In one aspect, the present disclosure refers to use of a liquid pharmaceutical formulation in the preparation of a medicament for treating edema, hypertension or heart failure or for treating a human exhibiting the symptoms of edema, hypertension or heart failure, wherein the liquid pharmaceutical formulation comprises: furosemide, or a pharmaceutically acceptable salt thereof, wherein furosemide is the sole therapeutically active agent in the liquid pharmaceutical formulation and the amount of furosemide in the pharmaceutical formulation is about 15 mg/mL or greater; and tris(hydroxymethyl)aminomethane, wherein the concentration of tris(hydroxymethyl)aminomethane in the liquid pharmaceutical formulation is in a range of 50 mM to 500 mM; wherein the liquid pharmaceutical formulation has a pH between about 7 to about 8.5, is isosmotic, and the molar ratio of tris(hydroxymethyl)aminomethane to furosemide is greater than or equal to one.

In another aspect, the present disclosure refers to a liquid pharmaceutical formulation comprising: furosemide, or a pharmaceutically acceptable salt thereof, wherein furosemide is the sole therapeutically active agent in the liquid pharmaceutical formulation and the amount of furosemide in the pharmaceutical formulation is about 15 mg/mL or greater; and tris(hydroxymethyl)aminomethane, wherein the concentration of tris(hydroxymethyl)aminomethane in the liquid pharmaceutical formulation is in a range of 50 mM to 500 mM, wherein the liquid pharmaceutical formulation has a pH between about 7 and about 8.5, is isosmotic, and the molar ratio of tris(hydroxymethyl)aminomethane to furosemide is greater than or equal to one.

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 preparation of a medicament for treating edema, hypertension or heart failure or for treating a human exhibiting the symptoms of edema, hypertension or heart failure, wherein the liquid pharmaceutical formulation comprises:

furosemide, or a pharmaceutically acceptable salt thereof, wherein furosemide is the sole therapeutically active agent in the liquid pharmaceutical formulation and the amount of furosemide in the pharmaceutical formulation is about 15 mg/mL or greater; and

tris(hydroxymethyl)aminomethane, wherein the concentration of tris(hydroxymethyl)aminomethane in the liquid pharmaceutical formulation is in a range of 50 mM to 500 mM;

wherein the liquid pharmaceutical formulation has a pH between about 7 to about 8.5, is isosmotic, and the molar ratio of tris(hydroxymethyl)aminomethane to furosemide is greater than or equal to one.

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 tris(hydroxymethyl)aminomethane is derived from tris(hydroxymethyl)aminomethane-HCl.

7. A liquid pharmaceutical formulation comprising:

furosemide, or a pharmaceutically acceptable salt thereof, wherein furosemide is the sole therapeutically active agent in the liquid pharmaceutical formulation and the

amount of furosemide in the pharmaceutical formulation is about 15 mg/mL or greater; and

tris(hydroxymethyl)aminomethane, wherein the concentration of tris(hydroxymethyl)aminomethane in the liquid pharmaceutical formulation is in a range of 50 mM to 500 mM,

wherein the liquid pharmaceutical formulation has a pH between about 7 and about 8.5, is isosmotic, and the molar ratio of tris(hydroxymethyl)aminomethane to furosemide is greater than or equal to one.

8. The liquid pharmaceutical formulation of claim 7, wherein the tris(hydroxymethyl)aminomethane is derived from tris(hydroxymethyl)aminomethane-HCl.

9. The liquid pharmaceutical formulation of claim 7 or 8, further comprising hydrochloric acid, sodium hydroxide, or combinations thereof.

10. The liquid pharmaceutical formulation of any one of claims 7-9, further comprising sodium chloride.

11. The liquid pharmaceutical formulation of any one of claims 7-10, wherein the liquid pharmaceutical formulation is loaded in a pump device.

12. The liquid pharmaceutical formulation of claim 11, wherein the pump device is a patch device.

13. The liquid pharmaceutical formulation of any one of claims 7-12 for use as a medicament.