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Impact of Material Chemistry and Morphology on Attrition Behavior of Excipients during Blending

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Abstract : Blending is a common process in the production of pharmaceutical dosage forms where the high shear is used to obtain a homogenous dosage. The shear required can lead to uncontrolled attrition of excipients and affect API's. This has an impact on the performance of the formulation as this can alter the structure of the mixture. Therefore, it is important to understand the driving mechanisms for attrition. The aim of this study was to increase the fundamental understanding of the attrition behavior of excipients. Attrition behavior of the excipients was evaluated using a high shear blender (Procept Form-8, Zele, Belgium). Twelve pure excipients are tested, with morphologies varying from crystalline (sieved), granulated to spray dried (round to fibrous). Furthermore, materials include lactose, microcrystalline cellulose (MCC), di-calcium phosphate (DCP), and mannitol. The rotational speed of the blender was set at 1370 rpm to have the highest shear with a Froude (Fr) number 9. Varying blending times of 2-10 min were used. Subsequently, after blending, the excipients were analyzed for changes in particle size distribution (PSD). This was determined (n = 3) by dry laser diffraction (Helos/KR, Sympatec, Germany). Attrition was found to be a surface phenomenon which occurs in the first minutes of the high shear blending process. An increase of blending time above 2 mins showed no change in particle size distribution. Material chemistry was identified as a key driver for differences in the attrition behavior between different excipients. This is mainly related to the proneness to fragmentation, which is known to be higher for materials such as DCP and mannitol compared to lactose and MCC. Secondly, morphology also was identified as a driver of the degree of attrition. Granular products consisting of irregular surfaces showed the highest reduction in particle size. This is due to the weak solid bonds created between the primary particles during the granulation process. Granular DCP and mannitol show a reduction of 80-90% in x10(µm) compared to a 20-30% drop for granular lactose (monohydrate and anhydrous). Apart from the granular lactose, all the remaining morphologies of lactose (spray dried-round, sieved-tomahawk, milled) show little change in particle size. Similar observations have been made for spray-dried fibrous MCC. All these morphologies have little irregular or sharp surfaces and thereby are less prone to fragmentation. Therefore, products containing brittle materials such as mannitol and DCP are more prone to fragmentation when exposed to shear. Granular products with irregular surfaces lead to an increase in attrition. While spherical, crystalline, or fibrous morphologies show reduced impact during high shear blending. These changes in size will affect the functionality attributes of the formulation, such as flow, API homogeneity, tableting, formation of dust, etc. Hence it is important for formulators to fully understand the excipients to make the right choices.

Keywords : attrition, blending, continuous manufacturing, excipients, lactose, microcrystalline cellulose, shear
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