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Research paper

Characterisation of density distributions in roller-compacted ribbons using micro-indentation and X-ray micro-computed tomography

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ABSTRACT

Roller compaction is one stage in a dry granulation process to produce free flowing granules. Its proper understanding is essential in optimising manufacturing efficiency and product quality. Roller compaction produces a compacted strip or "ribbon", which is then milled to produce granules. For a given milling condition, the density distribution in the ribbons determines the properties of the granules (particularly their size distribution and strength). Therefore, knowing the density distributions in the ribbons is very important in improving the effectiveness of the roller compaction process and the quality of the granules produced. In this paper, the density distribution in roller-compacted ribbons of microcrystalline cellulose (Avicel PH102) has been examined using three different techniques: (1) sectioning; (2) micro-indentation and (3) X-ray micro-computed tomography. It has been shown that with proper calibration all three techniques can essentially produce the same results, but with a different degree of resolution (scale of scrutiny). In addition, the influence of process conditions, such as roll gap, roll speed and the presence or absence of lubrication, on the ribbon density distributions has also been investigated. Flow into the press is often constrained by the presence of "cheek plates", which prevent lateral powder movement. In this type of arrangement, it is found that non-uniform powder feeding occurs in the compaction region, induced by the friction between the powder and the cheek plates; as a result, the densities in the middle of the ribbon width are generally higher than those close to the edges. It has also been shown that higher average ribbon densities are obtained when the roll gap, roll speed, or the friction between the powder and the side cheek plates is reduced.

1. Introduction

Roller compaction is one stage in a continuous dry granulation process for producing free flowing granules. In this process, powder blends are compressed between two counter-rotating rollers to form ribbons, flakes or briquettes, which are then milled to obtain granules [1,2]. Compared to other granulation processes, roller compaction has several advantages: (1) it is the most cost-effective process because of its low demand for space, personnel, energy and time consumption; (2) it is the most feasible granulation process for formulations with drugs sensitive to heat, moisture or solvents, as no liquid and additional heat are needed; (3) it is a continuous process with high throughput and relatively low energy consumption [1,2]; (4) it can produce more homogeneous products when compared to other dry granulation techniques, such as *slugging* [3,4]; and (5) it is possible to implement on-line control and automation of processing settings, so that batch-to-batch variations are minimised and the product quality is improved. Hence, roller compaction has attracted increasing attention over the last decade [1,3–14].

The properties of the granules (i.e., size distribution and strength) produced from roller-compacted ribbons depend upon the properties of the ribbons, such as density distribution and strength, and the milling conditions. Nyström and Alderborn [15] showed that the porosity and size of the granules were determined by these properties of ribbons for a given milling condition. Sheskey and Hendrey [16] showed that the change in the ribbon strength altered the grinding time in the mill to obtain granules of similar properties. In other words, under the same milling conditions, finer granules were produced with weaker ribbons (i.e., with lower tensile strength) while a larger proportion of coarse granules were obtained with stronger ribbons, as also demonstrated by many others [7,17,18]. Recent studies [19–21] revealed that the strength of compressed pharmaceutical compacts primarily depends on their relative densities, i.e., solid fraction. The

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variation of local densities in the ribbons will hence result in the difference in the localised ribbon strength and consequently will lead to a wide size distribution of the produced granules for a given milling condition. Therefore, knowing the density distributions of ribbons is very important in order to optimise roller compaction process, and thus to improve the quality of the granules produced. A drilling technique was developed by Funakoshi et al. [22] to estimate the compressive pressure applied to compact the powders along the roll width during roller compaction. For a given roller compaction setup, the variation in the compressive pressure would indicate the variations in ribbon density distribution. By correlating the force needed for drilling the produced compacts with the compression pressure, they found that the compression pressure in the middle of ribbon width is much higher than that at the edges, indicating that the density distribution in the compacted ribbon is not homogeneous. Nevertheless, little attention has been paid to the characterisation of density distributions of roller-compacted ribbons, although a variety of techniques, such as micro-hardness [23], mercury porosimetry [23], X-ray tomography [24,25] and NMR [26,27], have been used to characterise the density distribution of pharmaceutical tablets.

Therefore, the objectives of this paper were to characterise the variation of local density in the roller-compacted ribbons and to explore how the process conditions affect the density distributions in the ribbons. For these purposes, micro-indentation, X-ray micro-computed tomography (μCT) and sectioning methods are used to measure the local densities in the ribbons, so as to explore the local density variation. This paper is structured as follows. Firstly, the principles of micro-indentation and X-ray μCT micro will be briefly described. Secondly, the application of these techniques to characterise density distributions will be presented. Finally, the density distributions of ribbons produced under different roller compaction conditions are presented, the influence of the process conditions is discussed and the utility of the characterisation techniques employed is evaluated.

2. Micro-indentation

Micro-indentation is a technique for determining the hardness of materials at the micro-scale, which quantifies the resistance of a material to plastic deformation. During the micro-indentation test, an indenter of known shape and size is pressed into the material to be tested with a specified force. The size of the indentation depends on the dimensions of the indenter, the applied load and the hardness of the sample. The Vickers micro-hardness test used in this work is a standard micro-indentation test that uses a diamond indenter in the shape of a square-base pyramid. During Vickers tests, both diagonals of the indent are measured and the mean of these values is used to calculate the surface area of the indent, hence the hardness can be determined.

For pharmaceutical compacts, it is recognised that the local hardness is related to the local density. Generally, the higher the density is, the higher the hardness. Thus, micro-indentation tests have recently been performed to characterise the mechanical properties of pharmaceutical compacts [23,28–31]. For instance, the hardness of different compacted batches of lactose was determined by Busignies et al. [28], who showed that the hardness was indirectly proportional to the tablet porosity. The relationship between tablet density and hardness was established by Sinka et al. [29], which was used to obtain density distribution maps in the tablets produced with lubricated and non-lubricated dies. Micro-indentation was also used to examine the heterogeneity of the compact [30], to explore the effect of compaction parameters on the ribbon hardness [23] and to determine the endurance of polymeric film coating of ibuprofen tablets [31].

3. X-ray micro-computed tomography (X-ray micro-CT)

X-ray micro-CT is a non-destructive technique that provides three-dimensional images of micro-structures with a resolution of several microns. During the test, a sample is attached onto the turntable (see Fig. 1). An X-ray beam is then directed to the sample. In passing through the sample, some X-ray photons are attenuated (absorbed), whereas others will transmit through the sample and be detected by the detector. The absorption ability of a material for the X-ray photon energy is characterised using the linear attenuation coefficient μ, which can be approximated as in [32]

$$\mu = \rho \cdot \frac{Z}{A} \cdot N_{AV} \cdot \left(a + b \cdot \frac{Z^{3.8}}{E^{3.2}} \right) \quad (1)$$

where ρ is the material density, Z is the effective atomic number, A is the atomic weight, N_{AV} is Avogadro's number, a is the Klein–Nishina coefficient that is only weakly dependent on the X-ray photon energy, b is a constant with a value of 9.8×10^{24} and E is the photon energy. Thus, the linear attenuation coefficient μ depends upon the material density ρ, the atomic number Z and X-ray energy E. For a given X-ray energy and a compact of a single-component material (i.e., Z is constant), the linear attenuation coefficient is proportional to the bulk density, represented by ρ.

X-ray micro-CT has been widely used to examine the properties of powder compacts, including the density distribution [24,25,33,34], granule internal porosity distribution [35] and crack and fracture patterns inside the tablets [36,37]. Potential applications of X-ray micro-CT in pharmaceutical sciences are exemplified by Hancock and Mullarney [38]. Although this technique has been used to characterise the density distributions of the tablets [24,25], quantitative analysis of the density distribution of roller-compacted ribbons using this technique has not been reported. In this study, X-ray micro-CT is used to quantitatively determine the density distribution in the roller-compacted ribbons, to examine the effect of the process conditions on the pattern of density distributions and to explore the performance and utility of this technique in comparison with other density mapping techniques, such as the sectioning method and micro-indentation.

4. Materials and methods

Microcrystalline cellulose (MCC) of Avicel grade PH102 (FMC Biopolymer, USA) was used for all experiments. The true density of MCC was measured using helium pycnometry (AccuPyc 1330, Micrometrics®, Bedfordshire, UK). Magnesium stearate (MgSt) (Liga MF-2-V, Saville Whittle, UK) was employed as the lubricant.

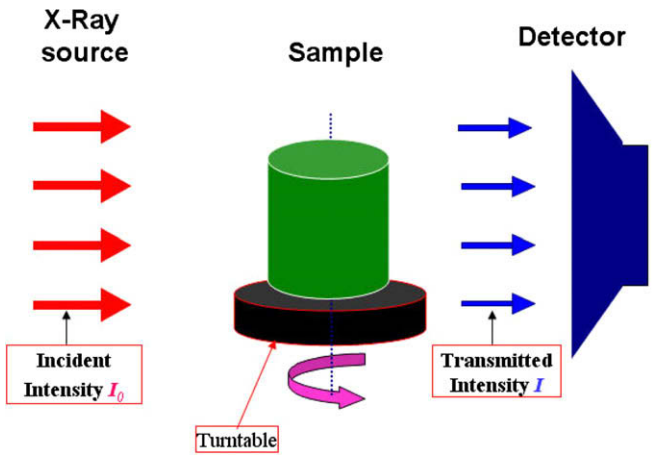

Fig. 1. Illustration of the principle of X-ray micro-computed tomography.