

ABSTRACT

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Title of Doctoral Thesis **Study of flow and consolidation behaviour of binary mixtures of Cellets and filler for preparation of multilayer tablets**

The manufacture and quality of solid dosage forms is influenced mainly by flow, consolidation and compaction properties of powder excipients. In this work, the behaviour of pellets made of microcrystalline cellulose (cellets), which might be used as a drug carrier in multilayer tablets, and their binary mixtures with microcrystalline cellulose was studied.

More than 20 powder excipients commonly used in tablet production and their binary mixtures were involved in preliminary studies. Measuring of the angle of repose, Hausner ratio and the mass flow rate through a hopper orifice was influenced by the particle shape, size and the width of the particle size distribution. In order to identify easily the free flowing substances, the hopper orifice having 10 mm diameter was useful. Excellent flow properties were confirmed for cellets with conventional testing methods thanks to their spherical shape and narrow particle size distribution. The avalanche testing using a rotational drum proved that the break energy representing the energy needed to start an avalanche correlates well with the powder cohesion and, moreover, it is sensitive in the prediction of the flow behaviour. Slumping avalanche behaviour, low cohesion estimated by rotational shear testing and low break energy values were found in cellets. It was showed that the angle of internal friction as an indicator of particle friction during powder bed packing can be predicted from the dynamic of gravitational consolidation and the change in porosity of powder bed. The values correlated well with those determined for seven lactose excipients by using the Jenike translational shear cell. Simple test equipment and fast procedure are the main advantages of using the gravitational consolidation method. The change in powder bed porosity of binary mixtures of cellets and microcrystalline cellulose during the gravitational consolidation showed also good correlation with the modified Heckel equation model introduced by Kuentz and Leuenberger for low compaction pressures. The compaction of cellets, microcrystalline cellulose and their binary mixtures with a compaction force in range of 2 - 20 kN showed significant correlation between the pre-compression energy E_1 and flow properties (Hausner ratio and cohesion). The energy of plastic deformation E_2 approved good compaction properties of microcrystalline cellulose and improved compactability of mixtures with cellets. Up to compaction force of 10 kN, the preparation of tablets made of cellets was not possible for low tensile strength. The tablet layer with the appropriate tensile strength in a range of 0,6 – 1,0 MPa and the axial relaxation up to 20 % can be obtained with mixtures containing 50 – 60 % of cellets at the compaction force of 10 kN. However, it will be necessary to specify the influence of a drug on these parameters in future studies.