Crystallization (or not) of active pharmaceutical ingredients in thin films

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Abstract

Utilizing surfaces for nucleation and growth is often adopted as a means to enhance crystallization. Certain surfaces can accelerate crystallization while other prevent it. On the other hand, constrains induced by the surface can trigger crystal growth on well-defined contact planes and thus along specific crystallographic directions i.e. texture or epitaxial growth can result. It has also been shown that surfaces can increase the crystallization rate when compared to the bulk. Furthermore, it has been shown for several organic semiconductors (organic molecules deposited on flat solid substrates as thin films, a hundred of nm thick) that new polymorphs could be stabilized only close to the substrate (called "substrate induced polymorphs or SSPs). In this presentation, we report two cases of thin film deposition of active pharmaceutical ingredients illustrating the ability of a solid surface and the confinement geometry to drastically change the crystallization outcome and therefore ultimately the properties of the drug product. The first example concerns pyrazinamide, an active pharmaceutical ingredient used in the treatment of tuberculosis, which possesses 4 polymorphic forms. Here, thin film deposition of pyrazinamide shows the long-time persistence of metastable polymorphs while the stable polymorph is never obtained. The second example pertains to ketoprofen (a non-steroidal anti-inflammatory) for which amorphous solid dispersions could be achieved upon thin film co-deposition with polyethylene oxide. It appears that these amorphous solid dispersions could be preserved for several months even when submitted to a high relative humidity atmosphere, depending on the film thickness.