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Introducing a novel gravitation-based high-velocity compaction analysis method for pharmaceutical powders

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ABSTRACT

With modern tableting machines large amounts of tablets are produced with high output. Consequently, methods to examine powder compression in a high-velocity setting are in demand. In the present study, a novel gravitation-based method was developed to examine powder compression. A steel bar is dropped on a punch to compress microcrystalline cellulose and starch samples inside the die. The distance of the bar is being read by a high-accuracy laser displacement sensor which provides a reliable distance-time plot for the bar movement. In-die height and density of the compact can be seen directly from this data, which can be examined further to obtain information on velocity, acceleration and energy distribution during compression. The energy consumed in compact formation could also be seen. Despite the high vertical compression speed, the method was proven to be cost-efficient, accurate and reproducible.

1. Introduction

1.1. Background

Understanding powder compression behavior is crucial when designing a tablet formulation. During tableting, when powder is compressed between punches, particles rearrange, fragment and deform under pressure resulting in a volume decrease and compact formation (Adolfsson and Nyström 1996; Antikainen and Yliruusi 2003; Hiestand et al., 1977; Zhang et al., 2003). As deformed particles are forced to pack into a smaller volume, new bonds are formed. Bonding occurs mostly due to Van der Waals interaction, electrostatic interaction, hydrogen bonding, local melting and mechanical interlocking. Perfectly plastic behavior refers to a phenomenon where this bonding allows the particle to retain its new shape whereas perfectly elastic particles do not create new bonds, causing the particle to recover to its original shape. Fragmentation refers to a phenomenon where particles break under pressure forming smaller particles, which can further rearrange and fill the voids between the larger particles. Plastic deformation is a time-dependent phenomenon whereas fragmentation occurs immediately when enough pressure has been applied.

Most materials are viscoelastic in nature and compression behavior of any material is a mixture of plastic deformation, elastic deformation and fragmentation. It is of importance to understand that the fraction of each phenomenon is condition-dependent meaning that, for instance, any material can presumably resist plastic flow if the compression speed is high enough (Tatavarti et al., 2008; Thoorens et al., 2014). Many other factors, for instance, compression pressure, humidity, temperature and particle surface characteristics in general may affect these phenomena as well (Amidon and Houghton 1995; Nokhodchi 2005; Rouèche et al., 2006). In a typical tableting setting microcrystalline cellulose (MCC) is dominantly known as a plastic material, starch as an elastic material and dicalcium phosphate as a fragmenting material, to name a few (Antikainen and Yliruusi 2003; Shlieout et al., 2002). However, such categorization is not unambiguous and the compression behavior varies depending on conditions.

1.2. Importance of compression behavior

Compacts consisting mostly of plastically deforming particles have a high probability of showing excessive hardness and possibly

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poor disintegration after administration. In contrast, pronounced elasticity promotes formation of weaker tablets or complete failure to form compacts (Hiestand et al., 1977; Katz et al., 2013). Tablet defects such as lamination or capping may also occur if the excipients are imbalanced in a formulation with regard to their properties (Tatavarti et al., 2008). Therefore, it is important to know the compression behavior of the individual components and the powder blend when designing a feasible formulation. A tablet should be hard enough to withstand the manufacturing and storage conditions and yet weak enough to disintegrate allowing the active ingredient to dissolve and absorb inside the GI-tract. Furthermore, it is crucial to remember that compression behavior alone does not dictate the properties of the compact, as each material contributes to the formulation with unique functional features such as disintegrating or binding effect.

1.3. Compaction simulators

Powder compaction simulators have been designed to assist in designing a tablet formulation. They are typically hydraulic or mechanically powered and are constructed to mimic the stages of tableting while consuming only minuscule amounts of material compared to common tableting processes (Michaut et al., 2010; Rees et al., 1972). Hydraulic machines tend to resemble eccentric tableting machines and mechanical machines mimic rotary tableting machines even though often being linear in design. At their best, compaction simulators can mimic all of the events of a tableting process ranging from die-filling to ejection and can be very useful tools in pharmaceutical formulation design. The main problem in utilizing some of the commercially available compaction simulators seems to be that a certain simulator may have to be paired with a certain tableting machine to get comparable results. Therefore, setting up the machines and testing them in various conditions to ensure comparable results may require extensive effort, as aptly demonstrated by Neuhaus (2007). Modern simulators are more user-friendly but the cost of these machines is still high.

1.4. Gravitation based high-velocity compaction analysis

In the present study, a gravitation-based high-velocity compaction analysis method is presented. A novel device was constructed to provide accurate information about powder compression. The device differs from current tableting machines and compaction simulators as it does not force the powder into a specified volume, but allows the powder to freely resist compression. Therefore, the properties of powder ultimately determine the maximum compression pressure. This enables acquiring pure substance or blend specific compression profiles. Tableting events other than compression itself, such as die-filling and ejection, are deliberately ignored in this setting in order to focus on compression and maintain the simplicity of the device. Thus, the device has not been constructed to replace a tableting simulator but to provide additional information about powder behaviour. All data obtained with the method is based on measuring distance as a function of time, and the basic physics accompanied is uncomplicated. The cost of the device is roughly 20 000 USD.

First, introductory testing was carried out to prove the accuracy of the setup. Following this, samples of MCC and starch were compressed consecutively to obtain compressibility profiles and energy distribution data. In the present study, we sought to prove that the presented method is valid for powder compression examination in an accurate and reproducible manner. Furthermore, we wanted to show that distance measurement with a known sampling frequency is the only requirement to derive information about the compression event.

2. Materials and methods

2.1. Materials

Powder compression studies were performed on microcrystalline cellulose (Avicel PH-102; FMC BioPolymer; Lot 7314C) and starch (Amioca powder TF; National Starch; Lot CGH-358/0439). The die walls and punches were lubricated using 5% w/w magnesium stearate (Ph. Eur) in acetone (technical grade).

2.2. Sample preparation

All samples were individually weighed using an analytical balance (Table 1). The water activity of the samples was measured with a water activity meter (AquaLab Series 3, Decagon Devices Inc., Pullman, Washington, USA) and the ambient room temperature and relative humidity were measured with a moisture tester (Mastech MS6900, Precision Mastech, City of Industry, California, USA). The height of the powder bed in the die before compression was derived from time-distance data recorded during compression.

2.3. High-speed gravitational compression device

2.3.1. Structure and function of the device

In the present study, a novel device was constructed to analyze the event of powder compression and compression properties of substances (Fig. 1). The device consists of a cylindrical steel bar with a length of 1 m and total mass of 6.27 kg mounted to a rigid frame. The bar is mounted onto a partially Teflon coated frame using Teflon coated bearings and extension pieces to restrict torsional and rotational motion, which combined result in nearly frictionless and strictly vertical motion of the bar. The bar is dropped from a controlled height of 0–200 mm onto an 18 mm high, circular flat faced punch with a diameter of 8 mm and corresponding die with a combined mass of 2.71 kg mounted on a steel anvil with a mass of 49.0 kg. The die consists of three different parts and can be dismantled to remove the compact after compression. The anvil is connected to an 11.5 kg concrete brick through 4 attachment pins. Rubber sheets are placed between the anvil and concrete brick and between the concrete brick and the ground to reduce horizontal motion of the device during impact. The anvil is made of decarbonized steel and all other metal parts are made of hardened steel (HRC 60–64). Decarbonized steel is

Table 1
Sample and compact characteristics (average ± standard deviation; n = 3).

T = 25–26 °C; R.H. = 32-33% (ambient)	Before compression			After compression		
Excipient	Water activity	Sample mass (mg)	Powder bed height (mm)	Out-of die tablet height (mm)	Out-of-die tablet width (mm)	Compact mass (mg)
MCC	0.228 ± 0.013	200.0 ± 0.2	7.757 ± 0.155	3.033 ± 0.031	8.326 ± 0.022	198.4 ± 1.7
Starch	0.215 ± 0.007	200.3 ± 0.1	5.690 ± 0.014	3.457 ± 0.016	8.269 ± 0.004	192.3 ± 1.2