilocybin.

72. The pharmaceutical composition of any one of claims 65-67, wherein the composition comprises 40 mg of psilocybin.

73. A composition of any one of claims 1-38 and 51, for use in therapy.