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Effect of colloidal silica dioxide on rheological properties of common pharmaceutical excipients

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Manufacturing of pharmaceutical solid dosage forms involves several processing steps including flow through hoppers, sieving, pouring, blending, die-filling, and compaction. These steps are highly sensitive to powder properties such as flowability and bulk density, which are to some extent inter-related. The knowledge of flow properties of raw excipients and their mixtures is essential for predicting their behaviour during blending, compression, handling or leaving in storage and these properties are critical for manufacturing since they can affect the final product quality and the efficiency of the processes.

Very effective tool for assessing properties such as flowability and powder cohesion is powder rheology. There are various commercially available instruments; one of them is the FT4 Universal Powder Rheometer (Freeman technology, UK). It allows the measurement of the powder response to various stress fields, thus simulating the range of processing conditions more closely. During the testing, materials are subjected to dynamic and shear tests which provide set of basic rheological characteristics. Moreover there is a conditioning procedure between each measurement which allows generation of a stable consolidation state and ensures the reproducibility of the data.

The flowability of powders can be improved significantly by the addition of small amounts of substances described as 'glidants' in the area of tableting technology. The primary particles of glidants exist in the form of agglomerates which are broken down into smaller aggregates during the blending process. These small glidant particles adsorb at the surface of the other solid component grains, increase the roughness of the host surface and thus improve the powder flow.

In this work, the rheological properties of silicified microcrystalline cellulose and pregelatinized starch was investigated in comparison to the characteristics of pure excipients. At first, pure materials were analysed on scanning electron microscopy (SEM) to obtain their particle size distribution and particle shape. Also the rheological properties of all three substances were examined by the Freeman FT4 rheometer. The observed properties were in accordance with known characteristics and typical behaviour of the excipients.

Then the binary mixtures of these excipients and different concentration of anhydrous colloidal silicon dioxide (Aerosil 200®) were prepared by blending in a Turbula® mixer for a defined period of time. The Freeman FT4 rheometer was used to measure flow properties of the mixtures. The bulk (conditioned and compressed densities, compressibility index), dynamic (basic flow energy) and shear (friction coefficient, flow factor) properties were determined. The optimum flowability was exhibited by the mixtures comprising 0.25 - 1 % of Aerosil, but the results revealed also additional more complex phenomena affecting the flowability of binary mixtures (blends). In order to support these findings and investigate the

blend behaviour in more detail, the mixtures of Aerosil and microcrystalline cellulose were selected for further experiments. A compressibility test on Gamlen Tablet Press GTP-1 (Gamlen Tableting, UK) was performed, confirming the binary mixture compressibility being affected by the composition, which allowed to explain poor flowability in Aerosil-rich blends. The samples were also subjected to Energy-dispersive X-ray spectroscopy to reveal the relationship between the rheological properties and the inter-particle structure of the materials. The images confirmed the theory that glidant fills cavities in the grains at first, and then covers the surface. In order to clarify the effect of particle size on the glidant action, the excipients were pre-sieved and selected fraction were mixed with Aerosil and re-tested by the rheometer. It was found that compressibility is mainly determined by the properties of the excipient itself and that the fraction with the larger particles are less compressible in general. Also the kinetics were studied with different time of mixing selected when preparing mixtures in the blender. The first results show that with the increasing time of mixing the compressibility decrease. Also, the basic flow energy is changing rapidly during prolonged mixing and it is lower at shorter mixing.