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~~ 5 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~~ 250 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 ~~1.5~~two.

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~~ 5 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~~ 250 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 ~~1.5~~two.

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.

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~~ 5 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~~ 250 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 ~~1.5~~two.

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~~ 5 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~~ 250 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 ~~1.5~~two.

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.