sonic energy source has a frequency between about 18 kHx and about 22 kHz, or about 20 kHz.

The methods may further comprise:

(e) receiving the plurality of particles through the outlet of the pressurizable chamber; and

(f) collecting the plurality of particles in a collection device.

In one embodiment, the compound is a taxane. The method of any one of claims 30-35 wherein the compound is a taxane. Exemplary taxanes may include paclitaxel, docetaxel, cabazitaxel, taxadiene, baccatin III, taxchinin A, brevifoliol, and taxuspine D, or a pharmaceutically acceptable salt thereof. In a specific embodiment, the taxane is selected from the group consisting of paclitaxel, docetaxel, and cabazitaxel, or a pharmaceutically acceptable salt thereof. In one embodiment, the solvent is selected from the group consisting of acetone, ethanol, methanol, dichloromethane, ethyl acetate, chloroform, acetonitrile, and suitable combinations thereof. In various embodiments, the compressed fluid and/or the anti-solvent may be super critical carbon dioxide. In one embodiment, the compound is paclitaxel and the solvent comprises acetone. In another embodiment, the compound is docetaxel and the solvent comprises ethanol. In a further embodiment, the method is carried out between 3 1.1°C to about 60°C, and at between about 1071 psi and about 1800 psi.

The invention also provides compound particles prepared by the method of any embodiment or combination of embodiments of the invention.

In another aspect, there is provided a composition, comprising particles including at least 95% by weight of a taxane, or a pharmaceutically acceptable salt thereof, wherein the particles have a specific surface area (SSA) of at least 18 m^2/g.

In another aspect, there is provided a use of the composition as described herein in the manufacture of a medicament for treating a tumor.

In another aspect, there is provided a method for making the composition as described herein comprising:

(a) introducing (i) a solution comprising at least one solvent and at least one solute comprising a taxane into a nozzle inlet, and (ii) a compressed fluid into an inlet of a vessel defining a pressurizable chamber;

(b) passing the solution out of a nozzle orifice and into the pressurizable chamber to produce an output stream of atomized droplets, wherein the nozzle orifice is located between 4 mm and 20 mm from a sonic energy source located within the output stream, wherein the sonic energy source produces sonic energy with an amplitude between 10% and 60% during the passing, and wherein the nozzle orifice has a diameter of between 20 μm and 125 μm;

(c) contacting the atomized droplets with the compressed fluid, to cause depletion of the solvent from the atomized droplets, to produce particles including at least 95% by weight of the taxane,

wherein steps (a), (b), and (c) are carried out under supercritical temperature and pressure for the compressed fluid

Brief Description of the Figures

Figure 1 is an electron micrograph of exemplary paclitaxel particles of the invention.

Figure 2 is an electron micrograph of raw paclitaxel particles.

Figure 3 illustrates a cross-section view of an example nozzle assembly, according to an example embodiment.

Figure 4 illustrates a cross-section view of another example nozzle assembly, according to an example embodiment.

Figure 5 illustrates a perspective view of a particle collection device, according to an example embodiment.

Figure 6 illustrates a top view of the particle collection device, according to an example embodiment.

Figure 7 illustrates a cross-section view of the particle collection device, according to an example embodiment.

We claim

1. A composition, comprising particles including at least 95% by weight of a taxane, or a pharmaceutically acceptable salt thereof, wherein the particles have a specific surface area (SSA) of at least 18 m^2/g.

2. The composition of claim 1, wherein the particles have a SSA of at least 20 m^2/g.

3. The composition of claim 1, wherein the taxane is selected from the group consisting of paclitaxel and docetaxel, or a pharmaceutically acceptable salt thereof.

4. The composition of claim 3, wherein the taxane is paclitaxel or a pharmaceutically acceptable salt thereof.

5. The composition of claim 4, wherein the paclitaxel particles have a specific surface area (SSA) of at least 20 m^2/g, 25 m^2/g, 30 m^2/g, 32 m^2/g, 34 m^2/g, or 35 m^2/g.

6. The composition of claim 4, wherein the paclitaxel particles have a SSA of between about 22 m^2/g and about 40 m^2/g, 25 m^2/g and about 40 m^2/g, 30 m^2/g and about 40 m^2/g, or between about 35 m^2/g and about 40 m^2/g.

7. The composition of any one of claims 4-6, wherein the paclitaxel particles have a bulk density of between about 0.060 g/cm^3 and about 0.11 g/cm^3 and a SSA of between about 22 m^2/g and about 40 m^2/g.

8. The composition of any one of claims 4-7, wherein at least 40% (w/w) of the paclitaxel is dissolved in 30 minutes or less in a solution of 50% methanol /50% water (v/v) at 37°C and pH 7.0 in a USP II paddle apparatus operating at 75 RPM.

9. The composition of claim 3, wherein the taxane is docetaxel or a pharmaceutically acceptable salt thereof.

10. The composition of claim 9, wherein the docetaxel particles have a SSA of at least 20 m^2/g, 25 m^2/g, 30 m^2/g, 35 m^2/g, 40 m^2/g, or 42 m^2/g.

11. The composition of claim 9, wherein the docetaxel particles have a SSA of between about 40 m^2/g and about 50 m^2/g, or between about 43 m^2/g and about 46 m^2/g.

12. The composition of any one of claims 9-11, wherein the docetaxel particles have a bulk density of between about 0.06 g/cm^3 and about 0.1 g/cm^3 and a SSA of between about 40 m^2/g and about 50 m^2/g .

13. The composition of any one of claims 9-12, wherein at least 20% (w/w) of the docetaxel is dissolved in 30 minutes or less in a solution of 15% methanol /85% water (v/v) at 37°C and pH 7.0 in a USP II paddle apparatus operating at 75 RPM.

14. The composition of any one of claims 1-13, wherein the particles have a mean particle size of between about 0.4 μm and about 1.2 μm, or between about 0.6 μm and about 1.0 μm.

15. The composition of any one of claims 1-14, wherein the particles are uncoated and exclude polymer, protein, polyethoxylated castor oil and polyethylene glycol glycerides composed of mono-, di- and triglycerides and mono- and diesters of polyethylene glycol.

16. The composition of any one of claims 1-15, wherein the composition comprises a suspension further comprising a pharmaceutically acceptable aqueous carrier.

17. The composition of any one of claims 1-16, further comprising one or more components selected from the group consisting of polysorbate, methylcellulose, polyvinylpyrrolidone, mannitol, and hydroxypropyl methylcellulose.

18. The composition of any one of claims 1-17, wherein the particles comprise at least 98%of the taxane.

19. Use of the composition of any one of claims 1-18 in the manufacture of a medicament for treating a tumor.

20. The use of claim 19, wherein the tumor is selected from the group consisting of a breast tumor, an ovarian tumor, a lung tumor, a bladder tumor, a prostate tumor, a bone tumor, a stomach tumor and a pancreatic tumor.

21. The use of claim 19 or 20, wherein the medicament is to be administered intraperitoneally.

22. The use of claim 21, wherein the medicament is to be administered by perfusion or as a bolus into the peritoneal cavity.

23. A method for making the composition of any one of claims 1-18, comprising:

(a) introducing (i) a solution comprising at least one solvent and at least one solute comprising a taxane into a nozzle inlet, and (ii) a compressed fluid into an inlet of a vessel defining a pressurizable chamber;

(b) passing the solution out of a nozzle orifice and into the pressurizable chamber to produce an output stream of atomized droplets, wherein the nozzle orifice is located between 4 mm and 20 mm from a sonic energy source located within the output stream, wherein the sonic

energy source produces sonic energy with an amplitude between 10% and 60% during the passing, and wherein the nozzle orifice has a diameter of between 20 μm and 125 μm;

(c) contacting the atomized droplets with the compressed fluid, to cause depletion of the solvent from the atomized droplets, to produce particles including at least 95% by weight of the taxane,

wherein steps (a), (b), and (c) are carried out under supercritical temperature and pressure for the compressed fluid.

24. The method of claim 23, further comprising:

(d) contacting the particles produced in step (c) with an anti-solvent to cause further depletion of the solvent from the taxane particles, wherein step (d) is carried out under supercritical temperature and pressure for the anti-solvent.

25. The method of any one of claims 23-24, wherein a flow rate of the solution through the nozzle has a range from about 0.5 mL/min to about 30 mL/min.

26. The method of any one of claims 23-25, wherein the sonic energy source comprises one of a sonic horn, a sonic probe, or a sonic plate.

27. The method of any one of claims 23-26, wherein the sonic energy source has a frequency between about 18 kHz and about 22 kHz, or about 20 kHz.

28. The method of any one of claims 23-27, further comprising:

(e) receiving the plurality of particles through the outlet of the pressurizable chamber; and

(f) collecting the plurality of particles in a collection device.

29. The method of any one of claims 23-28, wherein the taxane is selected from the group consisting of paclitaxel and docetaxel, or a pharmaceutically acceptable salt thereof.

30. The method of any one of claims 23-29, wherein the compressed fluid is super critical carbon dioxide.

31. The method of any one of claims 23-30, wherein the anti-solvent is super critical carbon dioxide.

32. The method of any one of claims 23-31, wherein the compound is paclitaxel and the solvent comprises acetone.

33. The method of any one of claims 23-31, wherein the compound is docetaxel and the solvent comprises ethanol.

34. The method of any one of claims 30-33, wherein the method is carried out between 31.1°C to about 60°C, and at between about 1071 psi and about 1800 psi.