Characterisation of insulin microcrystals in pharmaceutical formulations

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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 the crystal forms are used in pharmaceutical formulations for the treatment of diabetes. 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, but also because different polymorphs may adversely affect the stability, bioavailability and the therapeutic properties of the insulin. A direct crystallographic characterization of the crystalline 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 crystalline formulations of insulin. The results show that all the analyzed insulin 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 different formulations were clustered into distinct 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.