CHARACTERIZATION OF INSULIN MICROCRYSTALS IN PHARMACEUTICAL SUSPENSIONS

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Treatment of diabetes generally involves several daily injections of the protein hormone insulin. Insulin preparations with an extended action profile consist of microcrystalline suspensions that slowly dissolve and release the insulin into the blood stream. The action profiles are partly dependent on crystal form and on composition of crystals and soluble insulin. Careful chemical- and physical characterisation of the crystallinity of these suspensions is important, both for regulatory and patent related reasons, and also due to the fact that different polymorphs may adversely affect the stability, bioavailability and the therapeutic properties of the insulin.

Insulin was one of the first protein structures to be solved by X-ray crystallography. Since then, the structure has been solved from crystals originating from a number of different crystal forms. Some of these are used in pharmaceutical formulations for the treatment of diabetes. A direct crystallographic characterization of the crystals within the formulations has long been hampered due to the small size of the crystals (μm-scale). In his study X-ray powder diffraction has been used to characterize twelve crystalline formulations of insulin originating from six different crystal forms. The results show that all crystal forms give rise to distinct powder patterns. To facilitate a more efficient analysis, principal component analysis (PCA) was employed on the full profile patterns. The twelve different formulations were clustered into nine groups in the resulting score plot. Within each group, crystals from the same crystal system or with the same structural folding were gathered. The analysis shows that X-ray powder diffraction in combination with multivariate analysis provides efficient and reliable tools for characterization of pharmaceutical microcrystalline formulations of insulin. The methods are routinely used during research and development of new insulin formulations.