Role of Physical Form of the Active Pharmaceutical Ingredient (API) and Excipients

Raj Suryanarayanan (Sury), Department of Pharmaceutics, College of Pharmacy, University of Minnesota, Minneapolis, MN 55455, USA

The physical form of the active pharmaceutical ingredient (API) can influence the performance and stability of the dosage form. Even if the appropriate physical form of the API is selected, it may not be retained in the final dosage form. Stresses experienced during processing and drug-excipient interactions can lead to both physical and chemical transformations during product manufacture. In order to understand and interpret the effects of such transitions, it is often necessary to monitor the system during all the stages of pharmaceutical processing. While the focus will be on APIs, the processing-induced transitions of excipients can also influence product performance.

Tablet formulations. The amorphous state is increasingly recognized as a means to circumvent the challenge of poor aqueous solubility of compounds. However, during processing, compounds can undergo crystallization thereby negating the solubility advantage of the amorphous state. When amorphous indomethacin was compressed, its crystallization was not uniform throughout the tablets. The spatial information, gained by monitoring the different regions of a tablet (depth profiling), revealed progression of phase transformation from the surface to the tablet core as a function of storage time. Very low levels of crystallization on the tablet surface, while profoundly affecting product performance (decrease in dissolution rate), may not be readily detected by conventional analytical techniques.

Freeze-dried formulations. The phase behavior of the active pharmaceutical ingredient (API) and excipients in multi-component pharmaceutical systems, during the various stages of freeze-drying, is a complex interplay of formulation variables and processing conditions. The behavior of several pharmaceutical excipients, during the different stages of freeze-drying will be presented and the potential implications on product performance will be discussed. In all of these studies, X-ray powder diffractometry serves as a primary tool for phase identification as well as phase quantification.

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