There is a need for solid lipopeptide compositions that rapidly reconstitute (e.g., in less than about 5 minutes) in a pharmaceutical diluent to form reconstituted lipopeptide compositions that can be compounded as pharmaceutical compositions. For example, to reconstitute a 500 mg vial of lyophilized daptomycin for injection (CUBICI ®), the lyophilized powder is combined with 10 mL of 0.9% aqueous sodium chloride, allowed to stand for 10 minutes (or more) and then gently rotated or swirled "a few minutes" to form the reconstituted daptomycin composition prior to formation to prepare a parenteral daptomycin pharmaceutical composition.

There is also a need for solid daptomycin compositions with improved chemical stability in the solid and/or reconstituted form (i.e., higher total percent daptomycin purity over time), providing advantages of longer shelf life, increased tolerance for more varied storage conditions (e.g., higher temperature or humidity) and increased chemical stability after reconstitution as a liquid formulation for parenteral administration.

Summary

The present ~~invention~~ disclosure relates to solid lipopeptide compositions for reconstitution in aqueous diluent to form pharmaceutical compositions. The lipopeptide compositions are prepared by converting a pharmaceutically acceptable aqueous solution including the lipopeptide into the solid lipopeptide composition (e.g., by lyophilization, spray drying or the like). The solid lipopeptide composition can be subsequently reconstituted in an aqueous pharmaceutically acceptable diluent to form a pharmaceutical product for parenteral administration.

In a first embodiment, the time for reconstituting the solid lipopeptide compositions in the aqueous diluent can be unexpectedly reduced by increasing the pH of the aqueous lipopeptide solution (preferably to a pH of about 6.5-7.5, most preferably about 7.0) prior to lyophilizing the solution to form the solid lipopeptide composition. For example, solid daptomycin compositions prepared by lyophilizing liquid daptomycin solutions (without a sugar or glycine) at a pH of about 7.0 reconstituted more rapidly in 0.9% aqueous sodium chloride than otherwise comparable daptomycin formulations lyophilized at a pH of about 4.7.

The reconstitution rate of certain solid lipopeptide compositions in aqueous diluent was also accelerated by combining the lipopeptide with glycine or a sugar (preferably, a non-reducing sugar) prior to converting the solution to the solid lipopeptide. For example, 500 mg of the lyophilized pharmaceutical daptomycin compositions in Table 6 formed from

solutions including daptomycin and a non-reducing sugar or glycine at a pH of about 7.0 reconstituted in 0.9% aqueous sodium chloride in less than 2 minutes, with most compositions reconstituting in less than 1 minute.

The solid pharmaceutical lipopeptide preparations can be a product obtained by the following process: (a) forming an aqueous solution of the lipopeptide at a pH above the isoelectric point of the lipopeptide (e.g., above about 3.8 for daptomycin); (b) dissolving glycine or a sugar (preferably a non-reducing sugar) in the aqueous solution with the lipopeptide to form a liquid lipopeptide formulation; (c) adjusting the pH of the liquid lipopeptide formulation to about 6.5 to 7.5; and (d) converting the liquid lipopeptide formulation to the solid pharmaceutical lipopeptide composition (e.g., lyophilization). For example, a lyophilized daptomycin medicament preparation that reconstitutes in less than about 2 minutes in an aqueous 0.9% aqueous sodium chloride diluent can be prepared by: (a) forming an aqueous solution of daptomycin at a pH of about 4.5 - 5.0 (e.g., a pH of about 4.7); (b) adding a buffering agent including phosphate, citrate, maleate or a combination thereof to the aqueous solution of daptomycin to form a buffered daptomycin formulation; (c) dissolving one or more sugars in the buffered daptomycin formulation to form a buffered daptomycin sugar formulation containing about 2.5% w/v to about 25% w/v of the sugar(s) (e.g., about 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 1 1%, 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19%, 20%, 21%, 22%, 23%, or 24%), the sugar(s) being selected from the group consisting of trehalose, sucrose, mannitol, and combinations thereof; (d) adjusting the pH of the buffered daptomycin sugar formulation to a pH of about 6.5 to 7.5 (e.g., 7.0); and (e) lyophilizing the buffered daptomycin sugar formulation to form the solid pharmaceutical daptomycin composition. Preferably, the sugar(s) include sucrose, sucrose and mannitol, or trehalose.

In one aspect, there is provided a solid pharmaceutical daptomycin composition comprising at least one excipient selected from glycine and/or a sugar, characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 2 minutes at 25 degrees C, the solid pharmaceutical daptomycin composition obtainable by:

a. forming an aqueous daptomycin solution comprising 105 mg/mL (10.5% w/v) daptomycin at a pH of 6.5-7.5, and

b. converting the aqueous daptomycin formulation to the solid pharmaceutical daptomycin preparation.

In one aspect, there is provided a solid pharmaceutical daptomycin composition characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 2 minutes at 25 degrees C, the solid pharmaceutical daptomycin composition obtainable by:

a. forming an aqueous daptomycin solution comprising 105 mg/mL (10.5% w/v) daptomycin and 15% w/v sucrose at a pH of 7.0, and

b. converting the aqueous daptomycin formulation to the solid pharmaceutical daptomycin preparation.

In one aspect, there is provided a solid pharmaceutical daptomycin composition characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 5 minutes at 25 degrees C, the solid pharmaceutical daptomycin composition obtainable by:

a. forming an aqueous daptomycin solution comprising daptomycin and one or more sugars at a pH of 4.7, and

b. converting the aqueous daptomycin formulation to the solid pharmaceutical daptomycin preparation.

In one aspect, there is provided a solid pharmaceutical daptomycin composition characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 5 minutes at about 25 degrees C, the solid pharmaceutical daptomycin composition comprising daptomycin and at least one excipient selected from glycine and a sugar.

In one aspect, there is provided a solid pharmaceutical daptomycin composition characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 5 minutes at about 25 degrees C, wherein the solid pharmaceutical daptomycin composition is obtainable by:

a. forming an aqueous daptomycin solution comprising daptomycin at a pH of about 4.5-8.0, and

b. converting the aqueous daptomycin solution to the solid pharmaceutical daptomycin composition.

In a second embodiment, the present ~~invention~~ disclosure provides daptomycin compositions with improved daptomycin chemical stability, measured as higher total percent daptomycin purity over time (as determined by HPLC according to the method of Example 4).

Surprisingly, the daptomycin contained in solid preparations with certain preferred compositions (e.g., daptomycin combined with sucrose or trehalose) was more chemically stable than daptomycin in daptomycin solid preparations without sugar or glycine. The chemical stability of daptomycin in a solid form was measured by comparing total daptomycin purity measurements from multiple solid daptomycin preparations each obtained according to Example 4. Higher chemical stability was measured as higher comparative

daptomycin to form a buffered daptomycin sugar formulation; (d) adjusting the pH of the buffered daptomycin sugar formulation to about 6.5 to 8.0 (including, e.g., pH values of 6.5-7.5, 6.5-7.0, 6.5, 7.0. 7.5, 8.0, 7.0-8.0, 7.0-7.5 and values therebetween); and (e) lyophilizing the buffered daptomycin sugar formulation to form the solid pharmaceutical daptomycin preparation.

In one aspect, there is provided a vial comprising a solid pharmaceutical daptomycin composition as described herein, the vial containing 500 mg of daptomycin.

In one aspect, there is provided the vial as described herein for use in the treatment of a bacterial infection.

In one aspect, there is provided the use of a solid pharmaceutical daptomycin composition as described herein in the manufacture of a medicament for the treatment of a bacterial infection.

In one aspect, there is provided use of the pharmaceutical product as described herein for the manufacture of a medicament for the treatment of a bacterial infection.

In one aspect, there is provided a method of manufacturing a solid pharmaceutical daptomycin composition characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 2 minutes at 25 degrees C, the method of manufacturing the solid pharmaceutical daptomycin composition comprising the steps of:

a. forming an aqueous daptomycin solution comprising 105 mg/mL (10.5% w/v) daptomycin and 15% w/v sucrose at a pH of 7.0, and

b. converting the aqueous daptomycin formulation to the solid pharmaceutical daptomycin preparation.

In one aspect, there is provided a pharmaceutical product comprising a solid pharmaceutical daptomycin composition as described herein and a pharmaceutically acceptable diluent.

In one aspect, there is provided a method of manufacturing a solid pharmaceutical daptomycin composition, the method comprising:

a. forming an aqueous daptomycin solution comprising daptomycin and at least one excipient selected from glycine and a sugar at a pH of about 4.5-8.0, and

b. converting the aqueous daptomycin solution to the solid pharmaceutical daptomycin composition.

In one aspect, there is provided a method of manufacturing a solid pharmaceutical daptomycin composition, the method comprising:

a. forming an aqueous daptomycin solution comprising daptomycin at a pH of about 4.5-8.0, and

b. converting the aqueous daptomycin solution to the solid pharmaceutical daptomycin composition.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this ~~invention~~ disclosure belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present ~~invention~~disclosure, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

Other features and advantages of the ~~invention~~ disclosure will be apparent from the following detailed description, and from the claims.

Brief Description of the Drawings

Figure 1 is the chemical structure of daptomycin.

Figure 2 is the chemical structure of anhydro-daptomycin.

Figure 3 is the chemical structure of the beta-isomer of daptomycin.

Figure 4 is the chemical structure of the lactone hydrolysis product of daptomycin.

Figure 5 is Table 6 listing examples of preferred daptomycin compositions. These compositions were prepared as liquid solutions, then lyophilized to provide solid pharmaceutical daptomycin preparations that reconstitute in an aqueous pharmaceutical diluent within less than 2 minutes (including compositions that reconstitute in less than 1 minute). In Table 6, "Recon time" refers to the time required for about 500 mg the lyophilized daptomycin composition described in the "Formulation (solid state)" column to dissolve in 10 mL of 0.9% aqueous sodium chloride at room temperature (about 25 degrees C).

Figure 6 is Table 7 listing examples of other daptomycin compositions. These compositions were prepared as liquid solutions, then lyophilized to provide solid pharmaceutical lipopeptide preparations that reconstitute in an aqueous pharmaceutical diluent within 2 minutes or more. In Table 7, "Recon time" refers to the time required for

CLAIMS

1. A solid pharmaceutical daptomycin composition comprising at least one excipient selected from glycine and/or a sugar, characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 2 minutes at 25 degrees C, the solid pharmaceutical daptomycin composition obtainable by:
   a. forming an aqueous daptomycin solution comprising 105 mg/mL (10.5% w/v) daptomycin at a pH of 6.5-7.5, and
   b. converting the aqueous daptomycin formulation to the solid pharmaceutical daptomycin preparation.
2. The solid pharmaceutical daptomycin composition of claim 1, wherein the aqueous daptomycin solution is formed by combining daptomycin at a concentration of 125 – 130 mg/mL with water and sodium hydroxide.
3. The solid pharmaceutical daptomycin composition of claim 2, wherein the sodium hydroxide is provided to the aqueous daptomycin solution as 3N NaOH.
4. The solid pharmaceutical daptomycin composition of claim 3, wherein the aqueous daptomycin solution is formed at a temperature of 2 - 10°C.
5. The solid pharmaceutical daptomycin composition of claim 1, wherein the aqueous daptomycin solution is converted to the solid pharmaceutical composition by lyophilization.
6. The solid pharmaceutical daptomycin composition of claim 4, wherein the aqueous daptomycin solution is converted to the solid pharmaceutical composition by lyophilization.
7. The solid pharmaceutical daptomycin composition of claim 1, wherein the at least one excipient is glycine.
8. The solid pharmaceutical daptomycin composition of claim 1, wherein the at least one excipient is a non-reducing sugar.
9. The solid pharmaceutical daptomycin composition of claim 1, wherein the at least one excipient is sucrose.
10. The solid pharmaceutical daptomycin composition of claim 6, further comprising sucrose.
11. The solid pharmaceutical daptomycin composition of claim 9, wherein the aqueous daptomycin solution comprises 15% sucrose at a pH of 7.0.
12. A vial comprising the solid pharmaceutical daptomycin composition of any one of claims 1-11, the vial containing 500 mg of daptomycin.
13. The vial of claim 12 containing the solid pharmaceutical daptomycin composition dissolved in about 10 mL of 0.9% aqueous sodium chloride.
14. Use of the solid pharmaceutical daptomycin composition in any one of claims 1-11 in the manufacture of a medicament for the treatment of a bacterial infection.
15. The vial in any one of claims 12-13 for use in the treatment of a bacterial infection.

16. A solid pharmaceutical daptomycin composition characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 2 minutes at 25 degrees C, the solid pharmaceutical daptomycin composition obtainable by:
    a. forming an aqueous daptomycin solution comprising 105 mg/mL (10.5% w/v) daptomycin and 15% w/v sucrose at a pH of 7.0, and
    b. converting the aqueous daptomycin formulation to the solid pharmaceutical daptomycin preparation.
17. A solid pharmaceutical daptomycin composition characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 5 minutes at 25 degrees C, the solid pharmaceutical daptomycin composition obtainable by:
    a. forming an aqueous daptomycin solution comprising daptomycin and one or more sugars at a pH of 4.7, and
    b. converting the aqueous daptomycin formulation to the solid pharmaceutical daptomycin preparation.
18. The solid pharmaceutical daptomycin composition of claim 17, wherein the aqueous daptomycin solution comprises 105 mg/mL (10.5% w/v) daptomycin and one or more sugars selected from the group consisting of: sucrose, trehalose, mannitol, lactose, maltose, dextrose, and fructose.
19. The solid pharmaceutical daptomycin composition of claim 18, further characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 2 minutes.
20. A method of manufacturing a solid pharmaceutical daptomycin composition characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 2 minutes at 25 degrees C, the method of manufacturing the solid pharmaceutical daptomycin composition comprising the steps of:
    a. forming an aqueous daptomycin solution comprising 105 mg/mL (10.5% w/v) daptomycin and 15% w/v sucrose at a pH of 7.0, and
    b. converting the aqueous daptomycin formulation to the solid pharmaceutical daptomycin preparation.
21. A solid pharmaceutical daptomycin composition characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 5 minutes at about 25 degrees C, the solid pharmaceutical daptomycin composition comprising daptomycin and at least one excipient selected from glycine and a sugar.
22. The solid pharmaceutical daptomycin composition of claim 21, wherein the sugar is a non-reducing sugar.

23. The solid pharmaceutical daptomycin composition of claim 22, wherein the molar ratio of daptomycin to the sugar is about 1:1.12 to about 1:21.32.
24. The solid pharmaceutical daptomycin composition of claim 22 or 23, wherein the sugar is selected from trehalose, sucrose, and mannitol.
25. The solid pharmaceutical daptomycin composition of claim 21, wherein the solid pharmaceutical daptomycin composition comprises daptomycin and trehalose.
26. The solid pharmaceutical daptomycin composition of claim 25, wherein the molar ratio of daptomycin to trehalose is about 1:2.13 to about 1:21.32.
27. The solid pharmaceutical daptomycin composition of claim 21, wherein the solid pharmaceutical daptomycin composition comprises daptomycin and sucrose.
28. The solid pharmaceutical daptomycin composition of claim 27, wherein the molar ratio of daptomycin to sucrose is about 1:1.12 to about 1:8.98.
29. The solid pharmaceutical daptomycin composition of claim 21, wherein the solid pharmaceutical daptomycin composition comprises daptomycin and mannitol.
30. The solid pharmaceutical daptomycin composition of claim 29, wherein the molar ratio of daptomycin to mannitol is about 1:2.52 to about 1:5.04.
31. The solid pharmaceutical daptomycin composition of any one of claims 21-30, wherein the solid pharmaceutical daptomycin composition is obtainable by:
    a. forming an aqueous daptomycin solution comprising daptomycin and said excipient at a pH of about 4.5-8.0, and
    b. converting the aqueous daptomycin solution to the solid pharmaceutical daptomycin composition.
32. A solid pharmaceutical daptomycin composition characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 5 minutes at about 25 degrees C, wherein the solid pharmaceutical daptomycin composition is obtainable by:
    a. forming an aqueous daptomycin solution comprising daptomycin at a pH of about 4.5-8.0, and
    b. converting the aqueous daptomycin solution to the solid pharmaceutical daptomycin composition.
33. The solid pharmaceutical daptomycin composition of claim 31 wherein said Step a comprises forming an aqueous daptomycin solution at a pH of about 4.7-7.5.
34. The solid pharmaceutical daptomycin composition of claim 31 wherein said Step a comprises forming an aqueous daptomycin solution at a pH of about 5.0-7.5.
35. The solid pharmaceutical daptomycin composition of claim 32, wherein said Step a comprises forming an aqueous daptomycin solution at a pH of about 4.7-7.0.
36. The solid pharmaceutical daptomycin composition of claim 31 or 32, wherein said Step a comprises forming an aqueous daptomycin solution at a pH of about 6.5-7.5.

37. The solid pharmaceutical daptomycin composition of any one of claims 31-36, wherein the aqueous daptomycin solution further comprises a buffering agent.
38. The solid pharmaceutical daptomycin composition of any one of claims 31-37, wherein Step b comprises converting the aqueous daptomycin solution to a solid pharmaceutical composition by lyophilization, spray drying or fluid bed drying.
39. The solid pharmaceutical daptomycin composition of any one of claims 22-30, characterized in that an amount of the solid pharmaceutical daptomycin composition containing 500 mg of daptomycin dissolves in 10 mL of 0.9% aqueous sodium chloride in less than 2 minutes at about 25 degrees C.
40. A pharmaceutical product comprising the solid pharmaceutical daptomycin composition of any one of claims 21-39 and a pharmaceutically acceptable diluent.
41. Use of the solid pharmaceutical daptomycin composition in any one of claims 21-39 in the manufacture of a medicament for the treatment of a bacterial infection.
42. Use of the pharmaceutical product of claim 40 for the manufacture of a medicament for the treatment of a bacterial infection.
43. A method of manufacturing a solid pharmaceutical daptomycin composition, the method comprising:
    a. forming an aqueous daptomycin solution comprising daptomycin and at least one excipient selected from glycine and a sugar at a pH of about 4.5-8.0, and
    b. converting the aqueous daptomycin solution to the solid pharmaceutical daptomycin composition.
44. A method of manufacturing a solid pharmaceutical daptomycin composition, the method comprising:
    a. forming an aqueous daptomycin solution comprising daptomycin at a pH of about 4.5-8.0, and
    b. converting the aqueous daptomycin solution to the solid pharmaceutical daptomycin composition.
45. The method of claim 43, wherein said Step a comprises forming an aqueous daptomycin solution at a pH of about 4.7-7.5.
46. The method of claim 43, wherein said Step a comprises forming an aqueous daptomycin solution at a pH of about 5.0-7.5.
47. The method of claim 44, wherein said Step a comprises forming an aqueous daptomycin solution at a pH of about 4.7-7.0.
48. The method of claim 43 or 44, wherein said Step a comprises forming an aqueous daptomycin solution at a pH of about 6.5-7.5.

CLAIMS

1. A solid daptomycin preparation having improved reconstitution and increased daptomycin stability in powder and reconstituted forms compared to a daptomycin preparation compounded according to Example 1a, the solid daptomycin preparation comprising daptomycin, sucrose, and a phosphate buffering agent; wherein
   a. the solid daptomycin preparation is at least 92% pure daptomycin, as calculated by ratio of absorbance (area under curve) for the daptomycin divided by total area under a curve measured by high performance liquid chromatography (HPLC) of the reconstituted daptomycin solution at 214 nm according to Table 3 and Example 4; and
   b. the daptomycin preparation is obtainable by:
      i. forming an aqueous daptomycin solution comprising 105 mg/mL (10.5% w/v) daptomycin, a 7.1 mg/mL (50 mM) sodium phosphate dibasic buffering agent and 150 mg/mL (15% w/v) sucrose at a pH of about 7.0; and
      ii. converting the aqueous daptomycin formulation to the solid daptomycin preparation.
2. A solid daptomycin preparation comprising daptomycin and a material selected from the group consisting of glycine, one or more sugars, and a combination of two or more non-reducing sugars; the daptomycin preparation characterized in that 500 mg of the solid pharmaceutical daptomycin composition dissolves in 10 mL of 0.9% aqueous sodium chloride in 4 minutes or less at 25 degrees C.
3. The daptomycin preparation of claim 1, wherein the sugar is a non-reducing sugar and the daptomycin preparation further comprises a buffering agent.
4. The daptomycin preparation of any of claims 2-3, wherein
   a. at least 92% pure daptomycin, as calculated by a ratio of absorbance (area under curve) for the daptomycin divided by the total area under the curve measured by high performance liquid chromatography (HPLC) of the reconstituted daptomycin solution at 214 nm according to Table 3 and Example 4, and
   b. the daptomycin preparation is characterized in that 500 mg of the solid pharmaceutical daptomycin composition dissolves in 10 mL of 0.9% aqueous sodium chloride in 1 minute or less at 25 degrees C at a pH of between 4.7 and 7.0.
5. The daptomycin preparation of any of claims 2-4, wherein the sugars are selected from sucrose, trehalose, and mannitol.

6. The daptomycin preparation of any of claims 2-4, wherein the sugars comprise sucrose, and the daptomycin preparation is obtainable by:

a. forming an aqueous daptomycin solution comprising daptomycin and about 15.0% - about 20% w/v sucrose at a pH of about 4.7-7.0, and

b. converting the aqueous daptomycin formulation to the solid pharmaceutical daptomycin preparation.

7. The daptomycin preparation of claim 6, wherein the aqueous daptomycin solution is at a pH of about 7.0.

8. The daptomycin preparation of any of claims 6-7, wherein the daptomycin preparation is obtainable by:

a. forming an aqueous daptomycin solution comprising daptomycin, a sodium phosphate dibasic buffering agent and about 15.0% w/v sucrose at a pH of about 7.0, and

b. converting the aqueous daptomycin formulation to the solid pharmaceutical daptomycin preparation.

9. A solid pharmaceutical daptomycin preparation obtainable by:

a. forming an aqueous daptomycin solution comprising daptomycin, 50 mM of a phosphate containing buffering agent, and about 15.0% sucrose at a pH of about 7.0, and

b. converting the aqueous daptomycin formulation to the solid pharmaceutical daptomycin preparation,

wherein the solid pharmaceutical daptomycin preparation is characterized in that 500 mg of the solid pharmaceutical daptomycin composition dissolves in 10 mL of 0.9% aqueous sodium chloride in about 2 minutes or less at 25 degrees C.

10. The solid pharmaceutical daptomycin preparation of claim 9, wherein at least 92% pure daptomycin, as calculated by ratio of absorbance (area under curve) for the daptomycin divided by total area under the curve measured by high performance liquid chromatography (HPLC) of the reconstituted daptomycin solution at 214 nm according to Table 3 and Example 4.

11. The solid pharmaceutical daptomycin preparation of any of claims 1-10, further characterized in that the daptomycin preparation has a lower amount of one or more substances selected from the group consisting of anhydro-daptomycin (Figure 2), beta-isomer of daptomycin (Figure 3) and a lactone hydrolysis product of daptomycin (Figure 4) after storage for 1 month at 40 degrees C under nitrogen, compared to a solid

pharmaceutical daptomycin preparation obtained by lyophilizing daptomycin and daptomycin-related compounds in 0.9% aqueous sodium chloride diluent, wherein the amount of the substances is detected by HPLC at 214 nm according to the method of Example 4.

12. A liquid pharmaceutical daptomycin preparation having increased daptomycin chemical stability and being obtainable by:
    a. forming an aqueous daptomycin solution comprising daptomycin, 50 mM of a phosphate containing buffering agent, and about 15.0% sucrose at a pH of about 7.0,
    b. converting the aqueous daptomycin formulation to the solid pharmaceutical daptomycin preparation, and then
    c. reconstituting the solid pharmaceutical daptomycin preparation an aqueous diluent to form liquid pharmaceutical daptomycin preparation.
13. The liquid pharmaceutical daptomycin preparation of claim 12, wherein the liquid pharmaceutical daptomycin preparation is formulated for intravenous administration.
14. An article of manufacture comprising the pharmaceutical daptomycin preparations of any of claims 1-13.
15. A method of manufacturing a solid pharmaceutical daptomycin preparation having increased daptomycin chemical stability measured by a decrease in the rate of formation of substances structurally similar to daptomycin in the solid daptomycin preparation for 3-14 days after reconstitution in an aqueous diluent, wherein the substances structurally similar to daptomycin are selected from the group consisting of the anhydro-daptomycin (Figure 2), the beta-isomer of daptomycin (Figure 3) and the lactone hydrolysis product of daptomycin (Figure 4); the rate of formation of substances structurally similar to daptomycin is measured according to Example 4; and the method comprises:
    a. forming an aqueous daptomycin solution comprising daptomycin and about 5.0 – 20.0% w/v sucrose at a pH of about 4.5 to 7.5, and
    b. converting the aqueous daptomycin formulation to the solid pharmaceutical daptomycin preparation.
16. The method of claim 15, wherein the aqueous daptomycin solution has a pH of about 7.0 and comprises daptomycin, 15% w/v sucrose and 50 nM sodium phosphate buffer; and the aqueous daptomycin solution is converted to the solid pharmaceutical daptomycin preparation by lyophilization.

17. The method of any of claims 15-16, characterized in that the % purity of daptomycin in the solid pharmaceutical daptomycin preparation as measured by the method of Example 4 is increased by at least 10%, relative to the % purity of daptomycin in a solid pharmaceutical daptomycin preparation without sucrose measured by the method of Example 4 after 6 months at 40 degrees C.

18. The method of claim 17, wherein a Daptomycin Stability Ratio at 40 degrees C as calculated by Example 5 is less than 1.000.

19. The solid pharmaceutical daptomycin preparation of any one of claims 1-11, wherein a Daptomycin Stability Ratio at 40 degrees C as calculated by Example 5 is less than 1.000.

20. The solid pharmaceutical daptomycin preparation of any one of claims 1-11, wherein a Daptomycin Stability Ratio at 40 degrees C as calculated by Example 5 is less than 0.500.

21. The solid pharmaceutical daptomycin preparation of any one of claims 1-11, wherein a Daptomycin Stability Ratio at 40 degrees C as calculated by Example 5 is less than 0.300.