discreet, inconspicuous, unnoticeable and/or private manner, especially while in the company of another. ODFs can therefore be administered without the use of water, fulfilling the need of target population seeking convenience in drug administration, along with rapid onset of action with increased bioavailability due to bypassing the hepatic metabolism, consequently, leading to improved therapeutic response.

Just as with other dosage forms intended for oral administration, ODFs have typically been limited for use with specific active ingredients (e.g., those that are not moisture sensitive). What is needed, therefore, is an oral dissolvable film that can include additional classes of active ingredient (e.g., moisture sensitive, oxygen sensitive, pH sensitive, heat sensitive, etc.) not present in commercially manufactured ODFs, while maintaining the target aesthetics and performance characteristics of the ODF (e.g., desired content uniformity, desired thickness, and/or desired dissolution).

SUMMARY

The present disclosure provides for an orally disintegrating film matrix. The orally disintegrating film matrix can be in the form of an oral dissolvable film and is suitable for delivering one or more active ingredients to a subject. The orally disintegrating film matrix includes a rapidly dissolving binder (e.g., Kollicoat® Protect), a film forming polymer (e.g., Hypromellose), optionally a moisture deterring polymer (e.g., EUDRAGIT® EPO), and optionally a pH adjusting agent (e.g., anhydrous citric acid). The orally disintegrating film matrix can further include an active ingredient (e.g., the orally disintegrating film matrix can include a first active ingredient). Alternatively, the active ingredient can be absent from the orally disintegrating film matrix (e.g., the first active ingredient can be absent from the orally disintegrating film matrix). Either way, a second active ingredient can optionally be added after the orally disintegrating film matrix is formed.

In one aspect, the present disclosure refers to an orally disintegrating film matrix comprising:

rapidly dissolving binder comprising polyvinyl alcohol (PVA) and polyvinyl alcohol (PVA)–polyethylene glycol (PEG) copolymer; and

film forming polymer comprising hydroxypropyl methyl cellulose (HPMC);

wherein,

the orally disintegrating film matrix has a moisture content of less than 8 wt.%; and

upon contact with the oral cavity, the orally disintegrating film matrix disintegrates within 60 seconds.

In another aspect, the present disclosure refers to an orally disintegrating film matrix comprising:

at least one of a first and second active ingredient;

rapidly dissolving binder comprising polyvinyl alcohol (PVA) and polyvinyl alcohol (PVA)–polyethylene glycol (PEG) copolymer; and

film forming polymer comprising hydroxypropyl methyl cellulose (HPMC);

wherein,

the orally disintegrating film matrix has a moisture content of less than 8 wt.%, and

upon contact with the oral cavity, the orally disintegrating film matrix disintegrates within 60 seconds.

In a further aspect, the present disclosure refers to a method of forming an orally disintegrating film matrix comprising:

(a) contacting water, a rapidly dissolving binder, optionally a first active ingredient, and a film forming polymer, to form a homogeneous mixture;

(b) extruding the homogeneous mixture onto a substrate;

(c) curing the extruded homogeneous mixture to form the orally disintegrating film matrix;

(d) optionally impregnating a second active ingredient to the orally disintegrating film matrix; and

(e) optionally sizing the orally disintegrating film matrix to a desired surface area;

wherein,

the rapidly dissolving binder comprises polyvinyl alcohol (PVA) and polyvinyl alcohol (PVA)–polyethylene glycol (PEG) copolymer; and

the film forming polymer comprises hydroxypropyl methyl cellulose (HPMC).

In yet another aspect, the present disclosure refers to a method of forming an orally disintegrating film matrix comprising:

(a) contacting water, a first active ingredient, a rapidly dissolving binder, and a film forming polymer, to form a homogeneous mixture;

(b) extruding the homogeneous mixture onto a substrate;

(c) curing the extruded homogeneous mixture to form the orally disintegrating film matrix; and

(d) optionally sizing the orally disintegrating film matrix to a desired surface area;

wherein,

the rapidly dissolving binder comprises polyvinyl alcohol (PVA) and polyvinyl alcohol (PVA)–polyethylene glycol (PEG) copolymer; and

the film forming polymer comprises hydroxypropyl methyl cellulose (HPMC).

In yet another aspect, the present disclosure refers to a kit comprising

(a) the orally disintegrating film matrix disclosed herein or the orally disintegrating film matrix obtained by the method disclosed herein;

(b) a sealable and vapor impermeable container closure system;

wherein,

the orally disintegrating film matrix is contained within the sealable and vapor impermeable container closure system.

In another aspect, the present disclosure refers to the use of the orally disintegrating film matrix disclosed herein, or the orally disintegrating film matrix obtained by the method disclosed herein, in the manufacture of a medicament for delivering an active ingredient to a subject, wherein the medicament is to be orally administered to the subject.

The present disclosure also provides for a method of forming an orally disintegrating film matrix. The orally disintegrating film matrix can be in the form of an oral dissolvable film and is suitable for delivering one or more active ingredients to a subject. The method includes: (a) contacting water, a rapidly dissolving binder (e.g., Kollicoat® Protect), a film forming polymer (e.g., Hypromellose), optionally a moisture deterring polymer (e.g.,

EUDRAGIT® EPO), and optionally a pH adjusting agent (e.g., anhydrous citric acid) to form a homogeneous mixture; (b) extruding the homogeneous mixture onto a substrate; and (c) curing the extruded homogeneous mixture to form an orally disintegrating film matrix (which

can be in the form of an oral dissolvable film). The homogeneous mixture in (a) (alternatively referred to as a "slurry") can further include an active ingredient (e.g., the homogeneous mixture can include a first active ingredient). Alternatively, the active ingredient can be absent from the homogeneous mixture in (a) (e.g., the first active ingredient can be absent from the homogeneous mixture) and accordingly absent from the orally disintegrating film matrix. The second active ingredient can optionally be added after the orally disintegrating film matrix is formed.

The present disclosure also provides for an orally disintegrating film matrix in the form of an oral dissolvable film, suitable for delivering one or more active ingredients to a subject. The orally disintegrating film matrix includes a rapidly dissolving binder (e.g., Kollicoat® Protect), a film forming polymer (e.g., Hypromellose), an active ingredient, optionally a moisture deterring polymer (e.g., EUDRAGIT® EPO), and optionally a pH adjusting agent (e.g., anhydrous citric acid). A second active ingredient can optionally be added after the orally disintegrating film matrix is formed.

The present disclosure also provides for a kit that includes the orally disintegrating film matrix described herein (in the form of an oral dissolvable film), contained within a sealable and vapor impermeable container closure system.

The present disclosure also provides for a method of forming an orally disintegrating film matrix. The orally disintegrating film matrix can be in the form of an oral dissolvable film and is suitable for delivering one or more active ingredients to a subject. The method includes: (a) contacting water, a rapidly dissolving binder (e.g., Kollicoat® Protect), a film forming polymer (e.g., Hypromellose), a first active ingredient, optionally a moisture deterring polymer (e.g., EUDRAGIT® EPO), optionally a pH adjusting agent (e.g., anhydrous citric acid) to form a homogeneous mixture; (b) extruding the homogeneous mixture onto a substrate; and (c) curing the extruded homogeneous mixture to form an orally disintegrating film matrix (which can be in the form of an oral dissolvable film). Further, a second active ingredient can optionally be added after the orally disintegrating film matrix is formed. The second active ingredient can be impregnated to the orally disintegrating film matrix (e.g., via 3D printing).

The present disclosure also provides for a method of delivering one or more active ingredients to a subject in need thereof. The method includes administering to the subject the orally disintegrating film matrix (oral dissolvable film) described herein. The orally

disintegrating film matrix can include a first active ingredient as the only active ingredient. Alternatively, the orally disintegrating film matrix can include a second active ingredient as the only active ingredient. Alternatively, the orally disintegrating film matrix can include both a first and a second active ingredient. The first active ingredient is present when the orally disintegrating film matrix is formed (e.g., present in the slurry). The second active ingredient can be impregnated to the orally disintegrating film matrix (e.g., via 3D printing) after the orally disintegrating film matrix is formed.

The orally disintegrating film matrix described herein provides the advantages of achieving one or more of the significant and advantageous features (1)-(10): the orally disintegrating film matrix is (1) formulated as an oral dissolvable film to include a therapeutically effective amount of active ingredient that is at least one of: (a) moisture sensitive, (b) oxygen sensitive, (c) pH sensitive, (d) heat sensitive, (e) light (UV) sensitive, (f) having an unpleasant taste or odor, (g) water-insoluble, and (h) present in a small quantity; (2) formulated as a "thin film" having a suitable thickness, while (3) the oral dissolvable film has a desired kinetics of erodibility. Having the dissolvable oral film be "thin," and for it to have a desired (e.g., rapid) dissolution when placed in the mouth, is advantageous at least with small children who are at risk of choking on orally administered medications, as well as those patients suffering from dysphagia. Additionally, (4) the orally disintegrating film matrix can readily be printed on (e.g., via 3D printing). This includes (5) impregnating to the orally disintegrating film matrix (e.g., via 3D printing) an active ingredient. The orally disintegrating film matrix is formulated as an oral dissolvable film to (6) contain a low level of moisture (e.g., residual solvent), (7) target a specific pH range (e.g., inclusion of acid, base, and/or buffer), (8) effectively mask the taste of the active ingredient without the use of a taste masking agent and/or sweetener, (9) while being non-hygroscopic.

In those examples where an active ingredient is added after the orally disintegrating film matrix is formed, (10) the orally disintegrating film matrix can be formulated and stored (over extended periods of time) as a film roll. In doing so, the added active ingredient can include those that are (a) moisture sensitive, (b) oxygen sensitive, (c) pH sensitive, (d) heat sensitive, and/or (e) light (UV) sensitive, without unduly compromising the stability, physical integrity, safety and/or effectiveness of the orally disintegrating film matrix had the orally disintegrating film matrix included such active ingredient prior to the storage of the film roll.

As described herein, various examples of the present disclosure can independently include one or more of the significant and advantageous features (1)-(10) described above. Specifically, the significant and advantageous features possessed by the various examples can vary (or remain the same), across multiple examples. More specifically, the significant and advantageous features possessed by various examples can be the same as the significant and advantageous features possessed by other examples. Alternatively, the significant and advantageous features possessed by various examples can be different from the significant and advantageous features possessed by other examples. More specifically, a significant and advantageous feature possessed by any specific example can be independent of, and mutually exclusive of, any significant and advantageous feature possessed by any other example.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides for an orally disintegrating film matrix that includes a rapidly dissolving binder and film forming polymer. The present invention also provides for an orally disintegrating film matrix that includes a first active ingredient; a rapidly dissolving binder; and a film forming polymer.

The present invention provides for a method of forming an orally disintegrating film matrix that includes: (a) contacting water, a rapidly dissolving binder, and a film forming polymer, to form a homogeneous mixture; (b) extruding the homogeneous mixture onto a substrate; (c) curing the extruded homogeneous mixture to form the orally disintegrating film matrix; and (d) optionally sizing the orally disintegrating film matrix to a desired surface area.

The present invention also provides for a method of forming an orally disintegrating film matrix that includes: (a) contacting water, a rapidly dissolving binder, and a film forming polymer, to form a homogeneous mixture; (b) extruding the homogeneous mixture onto a substrate; (c) curing the extruded homogeneous mixture to form the orally disintegrating film matrix; (d) optionally impregnating a second active ingredient to the orally disintegrating film matrix; and (e) optionally sizing the orally disintegrating film matrix to a desired surface area.

The present invention also provides for a method of forming an orally disintegrating film matrix that includes: (a) contacting water, a rapidly dissolving binder, and a film forming polymer, to form a homogeneous mixture; (b) extruding the homogeneous mixture onto a

CLAIMS

1. An orally disintegrating film matrix comprising:

rapidly dissolving binder comprising polyvinyl alcohol (PVA) and polyvinyl alcohol (PVA)–polyethylene glycol (PEG) copolymer; and

film forming polymer comprising hydroxypropyl methyl cellulose (HPMC);

wherein,

the orally disintegrating film matrix has a moisture content of less than 8 wt.%; and

upon contact with the oral cavity, the orally disintegrating film matrix disintegrates within 60 seconds.

2. The orally disintegrating film matrix of claim 1, which does not include an active ingredient.

3. The orally disintegrating film matrix of claim 1, further comprising at least one of a first and second active ingredient.

4. An orally disintegrating film matrix comprising:

at least one of a first and second active ingredient;

rapidly dissolving binder comprising polyvinyl alcohol (PVA) and polyvinyl alcohol (PVA)–polyethylene glycol (PEG) copolymer; and

film forming polymer comprising hydroxypropyl methyl cellulose (HPMC);

wherein,

the orally disintegrating film matrix has a moisture content of less than 8 wt.%, and

upon contact with the oral cavity, the orally disintegrating film matrix disintegrates within 60 seconds.

5. A method of forming an orally disintegrating film matrix comprising:

(a) contacting water, a rapidly dissolving binder, optionally a first active ingredient, and a film forming polymer, to form a homogeneous mixture;

(b) extruding the homogeneous mixture onto a substrate;

(c) curing the extruded homogeneous mixture to form the orally disintegrating film matrix;

(d) optionally impregnating a second active ingredient to the orally disintegrating film matrix; and

(e) optionally sizing the orally disintegrating film matrix to a desired surface area;

wherein,

the rapidly dissolving binder comprises polyvinyl alcohol (PVA) and polyvinyl alcohol (PVA)–polyethylene glycol (PEG) copolymer; and

the film forming polymer comprises hydroxypropyl methyl cellulose (HPMC).

6. The method of claim 5, wherein the homogeneous mixture in (a) does not include a first active ingredient and the method comprises (d) impregnating a second active ingredient to the orally disintegrating film matrix.

7. The method of claim 5, wherein the homogeneous mixture in (a) further comprises a first active ingredient and the method optionally comprises (d) impregnating a second active ingredient to the orally disintegrating film matrix.

8. A method of forming an orally disintegrating film matrix comprising:

(a) contacting water, a first active ingredient, a rapidly dissolving binder, and a film forming polymer, to form a homogeneous mixture;

(b) extruding the homogeneous mixture onto a substrate;

(c) curing the extruded homogeneous mixture to form the orally disintegrating film matrix; and

(d) optionally sizing the orally disintegrating film matrix to a desired surface area;

wherein,

the rapidly dissolving binder comprises polyvinyl alcohol (PVA) and polyvinyl alcohol (PVA)–polyethylene glycol (PEG) copolymer; and

the film forming polymer comprises hydroxypropyl methyl cellulose (HPMC).

9. A kit comprising

(a) the orally disintegrating film matrix of any one of claims 1–4 or the orally disintegrating film matrix obtained by the method of any one of claims 5–8;

(b) a sealable and vapor impermeable container closure system;

wherein,

the orally disintegrating film matrix is contained within the sealable and vapor impermeable container closure system.

10. Use of the orally disintegrating film matrix of any one of claims 1 and 3–4, or the orally disintegrating film matrix obtained by the method of any one of claims 5–8, in the manufacture of a medicament for delivering an active ingredient to a subject, wherein the medicament is to be orally administered to the subject.

11. The orally disintegrating film matrix of any one of claims 1–4, further comprising a moisture deterring polymer comprising aminoalkyl methacrylate copolymers.

12. The orally disintegrating film matrix of claim 11, wherein the moisture deterring polymer comprises EUDRAGIT® EPO (aminoalkyl methacrylate copolymers).

13. The orally disintegrating film matrix of claim 11, wherein the moisture deterring polymer comprises 1-4 wt.% EUDRAGIT® EPO (aminoalkyl methacrylate copolymers).

14. The orally disintegrating film matrix of any one of claims 1–4 and 11–13, wherein the rapidly dissolving binder comprises Kollicoat® Protect (polyvinyl alcohol (PVA) and polyvinyl alcohol (PVA)–polyethylene glycol (PEG) copolymer).

15. The orally disintegrating film matrix of any one of claims 1–4 and 11–13, wherein the rapidly dissolving binder comprises 40-80 wt.% Kollicoat® Protect (polyvinyl alcohol (PVA) and polyvinyl alcohol (PVA)–polyethylene glycol (PEG) copolymer).

16. The orally disintegrating film matrix of any one of claims 1–4 and 11–15, wherein the film forming polymer comprises Hypromellose (hydroxypropyl methyl cellulose (HPMC)).

17. The orally disintegrating film matrix of any one of claims 1–4 and 11–15, wherein the film forming polymer comprises 5-20 wt.% Hypromellose (hydroxypropyl methyl cellulose (HPMC)).

18. The orally disintegrating film matrix of any one of claims 1–4 and 11–17, further comprising at least one of plasticizer, preservative, solvent, coloring agent, flavoring agent,

sweetening agent, filler, bulking agent, saliva stimulating agent, stabilizing and thickening agent, gelling agent, taste masking agent, pigment, lubricant, release modifier, adjuvant, solubilizer & emulsifier, fragrance, emulsifier, surfactant, lipid, glidant, stabilizer, antioxidant, anti-tacking agent, acid, base, buffer, and humectant.

19. The orally disintegrating film matrix of any one of claims 1–4 and 11–18, further comprising a second active ingredient impregnated to the orally disintegrating film matrix.

20. The orally disintegrating film matrix of any one of claims 1–4 and 11–18, further comprising a second active ingredient impregnated to the orally disintegrating film matrix via 3D printing.

21. The orally disintegrating film matrix of any one of claims 1–4 and 11–20, wherein upon contact with the oral cavity, the orally disintegrating film matrix disintegrates within 15 seconds.

22. The orally disintegrating film matrix of any one of claims 1–4 and 11–21, wherein the orally disintegrating film matrix has a moisture content of less than 4 wt.%.

23. The orally disintegrating film matrix of any one of claims 1–2 and 11–21, wherein the orally disintegrating film matrix does not comprise a first or second active ingredient; and wherein the orally disintegrating film matrix is configured to comprise a second active ingredient impregnated thereto.

24. The orally disintegrating film matrix of any one of claims 1, 3–4, and 11–21, wherein the orally disintegrating film matrix does not comprise a first active ingredient; and the orally disintegrating film matrix comprises a second active ingredient impregnated thereto.

25. The orally disintegrating film matrix of any one of claims 1, 3–4, and 11–24, further comprising citric acid, in an amount sufficient to adjust the pH of the orally disintegrating film matrix to a pH of 4.6 to 5; and wherein the orally disintegrating film matrix does not comprise a first active ingredient; and the orally disintegrating film matrix comprises a second active ingredient impregnated thereto.