ORAL DISSOLVABLE FILM AND METHOD OF MANUFACTURING AND USING THE SAME

RELATED APPLICATION

This application claims priority to U.S. Provisional Patent Application No. 62/955,484 filed December 31, 2019; the contents of which are incorporated herein in their entirety.

BACKGROUND OF THE INVENTION

Bioavailability of orally drugs administered is relatively low. Additionally, sensitive active ingredients (e.g., sensitive to moisture, oxygen, light, pH, and/or heat) present difficulties in the selection of the suitable dosage form and the route of administration. This includes those dosage forms configured for oral administration.

Currently, there is a need for pharmaceutical formulations having an increased barrier to moisture, oxygen, light, pH, and heat to thereby confer protection to sensitive active ingredient. There is also a need for an improved bioavailability of less potent and less bioavailable active ingredients which allows the less potent active ingredients to be used at low doses. Additionally, with various pharmaceutical formulations, there is a need for an increased penetration and crossing of the mucus layer by the active ingredients, thereby allowing active ingredients to enter into systemic circulation. The above are desirable while also reducing liver/GI toxicity.

SUMMARY

In an aspect of the present disclosure, there is provided a method of forming an oral dissolvable film, the method comprising:

(a) dissolving an active pharmaceutical ingredient in a first solvent-system to form a first mixture, wherein:

(i) when the active pharmaceutical ingredient is lipophilic or hydrophobic, dissolving the active pharmaceutical ingredient in a lipophilic or hydrophobic solvent, in a lipophilic or hydrophobic surfactant, or combination thereof; or

(ii) when the active pharmaceutical ingredient is hydrophilic or lipophobic, dissolving the active pharmaceutical ingredient in a hydrophilic or lipophobic solvent, in a hydrophilic or lipophobic surfactant, or combination thereof;

(b) contacting the first mixture and a lipophilic or hydrophobic surfactant to form a second mixture;

(c) contacting the second mixture with water and a hydrophilic or lipophobic surfactant to form a third mixture;

(d) contacting the third mixture with film forming ingredient to form a slurry; and

(e) casting the slurry on a substrate and curing to form the oral dissolvable film.

The present disclosure provides for an oral dissolvable film that includes: (a) active pharmaceutical ingredient; (b) surfactant; (c) solvent for the active pharmaceutical ingredient; (d) film matrix; and (e) water; wherein, (1) when the active pharmaceutical ingredient is lipophilic or hydrophobic: (i) the surfactant is lipophilic or hydrophobic, and (ii) the solvent for the active pharmaceutical ingredient is lipophilic or hydrophobic; and (2) when the active pharmaceutical ingredient is lipophobic or hydrophilic: (i) the surfactant is lipophobic or hydrophilic, and (ii) the solvent for the active pharmaceutical ingredient is lipophobic or hydrophilic.

The present disclosure also provides for an oral dissolvable film that includes: (a) lipophilic active pharmaceutical ingredient; (b) oil carrier for the lipophilic active pharmaceutical ingredient; (c) self–emulsifying lipophilic surfactant for the lipophilic active pharmaceutical ingredient; (d) one or more co–surfactants; (e) one or more hydrophilic surfactants; (f) film matrix; and (g) water.

The present disclosure also provides for an oral dissolvable film that includes: (a) hydrophilic active pharmaceutical ingredient; (b) water carrier for the hydrophilic active pharmaceutical ingredient; (c) hydrophilic surfactant for the hydrophilic active pharmaceutical ingredient; (d) one or more co–surfactants; (e) one or more self–emulsifying surfactants; (f) film matrix; and (g) water.

The present disclosure also provides for a method of forming an oral dissolvable film, the method includes: (a) dissolving an active pharmaceutical ingredient in a first solvent-system to form a first mixture, wherein: (i) when the active pharmaceutical ingredient is lipophilic or hydrophobic, dissolving the active pharmaceutical ingredient in a lipophilic or hydrophobic solvent, in a lipophilic or hydrophobic surfactant, or combination thereof; or (ii) when the active pharmaceutical ingredient is hydrophilic or lipophobic, dissolving the active pharmaceutical ingredient in a hydrophilic or lipophobic solvent, in a hydrophilic or lipophobic surfactant, or combination thereof; (b) contacting the first mixture and a lipophilic or hydrophobic surfactant to form a second mixture; (c) contacting the second mixture with water and a hydrophilic or lipophobic surfactant to form a third mixture; (d) contacting the third mixture with film forming ingredient to form a slurry; and (e) casting the slurry on a substrate and curing to form the oral dissolvable film.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides for an oral dissolvable film and a method of manufacturing and using the same.

Definitions

The term the following terms have the meanings ascribed to them unless specified otherwise.

The words “comprise,” “comprising,” “include,” “including,” and “includes” when used in this specification and claims are intended to specify the presence of stated substances, features, integers, components, or steps, but they do not preclude the presence or addition of one or more other substances, features, integers, components, steps, or combinations thereof.

CLAIMS

1. A method of forming an oral dissolvable film, the method comprising:

(a) dissolving an active pharmaceutical ingredient in a first solvent-system to form a first mixture, wherein:

(i) when the active pharmaceutical ingredient is lipophilic or hydrophobic, dissolving the active pharmaceutical ingredient in a lipophilic or hydrophobic solvent, in a lipophilic or hydrophobic surfactant, or combination thereof; or

(ii) when the active pharmaceutical ingredient is hydrophilic or lipophobic, dissolving the active pharmaceutical ingredient in a hydrophilic or lipophobic solvent, in a hydrophilic or lipophobic surfactant, or combination thereof;

(b) contacting the first mixture and a lipophilic or hydrophobic surfactant to form a second mixture;

(c) contacting the second mixture with water and a hydrophilic or lipophobic surfactant to form a third mixture;

(d) contacting the third mixture with film forming ingredient to form a slurry; and

(e) casting the slurry on a substrate and curing to form the oral dissolvable film.

2. The method of claim 1, wherein the film forming ingredient comprises at least one of mucoadhesive polymer, plasticizer, binder, filler, bulking agent, saliva stimulating agent, stabilizing and thickening agent, gelling agent, flavoring agent, taste masking agent, coloring agent, pigment, lubricant, release modifier, adjuvant, sweetening agent, solubilizer & emulsifier, fragrance, emulsifier, surfactant, pH adjusting agent, buffering agent, lipid, glidant, stabilizer, antioxidant, anti-tacking agent, humectant, solvent, permeation enhancer, and preservative.

3. The method of claim 1, wherein the lipophilic or hydrophobic solvent comprises an oil.

4. The method of claim 1, wherein the hydrophilic or lipophobic solvent comprises an aqueous liquid.

5. The method of claim 1, wherein the curing is carried out in a hot air oven at an air temperature of between about 38°C to about 110°C.

6. The method of claim 1, wherein the curing is carried out in a hot air oven at an air temperature of between about 45°C to about 80°C

7. The method of claim 1, wherein the curing is carried out in a hot air oven (at an air temperature of 50°C–70°C).

8. The method of claim 1, wherein the curing is carried out at a speed of between about 0.8 feet/min to about 2.5 feet/min.

9. The method of claim 1, wherein the curing is carried out at a speed of between about 0.8 feet/min to about 1.0 feet/min.

10. The method of claim 1, wherein the curing is carried out at a speed of between about 2.0 feet/min to about 2.5 feet/min.

11. The method of claim 1, wherein the oral dissolvable film comprises:

(a) hydrophilic active pharmaceutical ingredient;

(b) water carrier for the hydrophilic active pharmaceutical ingredient;

(c) hydrophilic surfactant for the hydrophilic active pharmaceutical ingredient;

(d) one or more co–surfactants;

(e) one or more self–emulsifying surfactants;

(f) film matrix; and

(g) water.

12. The method of claim 1, wherein the oral dissolvable film is configured to self-emulsify within 20 seconds upon contact with an oral mucosal surface of a subject.

13. The method of claim 1, wherein the oral dissolvable film is configured to form an oil–in–water (O/W) emulsion within 20 seconds upon contact with an oral mucosal surface of a subject.

14. The method of claim 1, wherein the oral dissolvable film is configured to form an oil–in–water (O/W) emulsion having an average droplet size of 0.1 microns to 120 microns within 20 seconds upon contact with an oral mucosal surface of a subject.

15. The method of claim 1, wherein the oral dissolvable film is configured to form an oil–in–water (O/W) emulsion having an average droplet size of

d(10): 0.5-10 micron,

d(50): 1-20 micron, and

d(90): 15-100 micron

within 20 seconds upon contact with an oral mucosal surface of a subject.

16. The method of claim 1, wherein the oral dissolvable film is suitable for oral administration (PO), buccal administration, sublingual administration, or mucosal administration.

17. The method of claim 1, wherein the oral dissolvable film has a moisture content of 3–13 wt.%.

18. The method of claim 1, wherein the oral dissolvable film is configured to disintegrate within 15 minutes upon buccal administration to a subject.

19. The method of claim 1, wherein the oral dissolvable film is configured to disintegrate within 30 seconds upon oral (PO) administration to a subject.

20. The method of claim 1, wherein the oral dissolvable film is configured for in vitro disintegration (USP<701> In-vitro Disintegration method) within 30 seconds.

21. The method of claim 1, wherein the oral dissolvable film exhibits at least one pharmacokinetic parameter selected from, (i) Tmax of between about 45 min to about 120 min, (ii) Cmax of at least 3.5 ng/ml, and (iii) AUC_{0-t} of at least 13 ng/hr/ml.

22. The method of claim 1, wherein the oral dissolvable film exhibits at least one pharmacokinetic parameter selected from, (i) Tmax of 1.5 hr, (ii) Cmax of 4.4 ng/ml, and (iii) AUC_{0-t} of 13.5 ng/hr/ml.

23. The method of claim 1, wherein the oral dissolvable film exhibits an in vivo dissolution time of no more than 20 minutes.

24. The method of claim 1, wherein the oral dissolvable film exhibits a bioavailability of at least 15%.

25. The method of claim 1, wherein the oral dissolvable film exhibits a stability of at least about 96% after nine months as measured under 40°C/75% RH accelerated conditions.