suspension or solution can be sprayed onto the surface of the API particles to form a coating film by evaporation of the solvent or water. Examples of technologies for wet particle coating include microencapsulation, fluid bed coating, solvent evaporation, spray drying, pan coating etc. In dry particle coating (also referred to as solventless coating), API particles are mechanically coated with fine particles of inactive ingredients (polymers and additives) to form particle composites. Examples of dry particle coating include hot melt coating, supercritical coating, impaction coating, electrostatic coating, etc. APIs particles coated with a taste-masking inactive ingredient may provide a more pleasant experience for a patient having difficulties swallowing or having a sensitivity to taste that would otherwise lead to a negative patient experience and poor compliance, in particular for pharmaceutical compositions that dissolve or disintegrate in the oral cavity. However, many of the materials used to coat APIs are hydrophobic. Thus, the coated API particles are hydrophobic.

[0006] To accurately dispense a pharmaceutical composition into a small, administrable form, a hydrophobic coated API particle can be placed in a matrix solution/suspension to form a pharmaceutical suspension. Mixing the API to form a pharmaceutical suspension allows for improved dosing accuracy. Oftentimes, this pharmaceutical suspension comprising the hydrophobic coated API particles can be dosed into molds, dried, and the molded article can then be transferred into a bottle, for example. However, this kind of handling of the pharmaceutical composition can increase risks such as damage and contamination.

[0007] Accordingly, many API suspensions today are dosed into preformed blister packs instead. Preformed blister packs eliminate one of the handling steps described above. Instead of dosing into a mold and then transferring the molded article to a bottle for packaging, preformed blister packs allow a manufacturer to dose the pharmaceutical suspension into a preformed blister pack that can be dried, then sealed and packaged. Thus, the preformed blister pack serves as both the mold and the package in which the pharmaceutical composition can be stored.

SUMMARY

[0007a] In a first aspect, the present disclosure refers to a method of making a pharmaceutical composition comprising:

providing a matrix solution/suspension comprising a matrix former, a structure former, an anti-aerating agent, and a solvent; and

mixing a plurality of hydrophobic particles into the matrix solution/suspension to form a pharmaceutical suspension; and

dosing the pharmaceutical suspension into preformed blister packs, wherein a dosed weight of the dosed pharmaceutical suspension is within 10% of a target dosed weight.

[0007b] In another aspect, the present disclosure refers to a pharmaceutical composition prepared by a process comprising the steps of:

providing a matrix solution/suspension comprising a matrix former, a structure former, an anti-aerating agent, and a solvent; and

mixing a plurality of hydrophobic particles into the matrix solution/suspension to form a pharmaceutical suspension; and

dosing the pharmaceutical suspension into preformed blister packs, wherein a dosed weight of the dosed pharmaceutical suspension is within 10% of a target dosed weight.

[0007c] In yet another aspect, the present disclosure refers to a pharmaceutical composition disclosed herein, for use in administering to a patient.

[0007d] In a further aspect, the present disclosure refers to a pharmaceutical composition comprising:

a plurality of API particles;

a coating material encapsulating each API particle of the plurality of API particles;

a matrix former;

a structure former; and

an anti-aerating agent.

[0008] Provided are compositions and methods for preparing compositions that can minimize aeration of hydrophobic API particles in a pharmaceutical suspension. For example, hydrophobic coated API particles may be mixed into matrix solution/suspension to form a pharmaceutical suspension to accurately dose into molds to form solid pharmaceutical compositions (i.e., article, tablet, etc.) for administering to a patient. However, the

hydrophobicity of the coated API particles causes the coated API particles to resist dispersing into the matrix solution/suspension. Consequently, this can cause air to become entrained with the pharmaceutical suspension, also known as aeration. Entrained air, or aeration of the pharmaceutical suspension, can cause phase separation of the coated API particles in the pharmaceutical suspension, causing a non-homogenous pharmaceutical suspension. Aeration and non-homogeneous pharmaceutical suspension can lead to poor dose weight accuracy of the pharmaceutical suspension comprising the hydrophobic API particles dosed into preformed blister packs and poor content uniformity in the finished product (i.e., pharmaceutical composition).

[0009] Traditional mechanical means of anti-aeration and/or minimizing aeration have not been found to be successful due to the high viscosity of the pharmaceutical suspension. For example, minimizing aeration may be achieved by applying vacuum to a pharmaceutical suspension, but depending on the composition and further processing requirements this approach may not be suitable. In particular, applying a vacuum to the pharmaceutical suspension can cause the suspension to rise because the viscous suspension "holds onto" the entrained air. Volatile formulation components may also be lost during vacuum processing. Further, traditional anti-aerating agents, such as ethanol or simethicone emulsion are similarly ineffective at anti-aerating the suspension.

[0010] Accordingly, compositions and methods provided herein minimize the aeration of a pharmaceutical suspension comprising hydrophobic coated API particles to improve the homogeneity of the pharmaceutical suspension and increase the dose weight accuracy. Specifically, examples provided can include matrix solutions/suspensions comprising chemical compounds comprising terpene and/or terpinol. In some examples, a matrix solution/suspension may comprise the terpene limonene. By introducing a terpene-comprising chemical compound such as limonene, the hydrophobic coated API particles may more readily incorporate into the matrix solution/suspension, minimizing the overall aeration of the pharmaceutical suspension.

[0011] The solutions, suspensions, and compositions provided herein are described with respect to hydrophobic coated API particles. However, solutions, suspensions, and compositions and methods of preparing solutions, suspensions, and compositions provided herein may be used to minimize the aeration of any hydrophobic material that can be mixed

into a pharmaceutical suspension. For example, other types of compositions may be mixed into the suspension composition according to some examples.

[0012] In some examples, a method of making a pharmaceutical composition is provided, the method comprising: providing a matrix solution/suspension comprising a matrix former, a structure former, an anti-aerating agent, and a solvent; and mixing a plurality of hydrophobic particles into the matrix solution/suspension to form a pharmaceutical suspension; and dosing the pharmaceutical suspension into preformed blister packs, wherein the dispensed or dosed weight of the dosed pharmaceutical suspension is within 10.0 percent of a target dosed weight. In some examples of the method, the dispensed weight percentage of the dosed pharmaceutical suspension is within 5.0 percent of a target dosed weight. In some examples of the method, the dispensed weight of the dosed pharmaceutical suspension is within 2.5 percent of a target dosed weight. In some examples of the method, the dispensed weight of the dosed pharmaceutical suspension is within 1.0 percent of a target dosed weight. In some examples of the method, the plurality of hydrophobic particles comprises coated active pharmaceutical ingredient (API). In some examples of the method, the coated API comprise one or more of anti-inflammatories, analgesics, anti-psychotics, anti-emetics, laxatives, anti-diarrheals, anti-histamines, or anti-depressants. In some examples of the method, the composition of the functionally-coated API comprises from 30-90 % w/w API. In some examples of the method, the matrix solution/suspension comprises a viscosity modifier. In some examples of the method, the viscosity modifier comprises xanthan gum. In some examples of the method, mixing a plurality of hydrophobic particles into the matrix solution/suspension comprises in-line mixing at 15-20°C degrees Celsius. In some examples of the method, the anti-aerating agent comprises one or more of a terpene or a terpinol. In some examples of the method, the anti-aerating agent comprises a liquid flavor. In some examples of the method, the anti-aerating agent comprises a liquid flavor comprising limonene. In some examples of the method, the anti-aerating agent comprises one or more of orange flavor, lemon flavor, grapefruit flavor, lime flavor, strawberry flavor, or peppermint flavor. In some examples of the method, the matrix solution/suspension or the pharmaceutical suspension comprises from 0.1-1.5 % w/w anti-aerating agent. In some examples of the method, the matrix solution/suspension or the pharmaceutical suspension comprises from 2.0-5.0 % w/w matrix former. In some

examples of the method, the matrix solution/suspension or the pharmaceutical suspension comprises from 1.0-5.0 % w/w structure former.

[0013] In some examples, a pharmaceutical composition is provided, the pharmaceutical composition prepared by a process comprising the steps of: providing a matrix solution/suspension comprising a matrix former, a structure former, an anti-aerating agent, and a solvent; and mixing a plurality of hydrophobic particles into the matrix solution/suspension to form a pharmaceutical suspension; and dosing the pharmaceutical suspension into preformed blister packs, wherein the dispensed weight percentage of dosed the pharmaceutical suspension is within 10.0 percent of a target dosed weight. In some examples of the pharmaceutical composition, the dispensed weight of the dosed suspension is within 5.0 percent of a target dosed weight. In some examples of the pharmaceutical composition, the dispensed weight of the dosed suspension within 2.5 percent of a target dosed weight. In some examples of the pharmaceutical composition, the dispensed weight of the dosed suspension within 1.0 percent of a target dosed weight. In some examples of the pharmaceutical composition, the plurality of hydrophobic particles comprises coated active pharmaceutical ingredient (API). In some examples of the pharmaceutical composition, the coated API comprise one or more of one or more of anti-inflammatories, analgesics, anti-psychotics, anti-emetics, laxatives, anti-diarrheals, anti-histamines, or anti-depressants. In some examples of the pharmaceutical composition, the composition of the functionally-coated API comprises from 30-90 % w/w API. In some examples of the pharmaceutical composition, the matrix solution/suspension comprises a viscosity modifier. In some examples of the pharmaceutical composition, the viscosity modifier comprises xanthan gum. In some examples of the pharmaceutical composition, mixing a plurality of hydrophobic particles into the matrix solution/suspension comprises in-line mixing at 15-20°C degrees Celsius. In some examples of the pharmaceutical composition, the anti-aerating agent comprises one or more of a terpene or a terpinol. In some examples of the pharmaceutical composition, the anti-aerating agent comprises a liquid flavor. In some examples of the pharmaceutical composition, the anti-aerating agent comprises a liquid flavor comprising limonene. In some examples of the pharmaceutical composition, the anti-aerating agent comprises one or more of orange flavor, lemon flavor, grapefruit flavor, lime flavor, strawberry flavor, or peppermint flavor. In some examples of the

pharmaceutical composition, the pharmaceutical composition comprises from 1-5 % w/w anti-aerating agent. In some examples of the pharmaceutical composition, the pharmaceutical composition comprises from 3-10 % w/w matrix former. In some examples of the pharmaceutical composition, the pharmaceutical composition comprises from 3-10 % w/w structure former.

[0014] In some examples, a method of treating a patient is provided, the method comprising administering to a patient the pharmaceutical composition. In some examples of the method, the patient is a human.

[0015] In some examples, a pharmaceutical composition is provided, the pharmaceutical composition comprising: a plurality of API particles; a coating material encapsulating each API particle of the plurality of API particles; a matrix former; a structure former; and an anti-aerating agent. In some examples of the pharmaceutical composition, the pharmaceutical composition is formed by creating a matrix solution/suspension comprising the matrix former, the structure former, and the anti-aerating agent. In some examples of the pharmaceutical composition, the plurality of API particles comprises one or more of one or more of anti-inflammatories, analgesics, anti-psychotics, anti-emetics, laxatives, anti-diarrheals, anti-histamines, or anti-depressants. In some examples of the pharmaceutical composition, the matrix solution/suspension comprises a viscosity modifier. In some examples of the pharmaceutical composition, the viscosity modifier comprises xanthan gum. In some examples of the pharmaceutical composition, the anti-aerating agent comprises one or more of a terpene or a terpinol. In some examples of the pharmaceutical composition, the anti-aerating agent comprises a liquid flavor. In some examples of the pharmaceutical composition, the anti-aerating agent comprises a liquid flavor comprising limonene. In some examples of the pharmaceutical composition, the anti-aerating agent comprises one or more of orange flavor, lemon flavor, grapefruit flavor, lime flavor, strawberry flavor, or peppermint flavor. In some examples of the pharmaceutical composition, the composition of the functionally coated API comprises from 30-90 % w/w API. In some examples of the pharmaceutical composition, the pharmaceutical composition comprises from 1-5 % w/w anti-aerating agent. In some examples of the pharmaceutical composition, the pharmaceutical composition

comprises from 3-10 % w/w matrix former. In some examples of the pharmaceutical composition, the pharmaceutical composition comprises from 3-10 % w/w structure former.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] The invention will now be described, by way of example only, with reference to the accompanying drawings, in which:

[0017] Fig. 1 shows a graph providing an evaluation of d10 particle size of hydrophobic coated API particles with various concentrations of liquid flavor;

[0018] Fig. 2 shows a graph providing an evaluation of d50 particle size of hydrophobic coated API particles with various concentrations of liquid flavor;

[0019] Fig. 3 shows a graph providing an evaluation of d90 particle size of hydrophobic coated API particles with various concentrations of liquid flavor;

[0020] Fig. 4 shows a graph providing an evaluation of d10 particle size of hydrophobic coated API particles with various concentrations of pure limonene;

[0021] Fig. 5 shows a graph providing an evaluation of d50 particle size of hydrophobic coated API particles with various concentrations of pure limonene;

[0022] Fig. 6 shows a graph providing an evaluation of d90 particle size of hydrophobic coated API particles with various concentrations of pure limonene; and

[0023] Fig. 7 shows a graph comparing the various particle size analyses of hydrophobic coated API with strawberry and orange liquid flavors.

DETAILED DESCRIPTION OF THE INVENTION

[0024] Described herein are exemplary embodiments of compositions formulated to minimize the aeration of pharmaceutical suspensions comprising hydrophobic coated API particles. Also provided are methods of minimizing the aeration of pharmaceutical suspensions comprising hydrophobic coated API particles. In some embodiments, embodiments provided herein may include adding a chemical compound comprising terpene and/or terpinol to the matrix solution/suspension. Specifically, embodiments of suspensions provided herein may include liquid flavors comprising terpene and/or terpinols. In some embodiments, the liquid flavor(s) may include the terpene limonene. Particular chemical

CLAIMS

1. A method of making a pharmaceutical composition comprising:

providing a matrix solution/suspension comprising a matrix former, a structure former, an anti-aerating agent, and a solvent; and

mixing a plurality of hydrophobic particles into the matrix solution/suspension to form a pharmaceutical suspension; and

dosing the pharmaceutical suspension into preformed blister packs, wherein a dosed weight of the dosed pharmaceutical suspension is within 10% of a target dosed weight.

2. The method of claim 1, wherein the dosed weight of the dosed pharmaceutical suspension is within 5% of a target dosed weight.

3. The method of claim 1, wherein the dosed weight of the dosed pharmaceutical suspension is within 2.5% of a target dosed weight.

4. The method of any of claims 1-3, wherein the plurality of hydrophobic particles comprises coated active pharmaceutical ingredient (API).

5. The method of claim 4, wherein the coated API comprise one or more of anti-inflammatories, analgesics, anti-psychotics, anti-emetics, laxatives, anti-diarrheals, anti-histamines, or anti-depressants.

6. The method of claim 4 or 5, wherein the composition of the functionally-coated API comprises from 30-90 % w/w API.

7. The method of any of claims 1-6, wherein the matrix solution/suspension comprises a viscosity modifier.

8. The method of claim 7, wherein the viscosity modifier comprises xanthan gum.

9. The method of any of claims 1-8, wherein mixing a plurality of hydrophobic particles into the matrix solution/suspension comprises in-line mixing at 15-20°C degrees Celsius.

10. The method of any of claims 1-9, wherein the anti-aerating agent comprises one or more of a terpene or a terpinol.

11. The method of any of claims 1-10, wherein the anti-aerating agent comprises a liquid flavor.

12. The method of any of claims 1-11, wherein the anti-aerating agent comprises a liquid flavor comprising limonene.

13. The method of any of claims 1-12, wherein the anti-aerating agent comprises one or more of orange flavor, lemon flavor, grapefruit flavor, lime flavor, strawberry flavor, or peppermint flavor.

14. The method of any of claims 1-13, wherein the matrix solution/suspension or pharmaceutical suspension comprises from 0.1-1.5 % w/w anti-aerating agent.

15. The method of any of claims 1-14, wherein the matrix solution/suspension or pharmaceutical suspension comprises from 2.0-5.0 % w/w matrix former.

16. The method of any of claims 1-15, wherein the matrix suspension/solution or pharmaceutical suspension comprises from 1.0-5.0 % w/w structure former.

17. A pharmaceutical composition prepared by a process comprising the steps of:

providing a matrix solution/suspension comprising a matrix former, a structure former, an anti-aerating agent, and a solvent; and

mixing a plurality of hydrophobic particles into the matrix solution/suspension to form a pharmaceutical suspension; and

dosing the pharmaceutical suspension into preformed blister packs, wherein a dosed weight of the dosed pharmaceutical suspension is within 10% of a target dosed weight.

18. The pharmaceutical composition of claim 17, wherein the dosed weight of the dosed pharmaceutical suspension is within 5% of a target dosed weight.

19. The pharmaceutical composition of claim 17, wherein the dosed weight of the dosed pharmaceutical suspension is within 2.5% of a target dosed weight.

20. The pharmaceutical composition of any of claims 17-19, wherein the plurality of hydrophobic particles comprises coated active pharmaceutical ingredient (API).

21. The pharmaceutical composition of claim 20, wherein the coated API comprise one or more of one or more of anti-inflammatories, analgesics, anti-psychotics, anti-emetics, laxatives, anti-diarrheals, anti-histamines, or anti-depressants.

22. The pharmaceutical composition of claim 20 or 21, wherein the pharmaceutical composition comprises from 65-85 % w/w API.

23. The pharmaceutical composition of any of claims 17-22, wherein the matrix solution/suspension comprises a viscosity modifier.

24. The pharmaceutical composition of claim 23, wherein the viscosity modifier comprises xanthan gum.

25. The pharmaceutical composition of any of claims 17-24, wherein mixing a plurality of hydrophobic particles into the matrix solution/suspension comprises in-line mixing at 15-20°C degrees Celsius.

26. The pharmaceutical composition of any of claims 17-25, wherein the anti-aerating agent comprises one or more of a terpene or a terpinol.

27. The pharmaceutical composition of any of claims 17-26, wherein the anti-aerating agent comprises a liquid flavor.

28. The pharmaceutical composition of any of claims 17-27, wherein the anti-aerating agent comprises a liquid flavor comprising limonene.

29. The pharmaceutical composition of any of claims 17-28, wherein the anti-aerating agent comprises one or more of orange flavor, lemon flavor, grapefruit flavor, lime flavor, strawberry flavor, or peppermint flavor.

30. The pharmaceutical composition of any of claims 17-29, wherein the matrix solution/suspension or pharmaceutical suspension comprises from 0.1-1.5 % w/w anti-aerating agent.

31. The pharmaceutical composition of any of claims 17-30, wherein the matrix solution/suspension or pharmaceutical suspension comprises from 2.0-5.0 % w/w matrix former.

32. The pharmaceutical composition of any of claims 17-31, wherein the matrix solution/suspension or pharmaceutical suspension comprises from 1.0-5.0 % w/w structure former.

33. A pharmaceutical composition of any of claims 17-32, for use in administering to a patient.

34. The pharmaceutical composition for use of claim 33, wherein the patient is a human.

35. A pharmaceutical composition comprising:

a plurality of API particles;

a coating material encapsulating each API particle of the plurality of API particles;

a matrix former;

a structure former; and

an anti-aerating agent.

36. The pharmaceutical composition of claim 35, wherein the pharmaceutical composition is formed by creating a matrix solution/suspension comprising the matrix former, the structure former, and the anti-aerating agent.

37. The pharmaceutical composition of claim 35 or 36, wherein the plurality of API particles comprises one or more of one or more of anti-inflammatories, analgesics, anti-psychotics, anti-emetics, laxatives, anti-diarrheals, anti-histamines, or anti-depressants.

38. The pharmaceutical composition of any of claims 35-37, wherein the matrix solution/suspension comprises a viscosity modifier.

39. The pharmaceutical composition of claim 38, wherein the viscosity modifier comprises xanthan gum.

40. The pharmaceutical composition of any of claims 35-39, wherein the anti-aerating agent comprises one or more of a terpene or a terpinol.

41. The pharmaceutical composition of any of claims 35-40, wherein the anti-aerating agent comprises a liquid flavor.

42. The pharmaceutical composition of any of claims 35-41, wherein the anti-aerating agent comprises a liquid flavor comprising limonene.

43. The pharmaceutical composition of any of claims 35-42, wherein the anti-aerating agent comprises one or more of orange flavor, lemon flavor, grapefruit flavor, lime flavor, strawberry flavor, or peppermint flavor.

44. The pharmaceutical composition of any of claims 35-43, wherein the pharmaceutical composition comprises from 65-85 % w/w API.

45. The pharmaceutical composition of any of claims 35-44, wherein the pharmaceutical composition comprises from 1-5 % w/w anti-aerating agent.

46. The pharmaceutical composition of any of claims 35-45, wherein the pharmaceutical composition comprises from 3-10 % w/w matrix former.

47. The pharmaceutical composition of any of claims 35-46, wherein the pharmaceutical composition comprises from 3-10 % w/w structure former.