compositions may also include pharmaceutically inactive components which contribute to one or more abuse-deterrent characteristics of the composition.

[0005] The present disclosure addresses these issues and provides related advantages.

SUMMARY

[0006] Dosage forms of the present disclosure are designed to deliver pharmacologically active agents in a controlled release manner. For instance, the present disclosure includes dosage forms with adequate time of onset of action and reduced lag times in the fed state. Such dosage forms find use in the treatment of a variety of conditions where a rapid onset of action is desired followed by an extended release phase for the pharmacologically active agent, for example in the treatment of attention deficit hyperactivity disorder (ADHD), pain or anxiety. In some embodiments, the present disclosure provides a dosage form including a drug composition including a pharmacologically active agent, a barrier layer covering at least a portion of the drug composition, and a drug layer covering at least a portion of the barrier layer, wherein the drug layer comprises the pharmacologically active agent. Related methods are also provided.

[0006a] In one aspect, provided herein is a dosage form, comprising:

a drug composition comprising sucrose acetate isobutyrate and a first pharmacologically active agent comprising methylphenidate;

a barrier layer covering at least a portion of the drug composition; and

a drug layer covering at least a portion of the barrier layer, wherein the drug layer comprises a second pharmacologically active agent comprising methylphenidate, and

wherein initial release of the first pharmacologically active agent from the dosage form occurs at a time of 5 minutes to 120 minutes when assayed by USP Apparatus II using 750 mL of 0.1 N HCl dissolution medium, a paddle speed of 50 rpm, and a dissolution medium temperature of 37 °C.

[0006b] In another aspect, provided herein is a dosage form, comprising:

a capsule comprising

an extended release (ER) composition encapsulated therein, the ER composition comprising

methylphenidate (MPH) at 15% to 25% w/w relative to the total weight of the ER composition,

sucrose acetate isobutyrate at 35% to 45% w/w relative to the total weight of the ER composition,

an organic solvent at 20% to 35% w/w relative to the total weight of the ER composition,

a first layer covering at least a portion of the capsule, the first layer comprising

a methacrylic acid copolymer at 60% to 90% w/w relative to the total weight of the first layer, and

a polyvinyl alcohol at 40% to 10% w/w relative to the total weight of the first layer;

a second layer covering at least a portion of the first layer,

the second layer comprising

MPH at 25% to 40% w/w relative to the total weight of the second layer, and

a bulking agent at 75% to 60% w/w relative to the total weight of the second layer.

[0006c] In another aspect, provided herein is an oral dosage form, comprising:

a capsule comprising

an extended release (ER) composition encapsulated therein, the ER composition comprising

methylphenidate (MPH) at 15% to 25% w/w relative to the total weight of the ER composition,

sucrose acetate isobutyrate (SAIB) at 25% to 40% w/w relative to the total weight of the ER composition,

triacetin at 25% to 35% w/w relative to the total weight of the ER composition,

isopropyl myristate (IPM) at 5% to 10% w/w relative to the total weight of the ER composition,

cellulose acetate butyrate (CAB) at 2% to 7% w/w relative to the total weight of the ER composition,

silicon dioxide at 0.5% to 1% w/w relative to the total weight of the ER composition, and

a polyoxylglyceride at 0.5% to 2.5% w/w relative to the total weight of the ER composition; and

a first layer covering the capsule, the first layer comprising

a methacrylic acid copolymer at 65% to 75% w/w relative to the total weight of the first layer, and

a polyvinyl alcohol-based moisture barrier material at 25% to 35% w/w relative to the total weight of the first layer;

a second layer covering the first layer, the second layer comprising

MPH at 30% to 40% w/w relative to the total weight of the second layer, and

hydroxypropyl methylcellulose (HPMC) at 70% to 60% w/w relative to the total weight of the second layer; and

a third layer covering the second layer.

[0006d] In another aspect, provided herein is a dosage form as described herein for use in therapy.

[0006e] In another aspect, provided herein is a use of the dosage form as described herein in the manufacture of a medicament for the treatment of Attention Deficit Disorder (ADD) or Attention Deficit Hyperactivity Disorder (ADHD) in a subject, wherein the medicament is to be administered orally to the subject on a once daily (QD) basis.

BRIEF DESCRIPTION OF THE DRAWINGS

[0007] The present invention is further described in the description of invention that follows, in reference to the noted plurality of non-limiting drawings, wherein:

[0008] **Figure 1A** provides a flow diagram showing the steps of an exemplary method of preparing an extended release (ER) composition in connection with preparation of exemplary dosage forms described herein.

[0009] **Figure 1B** provides a flow diagram showing the steps of an exemplary method of preparing a barrier coating solution utilized for the application of a barrier layer in connection with preparation of exemplary dosage forms described herein.

[0010] **Figure 2** provides a flow diagram showing the steps of an exemplary method of preparing a drug coating solution utilized for the application of a drug layer in connection with preparation of exemplary dosage forms described herein.

administering, a dosage form as described herein, wherein the pharmacologically active agent is methylphenidate.

***IN VITRO* DISSOLUTION AND PHARMACOKINETICS**

[00154] The dosage forms of the present disclosure may be characterized by a desirable *in vitro* dissolution profile. For example, in some embodiments the % cumulative release of the pharmacologically active agent from an oral dosage form according to the present disclosure is from 5% to 40%, e.g., 10% to 30%, at T = 1 hr when assayed by USP Apparatus II using 750 mL of 1-stage 0.1 N HCl dissolution medium, a paddle speed of 50 rpm, a dissolution medium temperature of 37 °C, and a sampling volume of 1 mL.

[00155] In some embodiments, the *in vitro* % cumulative release of the pharmacologically active agent from an oral dosage form according to the present disclosure is at least 80% at T = 12 hr when assayed by USP Apparatus II using a 2-stage dissolution protocol, a paddle speed of 50 rpm, a dissolution medium temperature of 37 °C, and a sampling volume of 1 mL, wherein the 2-stage dissolution protocol includes exposing the oral dosage form to 750 mL of 0.1 N HCl for T = 0 to T = 2 hrs, adding 200 mL of 0.19 M phosphate buffer to obtain a final dissolution medium volume of 950 mL, and exposing the oral dosage form to the final dissolution medium volume from T = 2 hrs to T = 24 hr.

[00156] In some embodiments, a dosage form of the present disclosure is constituted such that initial release from the dosage form, of a pharmacologically active agent comprised by the drug composition (or ER composition), occurs at a time of 5 minutes to 120 minutes when assayed by USP Apparatus II using 750 mL of 0.1 N HCl dissolution medium, a paddle speed of 50 rpm, and a dissolution medium temperature of 37 °C. For example, in some embodiments, a dosage form of the present disclosure is constituted such that initial release from the dosage form, of a pharmacologically active agent comprised by the drug composition (or ER composition), occurs at a time of 10 minutes to 120 minutes, 15 minutes to 120 minutes, 20 minutes to 120 minutes, 25 minutes to 120 minutes, 30 minutes to 120 minutes, 35 minutes to 120 minutes, 40 minutes to 120 minutes, 45 minutes to 120 minutes, 50 minutes to 120 minutes, 55 minutes to 120 minutes, 60 minutes to 120 minutes, 65 minutes to 120 minutes, 70 minutes to 120 minutes, 75 minutes to 120 minutes, 80 minutes to 120 minutes, 85 minutes to 120 minutes, 90 minutes to 120

CLAIMS

What is claimed is:

1. A dosage form, comprising:

    a drug composition comprising sucrose acetate isobutyrate and a first pharmacologically active agent comprising methylphenidate;

    a barrier layer covering at least a portion of the drug composition; and

    a drug layer covering at least a portion of the barrier layer, wherein the drug layer comprises a second pharmacologically active agent comprising methylphenidate, and

    wherein initial release of the first pharmacologically active agent from the dosage form occurs at a time of 5 minutes to 120 minutes when assayed by USP Apparatus II using 750 mL of 0.1 N HCl dissolution medium, a paddle speed of 50 rpm, and a dissolution medium temperature of 37 °C.

2. The dosage form of claim 1, wherein the first pharmacologically active agent is present in the drug composition at from 10% to 50% w/w relative to the total weight of the drug composition.

3. The dosage form of any one of claims 1 and 2, wherein the drug composition is encapsulated in a capsule and the barrier layer covers at least a portion of the capsule.

4. The dosage form of any one of claims 1 to 3, wherein the sucrose acetate isobutyrate is present at 30% to 60% w/w relative to the total weight of the drug composition.

5. The dosage form of any one of claims 1 to 4, wherein the drug composition comprises an organic solvent.

6. The dosage form of claim 5, wherein the organic solvent is present at 0.1% to 45% w/w relative to the total weight of the drug composition.

7. The dosage form of any one of claims 5 and 6, wherein the organic solvent comprises at least one member selected from triacetin, N-methyl-2-pyrrolidone, 2-pyrrolidone, dimethylsulfoxide, ethyl lactate, propylene carbonate, and glycofurol.

8. The dosage form of any one of claims 1 to 7, wherein the drug composition comprises a rheology modifier.

9. The dosage form of claim 8, wherein the rheology modifier is present at 0.1% to 20% w/w relative to the total weight of the drug composition.

10. The dosage form of any one of claims 8 and 9, wherein the rheology modifier comprises at least one member selected from a caprylic/capric triglyceride, isopropyl myristate, ethyl oleate, triethyl citrate, dimethyl phthalate, labrafil, labrasol, a polyglycolized glyceride, and benzyl benzoate.

11. The dosage form of any one of claims 1 to 10, wherein the drug composition comprises a network former.

12. The dosage form of claim 11, wherein the network former is present at 0.1% to 20% w/w relative to the total weight of the drug composition.

13. The dosage form of any one of claims 11 and 12, wherein the network former comprises at least one member selected from a cellulose acetate butyrate, a carbohydrate polymer, an organic acid of a carbohydrate polymer, a hydrogel, a cellulose acetate phthalate, an ethyl cellulose, a triblock copolymer, an acrylic polymer, hydroxyl propyl methyl cellulose, cellulose triacetate, and poly(methyl methacrylate).

14. The dosage form of any one of claims 1 to 13, wherein the drug composition comprises a viscosity enhancing agent.

15. The dosage form of claim 14, wherein the viscosity enhancing agent is present at 0.01% to 10% w/w relative to the total weight of the drug composition.

16. The dosage form of any one of claims 1 to 15, wherein the drug composition comprises a polyoxylglyceride.

17. The dosage form of claim 16, wherein the polyoxylglyceride is present at 0.1% to 5% w/w relative to the total weight of the drug composition.

18. The dosage form of any one of claims 1 to 17, wherein the barrier layer comprises at least one member selected from cellulose acetate phthalate, HPMC phthalate, HPMC acetate succinate, polyvinyl acetate phthalate, cellulose acetate trimelitate, methyacrylic acid copolymer, shellac, and zein.

19. The dosage form of any one of claims 1 to 18, wherein the barrier layer comprises at least one member selected from a hydrophobic cellulose, a polyalcohol, magnesium stearate, and silicon dioxide.

20. The dosage form of any one of claims 1 to 19, wherein the barrier layer comprises a methacrylic acid copolymer and a polyvinyl alcohol.

21. The dosage form of any one of claims 1 to 20, wherein the dosage form comprises a coating layer covering at least a portion of the drug layer.

22. The dosage form of claim 21, wherein the coating layer comprises a polyvinyl alcohol.

23. A dosage form, comprising:

a capsule comprising

an extended release (ER) composition encapsulated therein, the ER composition comprising

methylphenidate (MPH) at 15% to 25% w/w relative to the total weight of the ER composition,

sucrose acetate isobutyrate at 35% to 45% w/w relative to the total weight of the ER composition,

an organic solvent at 20% to 35% w/w relative to the total weight of the ER composition,

a first layer covering at least a portion of the capsule, the first layer comprising

a methacrylic acid copolymer at 60% to 90% w/w relative to the total weight of the first layer, and

a polyvinyl alcohol at 40% to 10% w/w relative to the total weight of the first layer;

a second layer covering at least a portion of the first layer,

the second layer comprising

MPH at 25% to 40% w/w relative to the total weight of the second layer, and

a bulking agent at 75% to 60% w/w relative to the total weight of the second layer.

24. An oral dosage form, comprising:

a capsule comprising

an extended release (ER) composition encapsulated therein, the ER composition comprising

methylphenidate (MPH) at 15% to 25% w/w relative to the total weight of the ER composition,

sucrose acetate isobutyrate (SAIB) at 25% to 40% w/w relative to the total weight of the ER composition,

triacetin at 25% to 35% w/w relative to the total weight of the ER composition,

isopropyl myristate (IPM) at 5% to 10% w/w relative to the total weight of the ER composition,

cellulose acetate butyrate (CAB) at 2% to 7% w/w relative to the total weight of the ER composition,

silicon dioxide at 0.5% to 1% w/w relative to the total weight of the ER composition, and

a polyoxylglyceride at 0.5% to 2.5% w/w relative to the total weight of the ER composition; and

a first layer covering the capsule, the first layer comprising

a methacrylic acid copolymer at 65% to 75% w/w relative to the total weight of the first layer, and

a polyvinyl alcohol-based moisture barrier material at 25% to 35% w/w relative to the total weight of the first layer;

a second layer covering the first layer, the second layer comprising

MPH at 30% to 40% w/w relative to the total weight of the second layer, and

hydroxypropyl methylcellulose (HPMC) at 70% to 60% w/w relative to the total weight of the second layer; and

a third layer covering the second layer.

25. The dosage form of any one of claims 1 to 24 for use in therapy.

26. Use of the dosage form of any one of claims 1 to 24 in the manufacture of a medicament for the treatment of Attention Deficit Disorder (ADD) or Attention Deficit Hyperactivity Disorder (ADHD) in a subject, wherein the medicament is to be administered orally to the subject on a once daily (QD) basis.