Whisker Growth of Glibenclamide in Solid Dispersions

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This contribution deals with observations of whisker growth of glibenclamide in solid dispersions with polyethylene glycol, in solid dispersion granules formed by layering and coalescence mechanism in a fluid-bed melt granulation process [1] as well as in the tableted granules. Dissolution data and tablet properties [2] indicate significant dependencies on aging. Dissolution and friability values decrease whereas crushing strength and disintegration times increase with time. These changes can be attributed to the growth of glibenclamide whiskers in the granules as well as the tablets which was observed by scanning electron microscopy. The extent of the whisker growth also depends on the melt granulation mechanisms. The first mechanism is defined as the layering of excipients on seeds of fusable materials and the second one as the distribution of the molten binder on the surface of powder particles. Drug loaded seeds or molten binder are solid dispersions of drugs (here glibenclamide) in a meltable polymer [1]. The appearance of whiskers in the SEM micrographs is very characteristic and could be used as diagnostical tool for the dominant granulation mechanism.

Whiskers are described as single crystals consisting of tiny filaments with about 2 microns in diameter and a few millimeters in length (high aspect ratios, often >1000). The axis of the whisker is frequently parallel to the major crystallographic direction. Whiskers tend to be high in purity and contain very few external or internal defects. Most of the research on whisker growth was carried out on inorganic or metallurgic substances. These results suggest that this phenomenon can be explained by the dislocation theory. Driving forces in whisker growth are a decrease in internal or applied stress (crystallization process) or a decrease in supersaturation (condensation, precipitation, electrodeposition). While most of the whiskers are straight, an amazing variety of shapes like polygonal spirals, kinks, twists or helices are observed [3,4].

Whisker growth has been also reported for pharmaceutical drug substances and excipients like menthol [5], nifedipine [6], acetylsalicylic acid [7], theophylline [8] and lactose [9].

As results of the studies it can be supposed that the duration of storage, the particle or granule size as well as the melt granulation mechanism can affect the whisker growth. Other factors that might lead to the crystal growth can be the presence of hygroscopic materials, the temperature und the relative humidity [7].

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