lubricating the resultant granulation using the lubricant; and

compressing the lubricated granulation into desired form.

[0010] Also ~~provided~~ disclosed is a method of treating a disease selected from acute heart failure and chronic heart failure, comprising administering a pharmaceutical formulation described herein to a patient in need thereof.

[0010a] Also provided is use of a pharmaceutical formulation as described herein in the manufacture of a medicament for treating a disease selected from acute heart failure and chronic heart failure.

DESCRIPTION OF THE FIGURES

[0011] Figure 1 is a flow diagram for the preparation of immediate release (IR) tablets of omecamtiv mecarbil (25 mg); see Example 1.

[0012] Figure 2 is a flow diagram for the preparation of matrix modified release compositions; see Example 2.

[0013] Figure 3 is a flow diagram for the preparation of matrix modified release compositions; see, Examples 3-5.

[0014] Figure 4 shows the exposure of healthy volunteers (plasma concentration (ng/ml) v. time (h)), fasted (top) and fed (bottom) for an immediate release composition (IR) and two matrix modified release compositions (MTX-F1 and MTX-F2); the study was a randomized, open-label, 4-way crossover incomplete block design study in healthy adult subjects:

- 60 subjects; 1 site in the US
- 12 total treatments (each treatment taken 20 times)
- Various formulations; Each taken fasted or fed
- Each subject will be randomized to 1 sequence
- Each subject receives 4 out of 12 possible treatments
- Each period ~7 days; Study duration: 27 days (Period 4:5 days).

[0015] Figure 5 is a table with data for an immediate release composition (IR) and two matrix modified release compositions (MTX-F1 and MTX-F2).

[0016] Figure 6 shows drug release at two pHs (2 and 6.8) for a matrix formulation of omecamtiv mecarbil free base (top) and for a omecamtiv mecarbil dihydrochloride hydrate salt form, Form A (bottom).

[0017] Figure 7 shows an X-ray powder diffraction pattern (XRPD) for Form A.

[0018] Figure 8 shows an XRPD of a omecamtiv mecarbil dihydrochloride hydrate salt form at varying relative humidity conditions.

pharmaceutically acceptable hydrate, or a pharmaceutically acceptable hydrate of a pharmaceutically acceptable salt thereof;

15-35% w/w control release agent;

20-45% w/w pH modifying agent;

25-65% w/w filler; and

0.1-1.0% w/w lubricant.

14. A process for making a pharmaceutical formulation according to Claim 1, comprising:

blending a mixture comprising omecamtiv mecarbil, or a pharmaceutically acceptable salt, a pharmaceutically acceptable hydrate, or a pharmaceutically acceptable hydrate of a pharmaceutically acceptable salt thereof, a control release agent, a pH modifying agent, and a filler;

lubricating the blended mixture using a lubricant;

granulating the lubricated blend;

lubricating the resultant granulation using the lubricant; and

compressing the lubricated granulation into desired form.

15. The process of claim 14, wherein the omecamtiv mecarbil is present as omecamtiv mecarbil dihydrochloride hydrate.

16. A pharmaceutical formulation prepared by the process of claim 14 or 15.

17. ~~A method of treating a disease selected from acute heart failure and chronic heart failure, comprising administering~~ Use of a pharmaceutical formulation according to any one of Claims 1-13 or 16 in the manufacture of a medicament for treating a disease selected from acute heart failure ~~to a patient in need thereof~~.

18. A pharmaceutical formulation according to any one of Claims 1-13, wherein the exposure of omecamtiv mecarbil from two to twelve hours after dosing in humans remains between 40 and 70 ng/ml.

19. The pharmaceutical composition according to Claim 18, wherein the exposure of omecamtiv mecarbil from two to twelve hours after dosing in humans remains between 40 and 55 ng/ml.