effects. Organic solvents, in particular, can present health and safety hazards and can influence product efficacy, safety and stability.

Summary

[0005a] In one aspect, there is provided a method of conditioning a micronized crystalline material comprising: providing aerosolized micronized crystalline particles, wherein said micronized crystalline particles contain one or both of an amorphous material and a residual solvent; continuously mixing the micronized crystalline particles with a conditioning gas comprising a carrier gas and a solvent vapor in a chamber connected directly to the exit of the micronization apparatus; maintaining the micronized crystalline particles in contact with the conditioning gas for sufficient time to result in annealing of said micronized crystalline particles, wherein said annealing results in one or both of reducing the presence of the amorphous material or reduction in the amount of residual solvent; and separating the micronized crystalline particles from the conditioning gas.

[0005b] In another aspect, there is provided a system for in-process conditioning of a micronized crystalline material comprising: a micronizing zone comprising a device for micronizing at least one crystalline material; a mixing zone in fluid communication with the micronizing zone, wherein the at least one micronized crystalline material is delivered from the micronizing zone to the mixing zone and therein mixed with a conditioning gas; a conditioning gas supply zone in fluid communication with the mixing zone, the conditioning gas supply zone providing the conditioning gas at a desired temperature and solvent vapor concentration to the mixing zone to be mixed with the at least one micronized crystalline material; a conditioning zone in fluid communication with the mixing zone, wherein the mixture of the at least one micronized crystalline material and the conditioning gas is delivered and remains in the conditioning zone for a desired residence time; a separation and collection zone, wherein the conditioned micronized crystalline material is separated from the conditioning gas and the conditioned active agent is collected.

[0005c] In yet another aspect, there is provided a conditioned micronized crystalline material prepared by the method as defined herein.

BRIEF DESCRIPTION OF THE Several Views of the DRAWINGS

[0006] Figure 1 is a diagram showing one embodiment of a system disclosed herein for in-process conditioning of micronized crystalline material.

[0007] Figure 2 is a diagram showing an embodiment of a system disclosed herein for in-process conditioning of micronized crystalline material.

[0008] Figure 3A is a drawing of one view of one embodiment of a dispersion head assembly as described in the present disclosure.

[0009] Figure 3B is a drawing of another view of one embodiment of a dispersion head assembly as described in the present disclosure.

[0010] Figure 3C is a drawing of a cross-sectional view of one embodiment of a dispersion head assembly.

[0011] Figure 4A is a cross-sectional drawing of one embodiment of a mixing head as described in the present disclosure.

[0012] Figure 4B is a cross-sectional drawing of another embodiment of a mixing head as described in the present disclosure.

[0013] Figure 5 is a graph depicting the unstable particle size distribution of a standard micronized glycopyrrolate sample as discussed in Example 1.

[0014] Figure 6A is an electron micrograph showing the amorphous morphology of a standard micronized glycopyrrolate sample as discussed in Example 1.

[0015] Figure 6B is an electron micrograph showing the fusing and agglomeration of a standard micronized glycopyrrolate sample after exposure as discussed in Example 1.

[0016] Figure 7 is a graph depicting the stable particle size distribution of a conditioned micronized glycopyrrolate sample as discussed in Example 1.

[0017] Figure 8A is an electron micrograph showing the crystalline morphology of a conditioned micronized glycopyrrolate sample as discussed in Example 1.

CLAIMS

1. A method of conditioning a micronized crystalline material comprising:

providing aerosolized micronized crystalline particles, wherein said micronized crystalline particles contain one or both of an amorphous material and a residual solvent;

continuously mixing the micronized crystalline particles with a conditioning gas comprising a carrier gas and a ~~conditioning~~ solvent vapor in a chamber connected directly to the exit of the micronization apparatus;

maintaining the micronized crystalline particles in contact with the conditioning gas for sufficient time to result in annealing of said micronized crystalline particles, wherein said annealing results in one or both of reducing the presence of the amorphous material or reduction in the amount of residual solvent; and

separating the micronized crystalline particles from the conditioning gas.

2. The method of claim 1, wherein the micronized crystalline material is mixed with the conditioning gas for between about 0.1 to 600 seconds before the micronized crystalline material exits the conditioning zone.

3. The method of claim 1, wherein the micronized crystalline material is mixed with the conditioning gas for between about 2 to 6 seconds before the micronized crystalline material exits the conditioning zone.

4. The method of claim 2, wherein the micronized crystalline material is mixed with the conditioning gas for about 3 seconds before the micronized crystalline material exits the conditioning zone.

5. The method of claim 1, wherein the micronized crystalline material is water soluble, the solvent vapor included in the conditioning gas is an aqueous solvent vapor, and the conditioning gas is provided at a temperature

ranging from about 20 °C to 100 °C and at a relative humidity ranging from about 0.05% to 95%.

6. The method of claim 1, wherein micronized crystalline material is not water soluble, the solvent vapor included in the conditioning gas is an organic solvent vapor, and the conditioning gas is provided at a temperature ranging from about 20 °C to 100 °C and at a relative saturation of a non-aqueous solvent in the range of about 0.05% to 95%.

7. The method of claim 1, wherein micronized crystalline material is an admixture of water soluble and non-water soluble materials, the solvent vapor included in the conditioning gas comprises an aqueous solvent vapor and an organic solvent vapor, and the conditioning gas is supplied at a temperature ranging from about 10 °C to 100 °C and at a relative humidity of the aqueous solvent in the range of about 0.05% to 95% and relative saturation of the non-aqueous solvent in the range of about 0.05% to 95%.

8. The method of any one of the preceding claims, wherein the micronized active agent is aerosolized within a delivery gas before mixing with the conditioning gas.

9. The method of any one of the preceding claims, wherein the micronized crystalline material is produced using a jet mill and is aerosolized in the jet mill gas flow.

10. The method of any one of the preceding claims, wherein the conditioning gas is mixed with the aerosolized micronized crystalline material in a ratio of about 1 to 10 parts conditioning gas with about 1 part of the aerosolized micronized crystalline material.

11. The method of any one of the preceding claims, wherein the micronized crystalline material has a particle size ranging from about 0.1 μm to about 100 μm.

a separation and collection zone, wherein the conditioned micronized crystalline material is separated from the conditioning gas and the conditioned active agent is collected.

17. The system of claim 16, wherein micronized crystalline material is water soluble and the conditioning gas supply zone is configured to provide the conditioning gas at a temperature ranging from about 20 °C to 100 °C and at a humidity ranging from about 0.05% to 90% relative humidity.

18. The system of claim 16, wherein micronized crystalline material is not water soluble and the conditioning gas supply zone is configured to provide the conditioning gas at a temperature ranging from about 20 °C to 100 °C and at a relative saturation of a non-aqueous solvent in the range of about 0.05% to 90% in the flowing conditioning gas stream.

19. The system of claim 16, wherein micronized crystalline material is an admixture of water soluble and non-water soluble materials, and the conditioning gas supply zone is configured to provide the conditioning gas at a temperature ranging from about 20 °C to 30 °C and at a relative humidity of 50 to 75% and a relative saturation of a non-aqueous solvent in the range of about 50% to 75% in the flowing conditioning gas stream.

20. The system of claim 16, wherein the conditioning gas supply zone is configured to provide the conditioning gas at a temperature of about 25 °C and with a humidity of about 65% relative humidity.

21. The system of claim 16, wherein the conditioning zone is configured to maintain the mixture of the at least one micronized crystalline material and the conditioning gas within the conditioning zone for a residence time of between about 0.5 to 60 seconds.

22. The system of claim 16, wherein the conditioning zone is configured to maintain the mixture of the at least one micronized crystalline material and

the conditioning gas within the conditioning zone for a residence time of between about 1 to about 10 seconds.

23. The system of claim 16 wherein the conditioning zone is configured to maintain the mixture of the at least one micronized crystalline material and the conditioning gas within the conditioning zone for a residence time of about 3 seconds.

24. The system of claim 16, wherein the micronizing zone comprises a jet mill configured for micronizing the at least one crystalline material.

25. The system of claim 16, wherein the conditioning gas supply zone is configured to provide the conditioning gas to the mixing zone at a flow rate ranging from about 150 standard cubic feet per minute (SCFM) up to about 300 SCFM.

26. The system of claim 16, wherein the micronizing zone is configured to deliver the at least one micronized crystalline material as an aerosolized particulate material to the mixing zone at a flow rate ranging from about 35 standard cubic feet per minute (SCFM) up to about 200 SCFM.

27. The system of claim 16, wherein the mixing zone comprises a dispersion head assembly, and wherein the conditioning gas and the micronized crystalline material are mixed in the dispersion head assembly.

28. The system of claim 27, wherein the dispersion head assembly comprises a mixing head configured to control the mixing of the conditioning gas and the at least one micronized crystalline material.

29. The system of claim 28, wherein the mixing head comprises an injection nozzle inlet configured to deliver the conditioning gas to an injection nozzle, and wherein the mixing head comprises a delivery gas inlet configured to deliver the micronized crystalline material to the injection nozzle, and wherein

37. A method of any one of claims 35 and 36, wherein the conditioned particles are maintained in a continuously fluidized state within the holding chamber.

38. A method of any one of claims 35-37, wherein secondary conditioning of the micronized particles results in one or both of reducing the presence of an amorphous material or reduction in the amount of a residual solvent.

39. The method of any one of claims 1-16, further comprising preparing a secondary conditioning gas and mixing the secondary conditioning gas with the conditioned micronized crystalline particles while said conditioned micronized crystalline particles are maintained in ~~the~~ a holding chamber, wherein said mixing of the secondary conditioning gas with the conditioned micronized crystalline particles is conducted for sufficient time to provide a secondary conditioning of the micronized crystalline particles.

40. A method according to claim 39, wherein the secondary conditioning of the micronized particles results in one or both of reducing the presence of an amorphous material or reduction in the amount of a residual solvent.

41. A conditioned micronized crystalline material prepared by the method of claim 1.

42. The conditioned micronized crystalline material according to claim 41, wherein the conditioned micronized crystalline material has reduced amorphous content relative to micronized crystalline material that has not been conditioned.

43. The conditioned micronized crystalline material according to claim 42 or claim 43, wherein the conditioned micronized crystalline material has

reduced residual solvent relative to micronized crystalline material that has not been conditioned.

44. The conditioned micronized crystalline material according to any one of claims 41-44, wherein the micronized crystalline particles comprise glycopyrrolate.

45. The conditioned micronized crystalline material according to any one of claims 41-44, wherein the micronized crystalline particles comprise budesonide.