

Claims

1. A sterile container, comprising a plinabulin monohydrate in crystalline solid form, wherein the plinabulin monohydrate exhibits an X-ray powder diffraction pattern comprising at least three characteristic peaks selected from the group consisting of peaks at approximately 8.1°, 13.1°, 16.3°, 23.9°, 24.2°, 24.5°, and 26.6° 2 θ .
2. A process of preparing a plinabulin monohydrate in crystalline form comprising the steps of: combining plinabulin and a first solvent system to form a first mixture, wherein the first solvent system is water, alcohol, or a mixture of water and alcohol, and wherein the alcohol, if present, is selected from the group consisting of methanol, ethanol, isopropyl alcohol, tert-butyl alcohol, n-butyl alcohol, and any mixtures thereof; heating the first mixture to a temperature in the range of about 50° C. to 90° C.; and cooling the first mixture to form a first precipitate, wherein the plinabulin monohydrate exhibits an X-ray powder diffraction pattern comprising at least three characteristic peaks selected from the group consisting of peaks at approximately 8.1°, 13.1°, 16.3°, 23.9°, 24.2°, 24.5°, and 26.6° 2 θ .
3. The process of claim 2, the first solvent system comprises ethanol.
4. The process of claim 2, wherein the heating step comprises: refluxing the first mixture; or heating the first mixture to a temperature in the range of about 70° C. to 78° C.
5. The process of claim 2, further comprising, prior to the cooling step, maintaining the first mixture at a temperature in the range of about 70° C. to 78° C. for about 1 hour.
6. The process of claim 2, wherein the cooling step comprises at least one of: adding water to the first mixture to produce the first precipitate; and stirring the first mixture for at least 4 hours.
7. The process of claim 2, wherein the heating step comprises heating the first mixture to a temperature of at least 65° C., and wherein the cooling step comprises cooling the first mixture to a temperature in the range of about 50° C. to 60° C.

8. The process of claim 2, further comprising one or more steps each independently selected from the group consisting of: filtering the heated first mixture prior to the first cooling step; filtering the first precipitate; washing the first precipitate; and analyzing the first precipitate using X-ray powder diffraction analysis.
9. The process of claim 2, further comprising the additional steps of: combining the first precipitate and a second solvent to form a second mixture, wherein the second solvent is water, alcohol, or a mixture of water and alcohol, and wherein the alcohol, if present, is selected from the group consisting of methanol, ethanol, isopropyl alcohol, tert-butyl alcohol, n-butyl alcohol, and mixtures thereof; heating the second mixture to a temperature in the range of about 50° C. to 90° C.; cooling the second mixture to a temperature in the range of about 15° C. to 30° C. to form a second precipitate; filtering the second precipitate; and washing the second precipitate.
10. The process of claim 9, wherein the second solvent is ethanol.
11. The process of claim 9, wherein the further heating step comprises: refluxing the second mixture; or heating the second mixture to a temperature in the range of about 70° C. to 78° C.
12. The process of claim 9, further comprising, prior to the further cooling step, maintaining the second mixture at a refluxing temperature for about 1 hour.
13. The process of claim 9, wherein the further cooling step comprises at least one of: adding water to the second mixture to produce the second precipitate; and stirring the second mixture for at least 4 hours.
14. The process of claim 9, further comprising the following steps: washing the first precipitate with an alcohol, selected from the group consisting of methanol, ethanol, isopropyl alcohol, tert-butyl alcohol, n-butyl alcohol, and mixtures thereof; collecting the alcohol wash; and adding the collected alcohol wash to the second mixture prior to the further heating step.
15. The process of claim 9, further comprising one or more steps each independently selected from the group consisting of: drying the second precipitate; and analyzing the second precipitate using X-ray powder diffraction analysis.

16. The process of claim 9, wherein the additional combining step, the additional cooling step, and the filtering step are repeated one or more times based on the amount of plinabulin in the second precipitate.
17. A process of preparing a plinabulin monohydrate in crystalline form, comprising mixing plinabulin, ethanol and water to form a mixture, wherein the plinabulin monohydrate exhibits an X-ray powder diffraction pattern comprising at least three characteristic peaks selected from the group consisting of peaks at approximately 8.1°, 13.1°, 16.3°, 23.9°, 24.2°, 24.5°, and 26.6° 2 θ .
18. The process of claim 17, wherein the volume ratio of ethanol to water is in the range of about 15:1 to about 25:1.
19. The process of claim 17, wherein the process is performed at a temperature in the range of about 20° C. to about 40° C.
20. The process of claim 17, further comprising stirring the mixture for at least 2 hours.