CLAIMS

1 A method of making cocrystals with at least a first substance and a second substance which are able to form cocrystals, wherein the first substance is an active pharmaceutical ingredient (API) or a pharmaceutically acceptable derivative, such as a salt, of an API, which method comprises the steps of:

a) feeding a molten mixture of the at least first substance and second substance into an atomizer;

b) atomizing the molten mixture to droplets;

c) solidifying the droplets to particles; and

d) collecting the said particles.

2. A method according to claim 1, wherein the method is a batch process or continuous process.

3. A method according to claim 1, wherein the first and second substances are combined in a stoichiometric ratio, such as 1:1, 1:2, 2:1 or another integer ratio.

4. A method according to claim 1, wherein the method is a method of making pharmaceutical co-crystals.

5. A method according to claim 1, wherein the first substance or its pharmaceutically acceptable derivative has at least one functional group selected from: thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, imine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, S-heterocyclic ring, thiophene, N-heterocyclic ring, pyrrole, O-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine.

6. A method according to any preceding claim, wherein the second substance is a coformer.

7. A method according to claim 6, wherein the coformer is an active or non-active ingredient.

8. A method according to any one of claims 6 or 7, wherein the coformer is a pharmaceutical excipient, vitamin, mineral or amino acid.

9. A method according to any one of claim 6 to 8, wherein the coformer has at least one functional group selected from: thioether, alcohol, thiol, aldehyde, ketone, thioketone, nitrate ester, phosphate ester, thiophosphate ester, ester, thioester, sulfate ester, carboxylic acid, phosphonic acid, phosphinic acid, sulfonic acid, amide, primary amine, secondary amine, ammonia, tertiary amine, imine, thiocyanate, cyanamide, oxime, nitrile, diazo, organohalide, nitro, S-heterocyclic ring, thiophene, N-heterocyclic ring, pyrrole, O-heterocyclic ring, furan, epoxide, peroxide, hydroxamic acid, imidazole, and pyridine.

10. A method according to any preceding claim, wherein the first and second substances are exposed to heat for at least 1 minute, optionally 2 minutes or longer, until a homogenous and molten mixture is formed.

11. A method according to any preceding claim, wherein shear and/or pressure are employed to facilitate the mixture and entanglement of the components in the mixture, as well as to decrease their viscosity.

12. A method according to claim 11, wherein shear and pressure are promoted by magnetic stirrer bars, paddles, or by an extrusion method.

13. A method according to claim 12, wherein the extrusion method is a screw-based extrusion apparatus connected to the atomization system.

14. A method according to claim 13, wherein the screw-based extrusion apparatus connected to the atomization system is a single-screw or twin-screw extrusion apparatus, optionally wherein the twin-screw extrusion apparatus is a co-rotating or counter-rotating system.

15. A method according to any preceding claim, wherein the melting temperature of the mixture is between -120 to +300°C, typically between 0 and 200°C, optionally between 20 and 180°C.

16. A method according to any preceding claim, wherein the mixture further comprises one or more functional matrix material(s) to promote mixing between the first and second substances, and/or to decrease the melting temperature of the mixture, and/or to add functionality to the final product, optionally wherein the one or more functional matrix material(s) comprises an, agent with a plasticizing effect, such as polyethylene glycol, or carbon dioxide, or one or more surfactant, or one or more polymers.

17. A method according to any preceding claim, wherein in step b) the atomizing nozzle has a rotary, pressure, fluid, or ultrasonic configuration.

18. A method according to any preceding claim, wherein in step c) cooling is promoted by a stream of co-current or counter-current cooling gas or liquid, with respect to the melt spray direction.

19. A method according to any preceding claim, wherein the residence time of the droplets is controlled through a counter-current stream of cooling gas or liquid.

20. A method according to any one of claims 18 or 19, further comprising one or more of the following:

(i) wherein the initial temperature of the stream of gas or liquid is between -20 and 200°C;

(ii) wherein the counter-current stream of cooling gas is air, nitrogen or carbon dioxide;

(iii) wherein the counter-current stream of cooling liquid is liquid carbon dioxide or liquid nitrogen.

21. A method according to any one of claims 18, 19 or 20(i), further comprising one or more of the following:

(i) wherein the cooling gas is air, nitrogen or carbon dioxide;

(ii) wherein the cooling liquid is liquid carbon dioxide or liquid nitrogen.

22. A method according to any preceding claim, further comprising one or more of the following:

(i) wherein the particles obtained comprise at least 50% (w/w) cocrystal purity, more preferably at least 75% (w/w) cocrystal purity, especially 90% (w/w) or more cocrystal purity;

(ii) wherein the particles obtained have a particle size from 1 to 500 μm.