Study of Crystallization of Drug Substances under Solvent Vapour Atmosphere by Microcalorimetry

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The final steps of chemical syntheses of solid drug substances are generally crystallisation followed by milling or sieving. In pharmaceutical industry, several polymorphs and solvates may be present. A change of the crystalline form and/or the presence of an amorphous part may induce important changes concerning the physical properties (dissolution rate, bioavailability, stability, processability…) of the corresponding drug product. Therefore, it is mandatory for the development of robust processes to determine the influence of significant parameters, such as temperature and solvents of crystallization, drying, milling, storage conditions, on the crystalline form and on its crystallinity.

Microcalorimetry has been shown to be a powerful tool for the quantification of small amounts of amorphous in solid compound based on the measurement of the energy of crystallization. [1] Generally, the corresponding sample is subjected to various relative humidities, but any organic vapour can also be used and should have a similar effect on the crystallisation behaviour of the amorphous part. [2, 3] In the same way, this technique can also be applied to detect a phase transformation of one crystalline form into another by submitting the sample to an organic atmosphere.

This communication will discuss the applications of different organic vapours in microcalorimetry for crystallisation studies of drug substances. The first part will focus on the study of phase transition of a drug substance by using microcalorimetry as an additional technique for qualitative information. The second part will present development of methods to quantify the amorphous part in drug substances.

References

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