concentration, until the drug gets excreted through the kidneys or through other metabolic routes (e.g., hepatic). As a result, IV drugs may cause unwanted side effects. Drugs administered via the IV route are significantly diluted in the venous blood volume and lungs before reaching the cardiac circulation.

[0011] Injecting a drug to the heart directly is usually a last-resort taken by a cardiologist as a life saving measure in an emergency. The doses of the drugs injected directly into the heart in this manner are usually less than their IV and/or oral doses.

[0012] In some cases, an unplanned surgery is necessary to save the patient's life. Of course, unplanned surgeries are expensive and risky to the patient.

[0013] Cardiac arrhythmias are associated with disabling symptoms like tightness around the chest, palpitations, feeling tired, shortness of breath, and sometimes chest pain.

[0014] In view of the above, arrhythmias frequently result in emergency room (ER) visits, where intravenous drugs are administered, sometimes necessitating an extended stay in the hospital and in some cases also leading to unplanned invasive procedures. Pipeline Insights: Antiarrhythmics, Datamonitor (06/2006); and TWISS et al., "Efficacy of Calcium Channel Blockers as Maintenance Therapy for Asthma," British J of Clinical Pharmacology (November 2001).

[0015] There remains, however, a need for improved compositions and methods for treating heart conditions. Accordingly, there also remains a need for methods of making these compositions.

SUMMARY

[0015a] In an aspect of the present disclosure, there is provided a kit, comprising:

(1) a pharmaceutical composition that comprises:

(a) a flecainide acetate,

(b) a cyclodextrin, and

(c) an acid;

(2) a receptacle containing said pharmaceutical composition; and

(3) instructions for use of a nebulizer to inhalationally administer a dose of said pharmaceutical composition in aerosol to a subject, wherein said dose contains from 50 mg to 250 mg of said flecainide acetate, and said aerosol of said pharmaceutical composition has droplets that have a mass median aerodynamic diameter of less than 10 μm; and

wherein said pharmaceutical composition is in the form of a liquid solution that has:

(i) said flecainide acetate at a concentration range of 65 mg/mL to 95 mg/mL;

(ii) said cyclodextrin at a concentration of from 10% (w/v) to 30% (w/v) of said liquid solution;

(iii) said acid at a concentration of from 2 mM to 10 mM; and

(iv) a pH range of from 5.5 to 6.5 when said pH is measured at room temperature.

[0015b] In another aspect of the present disclosure, there is provided a pharmaceutical composition, comprising:

(1) a therapeutically effective amount of a flecainide acetate,

(2) a cyclodextrin, and

(3) an acid,

wherein said pharmaceutical composition is in the form of a liquid solution that has said flecainide acetate at a concentration range of 60 mg/mL to 120 mg/mL, said cyclodextrin at a concentration of from 5% (w/v) to 50% (w/v) of said liquid solution, said acid at a concentration of 2 mM to 10 mM, and a pH range of 5.5 to 6.3 when measured at room temperature.

[0015c] In a further aspect of the present disclosure, there is provided a unit dose of a pharmaceutical composition that comprises: a flecainide acetate, a cyclodextrin, and an acid,

wherein said pharmaceutical composition is in the form of a liquid solution that has said flecainide acetate at a concentration range of 60 mg/mL to 120 mg/mL, said cyclodextrin at a concentration of from 5% (w/v) to 50% (w/v) of said liquid solution, said acid at a concentration of 2 mM to 10 mM, and a pH range of 5.5 to 6.3 when measured at room temperature, and

wherein said unit dose comprises from 50 mg to 350 mg of said flecainide acetate.

[0016] Described herein, in some examples, is a pharmaceutical composition, comprising: a therapeutically effective amount of a salt of flecainide, wherein the pharmaceutical composition is in the form of a liquid solution that has the salt of flecainide at a concentration above 60 mg/mL.

[0017] In some cases, the pharmaceutical composition further comprises a cyclodextrin. In some cases, a pH of the solution is above 5.5 when the pH is measured at room temperature. In some cases, a pH of the solution is from about 5.5 to about 6.5 when the pH is measured at room temperature. In some cases, the pharmaceutical composition further comprises a cyclodextrin, and wherein a pH of the solution is above 5.5 when the pH is measured at room temperature. In some cases, the cyclodextrin is selected from the group consisting of: α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin, derivatized α -cyclodextrins, derivatized β-cyclodextrins, and derivatized γ-cyclodextrins. In some cases, the cyclodextrin is selected from the group consisting of: α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin, hydroxypropyl-β-cyclodextrin,

CLAIMS

What is claimed is:

1. A kit, comprising:

(1) a pharmaceutical composition that comprises:

(a) a flecainide acetate,

(b) a cyclodextrin, and

(c) an acid;

(2) a receptacle containing said pharmaceutical composition; and

(3) instructions for use of a nebulizer to inhalationally administer a dose of said pharmaceutical composition in aerosol to a subject, wherein said dose contains from 50 mg to 250 mg of said flecainide acetate, and said aerosol of said pharmaceutical composition has droplets that have a mass median aerodynamic diameter of less than 10 μm; and

wherein said pharmaceutical composition is in the form of a liquid solution that has:

(i) said flecainide acetate at a concentration range of 65 mg/mL to 95 mg/mL;

(ii) said cyclodextrin at a concentration of from 10% (w/v) to 30% (w/v) of said liquid solution;

(iii) said acid at a concentration of from 2 mM to 10 mM; and

(iv) a pH range of from 5.5 to 6.5 when said pH is measured at room temperature.

2. The kit of claim 1, wherein said concentration of said flecainide acetate is from 70 mg/mL to 80 mg/mL.

3. The kit of claim 1, wherein said concentration of said flecainide acetate is about 75 mg/mL.

4. The kit of claim 1, wherein said acid is selected from the group consisting of: acetic acid, citric acid, nitric acid, hydrochloric acid, ascorbic acid, lactic acid, sulfuric acid, maleic acid, tartaric acid, phosphoric acid, aconitic acid, adipic acid, benzoic acid, caprylic acid, cholic acid, formic acid, glutamic acid, lactic acid, propionic acid, sorbic acid, stearic acid, and succinic acid.

5. The kit of claim 1, wherein said acid comprises acetic acid.

6. The kit of claim 1, wherein said acid comprises citric acid.

7. The kit of claim 1, wherein said concentration of said acid is about 5 mM.

8. The kit of claim 1, wherein said pH of said liquid solution is about 5.9 when measured at room temperature.

9. The kit of claim 1, wherein said cyclodextrin is selected from the group consisting of: α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin, hydroxypropyl-β-cyclodextrin, hydroxyethyl-β-cyclodextrin, hydroxypropyl-γ-cyclodextrin, hydroxyethyl-γ-cyclodextrin, dihydroxypropyl-β-cyclodextrin, glucosyl-α-cyclodextrin, glucosyl-β-cyclodextrin, diglucosyl-β-cyclodextrin, maltosyl-α-cyclodextrin, maltosyl-β-cyclodextrin, maltosyl-γ-cyclodextrin, maltotriosyl-β-cyclodextrin, maltotriosyl-γ-cyclodextrin, dimaltosyl-β-cyclodextrin, succinyl-β-cyclodextrin, 6A-amino-6A-deoxy-N-(3-hydroxypropyl)-β-cyclodextrin, sulfobutylether-β-cyclodextrin, sulfobutylether-γ-cyclodextrin, sulfoalkylether-β-cyclodextrins, and sulfoalkylether-γ-cyclodextrins.

10. The kit of claim 1, wherein said cyclodextrin comprises hydroxypropyl-β-cyclodextrin.

11. The kit of claim 1, wherein said concentration of said cyclodextrin is from 15% (w/v) to 25% (w/v) of said liquid solution.

12. The kit of claim 1, wherein said concentration of said cyclodextrin is about 20% (w/v) of said liquid solution.

13. The kit of claim 1, wherein said pharmaceutical composition further comprises an artificial sweetener.

14. The kit of claim 1, wherein said dose contains from 150 mg to 250 mg of said flecainide acetate.

15. The kit of claim 14, wherein said dose contains about 200 mg of said flecainide acetate.

16. The kit of claim 1, further comprising a nebulizer selected from the group consisting of: a breath-actuated jet nebulizer, a vibrating mesh nebulizer, and an ultrasonic nebulizer.

17. The kit of claim 1, wherein said pharmaceutical composition is formulated for administration via a breath-actuated jet nebulizer, a vibrating mesh nebulizer, or an ultrasonic nebulizer.

18. The kit of claim 14, wherein said dose contains about 175 mg of said flecainide acetate.

19. The kit of claim 1, wherein:

(a) said concentration of said flecainide acetate is about 75 mg/mL;

(b) said acid comprises acetic acid; and

(c) said cyclodextrin comprises hydroxypropyl-β-cyclodextrin, and said concentration of said cyclodextrin is about 20% (w/v) of said liquid solution.

20. A pharmaceutical composition, comprising:

(1) a therapeutically effective amount of a flecainide acetate,

(2) a cyclodextrin, and

(3) an acid,

wherein said pharmaceutical composition is in the form of a liquid solution that has said flecainide acetate at a concentration range of 60 mg/mL to 120 mg/mL, said cyclodextrin at a concentration of from 5% (w/v) to 50% (w/v) of said liquid solution, said acid at a concentration of 2 mM to 10 mM, and a pH range of 5.5 to 6.3 when measured at room temperature.

21. The pharmaceutical composition of claim 20, wherein said concentration of said cyclodextrin is from 15% (w/v) to 25% (w/v) of said liquid solution.

22. The pharmaceutical composition of claim 20, wherein said concentration of said cyclodextrin is about 20% (w/v) of said liquid solution.

23. The pharmaceutical composition of claim 20, wherein said cyclodextrin is selected from the group consisting of: α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin, hydroxypropyl-β-cyclodextrin, hydroxyethyl-β-cyclodextrin, hydroxypropyl-γ-cyclodextrin, hydroxyethyl-γ-cyclodextrin, dihydroxypropyl-β-cyclodextrin, glucosyl-α-cyclodextrin, glucosyl-β-cyclodextrin, diglucosyl-β-cyclodextrin, maltosyl-α-cyclodextrin, maltosyl-β-cyclodextrin, maltosyl-γ-cyclodextrin, maltotriosyl-β-cyclodextrin, maltotriosyl-γ-cyclodextrin, dimaltosyl-β-cyclodextrin, succinyl-β-cyclodextrin, 6A-amino-6A-deoxy-N-(3-hydroxypropyl)-β-cyclodextrin,

sulfobutylether-β-cyclodextrin, sulfobutylether-γ-cyclodextrin, sulfoalkylether-β-cyclodextrins, and sulfoalkylether-γ-cyclodextrins.

24. The pharmaceutical composition of claim 20, wherein said cyclodextrin comprises hydroxypropyl-β-cyclodextrin.

25. The pharmaceutical composition of claim 20, wherein said concentration of said flecainide acetate is from 65 mg/mL to 95 mg/mL.

26. The pharmaceutical composition of claim 20, wherein said concentration of said flecainide acetate is about 75 mg/mL.

27. The pharmaceutical composition of claim 20, wherein said acid is selected from the group consisting of: acetic acid, citric acid, nitric acid, hydrochloric acid, sulfuric acid, maleic acid, tartaric acid, phosphoric acid, aconitic acid, adipic acid, ascorbic acid, benzoic acid, caprylic acid, cholic acid, formic acid, glutamic acid, lactic acid, propionic acid, sorbic acid, stearic acid, and succinic acid.

28. The pharmaceutical composition of claim 20, wherein said acid comprises acetic acid.

29. The pharmaceutical composition of claim 20, wherein said acid comprises citric acid.

30. The pharmaceutical composition of claim 20, wherein said concentration of said acid is about 5 mM.

31. The pharmaceutical composition of claim 20, wherein said pH of said liquid solution is about 5.9 when measured at room temperature.

32. The pharmaceutical composition of claim 20, wherein said pharmaceutical composition further comprises a sweetener.

33. The pharmaceutical composition of claim 33, wherein said sweetener is selected from the group consisting of acesulfame potassium, aspartame, cyclamate, mogrosides, saccharin, *stevia*, sucralose, neotame, mannitol, sorbitol, xylitol, lactitol, isomalt, maltitol, and pharmaceutically acceptable salts thereof.

34. The pharmaceutical composition of claim 20, wherein said pharmaceutical composition is formulated for administration via inhalation.

35. A unit dose of a pharmaceutical composition that comprises: a flecainide acetate, a cyclodextrin, and an acid,
wherein said pharmaceutical composition is in the form of a liquid solution that has said flecainide acetate at a concentration range of 60 mg/mL to 120 mg/mL, said cyclodextrin at a concentration of from 5% (w/v) to 50% (w/v) of said liquid solution, said acid at a concentration of 2 mM to 10 mM, and a pH range of 5.5 to 6.3 when measured at room temperature, and
wherein said unit dose comprises from 50 mg to 350 mg of said flecainide acetate.

36. The unit dose of claim 35, comprising from 250 mg to 350 mg of said flecainide acetate.

37. The unit dose of claim 36, comprising from 100 mg to 250 mg of said flecainide acetate.

38. The unit dose of claim 37, wherein:
(i) said concentration of said flecainide acetate is about 75 mg/mL;
(ii) said acid comprises acetic acid; and
(iii) said cyclodextrin comprises hydroxypropyl-β-cyclodextrin, and said concentration of said cyclodextrin is about 20% (w/v) of said liquid solution.

39. The unit dose of claim 35, wherein said concentration of flecainide acetate is from 65 mg/mL to 95 mg/mL.

40. The unit dose of claim 35, wherein said cyclodextrin comprises hydroxypropyl-β-cyclodextrin, and said concentration of said cyclodextrin is from 15% (w/v) to 25% (w/v) of said liquid solution.

41. The unit dose of claim 40, wherein said pH is 5.8 to 6.2 when measured at room temperature.

42. The composition of claim 20, wherein:

(a) said concentration of said flecainide acetate is about 75 mg/mL;

(b) said acid comprises acetic acid; and

(c) said cyclodextrin comprises hydroxypropyl-β-cyclodextrin, and said concentration of said cyclodextrin is about 20% (w/v) of said liquid solution.