34b Use of a Novel Shear Cell to Study the Influence of Shear Intensity and Total Shear on the Properties of Pharmaceutical Blends

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Shear plays an important role in the processing of pharmaceutical blends, affecting the performance of mixtures as well as their scale-up requirements. However, in spite of its significant impact, shear has not been studied systematically. Typically, shear is applied (often unintentionally) both in the blender and in feed frame. In both these environments the granular flow is poorly understood and we do not know either the intensity or the uniformity of shear that is imparted to the system. In order to carefully examine this issue, we developed a "controlled shear environment" and use it to study homogenization of Magnesium Stearate (MgSt) under carefully controlled, homogeneously applied shear rates. Experiments were performed in order to examine the effect of total shear and MgSt content on blend flow properties, MgSt homogeneity, bulk density and tablet hardness, using a blend of 58-60%Fast-flo lactose, 40% Avicel 102, 0-2% MgSt. Blends were sheared at various rates in the range from 10 to 245 RPM (corresponding to shear rates between 0.45 s-1 and 109.03s-1) for a total of 10 to 5000 revolutions corresponding to 270 to 135,000 total dimensionless shear units), and were subsequently sampled. As the total shear increases, MgSt RSD decrease and then reaches a distinctive plateau, suggesting the existence of two separate regimes, one where MgSt homogeneity depends on shear, and another where a maximum degree of lubrication (or over-lubrication) has been "achieved". Bulk density, which has a strong effect on tablet weight and content uniformity, is another very important variable that is deeply affected by total amount of applied shear. Bulk density increases and then reaches a plateau, suggesting the existence of two regimes closely related to those observed for MgSt RSD. Flow properties of prepared samples were strongly affected by shear. The mixture flow properties were characterized in terms of the size of avalanches observed under dilated conditions in the "Rutgers Gravitational Displacement Rheometer". Finally, and perhaps most importantly, tablet hardness is consistently and reproducibly affected by the total amount of shear imposed on the blend. Results show that there is no effect of shear rate on the tablet hardness, however, as the total shear is increased, the tablet hardness decreases. These results demonstrate feasibility of the proposed method for characterizing shear effects, and provide an excellent starting point for a systematic study of the effect of shear on critical blend properties (particle size and shape, bulk density, flow properties, level of cohesion) and tablet properties (hardness, dissolution, friability, weight variability).