In one aspect, disclosed herein is a use of a liquid pharmaceutical formulation in the manufacture of a medicament for treating edema, hypertension or heart failure or for the symptoms of edema, hypertension or heart failure, wherein the liquid pharmaceutical formulation comprises: 2 mg/mL to 20 mg/mL furosemide, or a pharmaceutically acceptable salt thereof, wherein furosemide is the sole therapeutically active agent in the liquid pharmaceutical formulation; and greater than or equal to 50 mM tris(hydroxymethyl)aminomethane; wherein the liquid pharmaceutical formulation has a pH between 7.2 to 8.5, and the molar ratio of tris(hydroxymethyl)aminomethane to furosemide is greater than or equal to 1.5.

In another aspect, disclosed herein is a liquid pharmaceutical formulation comprising: 2 mg/mL to 20 mg/mL furosemide, or a pharmaceutically acceptable salt thereof, wherein furosemide is the sole therapeutically active agent in the liquid pharmaceutical formulation; and greater than or equal to 50 mM tris(hydroxymethyl)aminomethane, wherein the liquid pharmaceutical formulation has a pH between 7.2 to 8.5, and the molar ratio of tris(hydroxymethyl)aminomethane to furosemide is greater than or equal to 1.5.

In another aspect, disclosed herein is a liquid pharmaceutical formulation as disclosed herein for use as a medicament.

Thus, in one example, the present teachings provide methods for treating a patient with edema or hypertension, which can be due to congestive heart failure, or renal or hepatic insufficiency or failure. The methods generally include administering to a patient a pharmaceutical formulation of the present teachings, where the pharmaceutical formulation includes furosemide, or a pharmaceutically acceptable salt, hydrate or ester thereof; and a pharmaceutically acceptable buffer including Tris, where the concentration of Tris in the pharmaceutical formulation can be greater than or equal to about 50 mM, and the pharmaceutical formulation has a molar excess of Tris to furosemide and a pH in the range of about 7 to about 8.5. In various examples, the pharmaceutical formulation can be isoosmotic.

In particular examples, methods of treating a patient with or exhibiting the symptoms of edema, hypertension or heart failure can include

administering subcutaneously to a patient using a patch device a pharmaceutical formulation including between about 6 mg/mL to about 10 mg/mL of furosemide, or a pharmaceutically acceptable salt, hydrate or ester thereof; and a pharmaceutically acceptable buffer comprising Tris, where the concentration of Tris in the pharmaceutical formulation is greater than or equal to about 50 mM; and where the molar ratio of Tris to furosemide is greater than or equal to 1.65, and the pharmaceutical formulation has a pH between about 7.2 to about 8 and is isoosmotic.

In another example, the present teachings provide pharmaceutical formulations including furosemide, or pharmaceutically acceptable salt, hydrate or ester thereof; and a pharmaceutically acceptable buffer including Tris in an amount greater than or equal to about 50 mM, where the molar ratio of Tris to furosemide is greater than one and the pharmaceutical formulation can have a pH in the range of about 7 to about 8.5 and can be isoosmotic.

The foregoing as well as other features and advantages of the present teachings will be more fully understood from the following figures, description, examples, and claims.

CLAIMS

1. Use of a liquid pharmaceutical formulation in the manufacture of a medicament for treating edema, hypertension or heart failure or for the symptoms of edema, hypertension or heart failure, wherein the liquid pharmaceutical formulation comprises:

2 mg/mL to 20 mg/mL furosemide, or a pharmaceutically acceptable salt thereof, wherein furosemide is the sole therapeutically active agent in the liquid pharmaceutical formulation; and

greater than or equal to 50 mM tris(hydroxymethyl)aminomethane;

wherein the liquid pharmaceutical formulation has a pH between 7.2 to 8.5, and the molar ratio of tris(hydroxymethyl)aminomethane to furosemide is greater than or equal to 1.5.

2. The use of claim 1, wherein the liquid pharmaceutical formulation is to be administered subcutaneously.

3. The use of claim 2, wherein the liquid pharmaceutical formulation is to be administered subcutaneously using a pump device.

4. The use of claim 3, wherein the pump device is a patch device.

5. The use of claim 1, wherein the liquid pharmaceutical formulation is to be administered intravenously.

6. The use of any one of claims 1-5, wherein the liquid pharmaceutical formulation comprises 2 mg/mL to 15 mg/mL furosemide.

7. The use of any one of claims 1-6, wherein the tris(hydroxymethyl)aminomethane is derived from tris(hydroxymethyl)aminomethane-HCl.

8. The use of any one of claims 1-7, wherein the liquid pharmaceutical formulation comprises 50 mM to 250 mM Tris.

9. The use of any one of claims 1-8, wherein liquid pharmaceutical formulation has a pH between 7.2 to 8.

10. The use of any one of claims 1-9, wherein the liquid pharmaceutical formulation further comprises hydrochloric acid, sodium hydroxide, or combinations thereof.

11. The use of any one of claims 1-10, wherein the liquid pharmaceutical formulation further comprises sodium chloride.

12. A liquid pharmaceutical formulation comprising:

2 mg/mL to 20 mg/mL furosemide, or a pharmaceutically acceptable salt thereof, wherein furosemide is the sole therapeutically active agent in the liquid pharmaceutical formulation; and

greater than or equal to 50 mM tris(hydroxymethyl)aminomethane,

wherein the liquid pharmaceutical formulation has a pH between 7.2 to 8.5, and the molar ratio of tris(hydroxymethyl)aminomethane to furosemide is greater than or equal to 1.5.

13. The liquid pharmaceutical formulation of claim 12, wherein the tris(hydroxymethyl)aminomethane is derived from tris(hydroxymethyl)aminomethane-HCl.

14. The liquid pharmaceutical formulation of claim 12 or 13, further comprising hydrochloric acid, sodium hydroxide, or combinations thereof.

15. The liquid pharmaceutical formulation of any one of claims 10-14, further comprising sodium chloride.

16. The liquid pharmaceutical formulation of any one of claims 10-15, comprising 2 mg/mL to 15 mg/mL of furosemide.

17. The liquid pharmaceutical formulation of any one of claims 10-16, wherein the tris(hydroxymethyl)aminomethane is derived from tris(hydroxymethyl)aminomethane-HCl.

18. The liquid pharmaceutical formulation of any one of claims 10-17 comprising 50 mM to 250 mM Tris.

19. The liquid pharmaceutical formulation of any one of claims 10-18, having a pH between 7.2 to 8.

20. The liquid pharmaceutical formulation of any one of claims 10-19 for use as a medicament.