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:

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

a first and second active ingredient;

a moisture deterring polymer;

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 first active ingredient, 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) after the curing of the extruded homogeneous mixture to form the orally disintegrating film matrix, impregnating via 3D printing, a second active ingredient to the cured orally disintegrating film matrix; and

(e) sizing the impregnated 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 a first and second 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.,

CLAIMS

1. An orally disintegrating film matrix comprising:

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.

2. An orally disintegrating film matrix comprising:

a first and second active ingredient;

a moisture deterring polymer;

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.

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

(a) contacting water, a first active ingredient, 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) after the curing of the extruded homogeneous mixture to form the orally disintegrating film matrix, impregnating via 3D printing, a second active ingredient to the cured orally disintegrating film matrix; and

(e) sizing the impregnated 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).

4. A kit comprising

(a) the orally disintegrating film matrix of any one of claims 1 or 2 or the orally disintegrating film matrix obtained by the method of claim 3;

(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.

5. Use of the orally disintegrating film matrix of any one of claims 1 or 2, or the orally disintegrating film matrix obtained by the method of claim 3, in the manufacture of a medicament for delivering a first and second active ingredient to a subject, wherein the medicament is to be orally administered to the subject.

6. The orally disintegrating film matrix of any one of claims 1 or 2, further comprising a moisture deterring polymer comprising aminoalkyl methacrylate copolymers.

7. The orally disintegrating film matrix of claim 6, wherein the moisture deterring polymer comprises aminoalkyl methacrylate copolymers (EUDRAGIT® EPO).

8. The orally disintegrating film matrix of claim 6, wherein the moisture deterring polymer comprises 1-4 wt.% aminoalkyl methacrylate copolymers (EUDRAGIT® EPO).

9. The orally disintegrating film matrix of any one of claims 1 or 2 and 6–8, wherein the rapidly dissolving binder comprises polyvinyl alcohol (PVA) and polyvinyl alcohol (PVA)–polyethylene glycol (PEG) copolymer (Kollicoat® Protect).

10. The orally disintegrating film matrix of any one of claims 1 or 2 and 6–8, wherein the rapidly dissolving binder comprises 40-80 wt.% polyvinyl alcohol (PVA) and polyvinyl alcohol (PVA)–polyethylene glycol (PEG) copolymer (Kollicoat® Protect).

11. The orally disintegrating film matrix of any one of claims 1 or 2 and 6–10, wherein the film forming polymer comprises 5-20 wt.% Hypromellose (hydroxypropyl methyl cellulose (HPMC)).

12. The orally disintegrating film matrix of any one of claims 1 or 2 and 6–11, 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.

13. The orally disintegrating film matrix of any one of claims 1 or 2 and 6–12, further comprising the second active ingredient impregnated to the orally disintegrating film matrix.

14. The orally disintegrating film matrix of any one of claims 1 or 2 and 6–12, further comprising the second active ingredient impregnated to the orally disintegrating film matrix via 3D printing.

15. The orally disintegrating film matrix of any one of claims 1 or 2 and 6–14, wherein upon contact with the oral cavity, the orally disintegrating film matrix disintegrates within 15 seconds.

16. The orally disintegrating film matrix of any one of claims 1 or 2 and 6–15, wherein the orally disintegrating film matrix has a moisture content of less than 4 wt.%.

17. The orally disintegrating film matrix of any one of claims 1 or 2, and 6–16, 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.