Method and Apparatus

The present invention relates to a method of processing active pharmaceutical ingredients and to apparatus for use in such methods.

In particular the present invention relates to the use of twin screw extruders in the processing of active pharmaceutical ingredients (APIs).

Prior to their incorporation into a formulation for dosage, active pharmaceutical ingredients need to be provided in a ready to handle form which is highly purified and comprises minimum levels of solvent. Most APIs are desirably provided as dry materials in particulate form, as powders or granules. The size of these particles needs to be uniform and it is necessary for a synthetic method to provide particles of consistent size.

The synthesis of APIs typically involves a number of steps often including a crystallisation step as a purification means to provide the actual active ingredient. The isolated crystals may still contain high levels of solvent (typically more than 5 wt% and often much higher) and are not usually of a consistent size or indeed the desired size for inclusion in a pharmaceutical formulation.

Thus additional steps are usually needed after crystallisation to provide an API in a form ready for formulation. This further processing will usually involve a milling step and/or granulation step to provide particles of the desired size distribution and a drying step. In current methods the granulation and drying steps are carried out separately and usually involve batch processes.

For example particles may be granulated using high shear mixer granulators or twin screw extruders. The material is then dried using fluid bed dryers, vacuum drying, microwave drying, spray dryers, tray dryers, rotary core dryers, paddle dryers, tumble dryers or belt dryers.

However these drying processes take up considerable space and can be labour intensive. The product often requires further post-drying processing such as milling, screening or blending to provide homogeneity.

The present invention seeks to provide a method of processing active pharmaceutical ingredients which offers advantages over methods of the prior art.

Summary

In one aspect of the present disclosure, there is provided a method of processing an active pharmaceutical ingredient, the method comprising passing a precursor composition comprising the active pharmaceutical ingredient and a solvent through a twin screw extruder wherein the twin screw extruder is heated at ambient pressure, wherein at least a portion of the extruder is heated to a temperature above the boiling point of the solvent(s) present in the precursor composition; the portion of the extruder is heated to a temperature below the melting point of the API; the APIs and solvents together provide at least 90 wt% of the precursor composition; and wherein the barrel of the twin screw extruder includes one or more vents along its length.

In another aspect, there is provided a method of preparing a formulated pharmaceutical product, the method comprising a) providing an active pharmaceutical ingredient using the method of claim 1; and b) admixing the treated composition obtained in step (a) with one or more further components.

In yet another aspect, there is provided an apparatus for processing an active pharmaceutical ingredient, the apparatus comprising: a barrel, two screws located within the barrel, means for inputting material into the barrel, exit means for collected material from the barrel, one or more heating elements arranged to heat material inside the barrel,
one or more vents along the length of the barrel.

In a further aspect of the present disclosure, there is provided a use of a heated twin screw extruder to concurrently dry and granulate an active pharmaceutical ingredient.

Description

According to a first aspect of the present invention there is provided a method of processing an active pharmaceutical ingredient, the method comprising passing a precursor composition

Claims

1. A method of processing an active pharmaceutical ingredient, the method comprising passing a precursor composition comprising the active pharmaceutical ingredient (API) and a solvent through a twin screw extruder wherein the twin screw extruder is heated at ambient pressure, wherein at least a portion of the extruder is heated to a temperature above the boiling point of the solvent(s) present in the precursor composition; the portion of the extruder is heated to a temperature below the melting point of the API; the APIs and solvents together provide at least 90 wt% of the precursor composition; and
wherein the barrel of the twin screw extruder includes one or more vents along its length.

2. A method of preparing a formulated pharmaceutical product, the method comprising:

(a) providing an active pharmaceutical ingredient using the method of claim 1; and
(b) admixing the treated composition obtained in step (a) with one or more further components.

3. A method according to any preceding claim wherein the active pharmaceutical ingredient is selected from paracetamol, ibuprofen, aspirin, felodipine, piracetam, irbesartan, hydrochlorothiazide, caffeine, amoxiciline, griseofulvin, metformin, chlorpheniramine maleate, simvastatin, etoricoxib, eprosartan, levofloxacin and sevelamer.

4. A method according to any preceding claim wherein the solvent is selected from water, ethanol, isopropanol, glycerol, ethyl acetate, hexane, cyclohexane, acetone, methanol and propylene glycol.

5. A method according to any preceding claim wherein the precursor composition comprises at least 5 wt% solvent.

6. A method according to any preceding claim which provides a treated composition comprising less than 1 wt% solvent.