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The effect of lubrication on density distributions of roller compacted ribbons

A.M. Miguélez-Morán[a,b], C.-Y. Wu[a,*], J.P.K. Seville[c]

[a] Department of Chemical Engineering, University of Birmingham, Birmingham, B15 2TT, UK
[b] Department of Pharmaceutical Technology and Biopharmacy, University of Heidelberg, Im Neuenheimer Feld 366, D69120, Heidelberg, Germany
[c] School of Engineering, University of Warwick, Coventry, CV4 7AL, UK

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ABSTRACT

Roller compaction is a continuous dry granulation process for producing free flowing granules in order to increase the bulk density and uniformity of pharmaceutical formulations. It is a complicated process due to the diversity of powder blends and processing parameters involved. The properties of the produced ribbon are dominated by a number of factors, such as the powder properties, friction, roll speed, roll gap, feeding mechanisms and feeding speed, which consequently determine the properties of the granules (size distribution, density and flow behaviour). It is hence important to understand the influence of these factors on the ribbon properties. In this study, an instrumented roller press developed at the University of Birmingham is used to investigate the effect of lubrication on the density distribution of the ribbons. Three different cases are considered: (1) no lubrication, (2) lubricated press, in which the side cheek plates of the roller press are lubricated, and (3) lubricated powder, for which a lubricant is mixed into the powder. In addition, how the powders are fed into the entry region of the roller press and its influence on ribbon properties are also investigated. It is found that the method of feeding the powder into the roller press plays a crucial role in determining the homogeneity of the ribbon density. For the roller press used in this study, a drag angle (i.e., the angle formed when the powder is dragged into the roller press) is introduced to characterise the powder flow pattern in the feeding hopper. It is shown that a sharper drag angle results in a more heterogeneous ribbon. In addition, the average ribbon density depends upon the peak pressure and nip angle. The higher the peak pressure and nip angle are, the higher the average ribbon density is. Furthermore, the densification behaviour of the powder during roller compaction is compared to that during die compaction. It has been shown that the densification behaviour during these two processes is similar if the ribbons and the tablets have the same thickness.

1. Introduction

Roller compaction is a dry granulation process in which powder blends are compressed between two counter-rotating rollers to form strips, flakes or briquettes, which are subsequently milled to obtain granules with desirable size and size distribution for making capsules or tablets (Guigon et al., 2007). Low demand for space, personnel, energy and time consumption makes roller compaction the most cost-effective agglomeration process. For formulations with drugs that are sensitive to heat, moisture or solvents, roller compaction is the most feasible granulation process because no moisture and additional heat are involved. In addition, compared to other dry granulation techniques, such as *slugging*, roller compaction is a continuous process with higher productivity but less energy consumption and can produce more homogeneous products. Furthermore, on-line control and automation of processing settings can be readily implemented in the roller compaction process so that batch-to-batch variations are minimised and the product quality is improved.

During roller compaction, the powder blends are fed into the compaction zone (the gap between two rollers). The compaction zone can be divided into three regions (Johanson, 1965, see also Fig. 1): (i) an entry (slip) region, (ii) a nip region and (iii) a release region. In the slip region, particle rearrangement, permeation of entrapped air and pre-agglomeration may occur. In the nip region, the powder blend is gripped and compressed between the two rollers as they continue to rotate. The velocity of the powder becomes close to the rotation speed and it is compacted as it is “nipped” between the two rollers. The compaction continues until the powder reaches the neutral angle at which the compression pressure is a maximum. Thereafter, the compressed powder moves to the release region in which relaxation (elastic recovery)

* Corresponding author. Tel.: +44 121 4145365; fax: +44 121 4145324.
E-mail addresses: c.y.wu@bham.ac.uk, miguelez@uni-hd.de (C.-Y. Wu).

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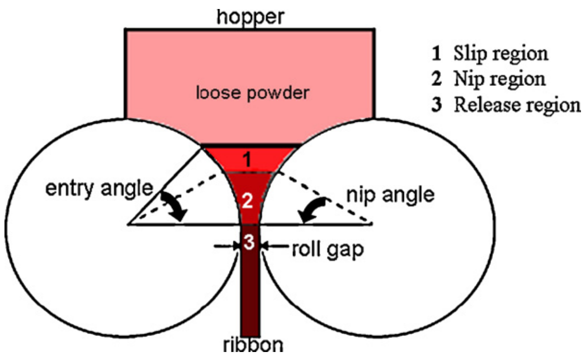

Fig. 1. Illustration of the main regions during roll compaction.

of the compressed powder may take place. The sizes of these three regions and the transition from one region to another depend on the material properties and the processing conditions. The densification behaviour of powders during roller compaction is governed by two key parameters: (1) the nip angle α and the maximum pressure (P_{max}). The nip angle defines the size of the nip region and the compression duration, while the maximum pressure (P_{max}) at the neutral angle indicates the maximum degree of densification. These two parameters are determined by both the inherent powder properties (internal friction, cohesion and the friction between the powder and the tooling) and processing conditions, such as roll speed and roll gap (Miller, 1997; Shlieout et al., 2002; Guigon and Simon, 2003; Simon and Guigon, 2003; Bindhumadhavan et al., 2005; Weyenberg et al., 2005; Mansa, 2004) in a very complicated manner. Due to the diversity of pharmaceutical powder blends and the large number of variables involved, roller compaction is still not well understood although it has attracted increasing attention over the last decade (Miller, 1997; Kleinebudde, 2004; Guigon et al., 2007).

Generally, the ribbons are subsequently milled into granules that are usually compressed into tablets. Wikberg and Alderborn (1991) studied the effect of shape and porosity of the granules on tablet properties and demonstrated that both shape and porosity affected the potential for granule deformation and hence the tablet properties. Nystrom and Alderborn (1993) showed that the main factors contributing to the strength of compacts were granule porosity and size, which were indeed determined by the properties of ribbons for a given milling condition. Sheskey and Hendren (1999) showed that the change in the ribbon strength varied with the grinding time at the mill. Thus, under the same milling condition, finer granules are produced with weaker ribbons (i.e., with lower tensile strength) than stronger ribbons, as demonstrated by Inghelbrecht and Remon (1998) and Von Eggelkraut-Gottanka (2002). Also Weyenberg et al. (2005) characterised the granules used to produce ocular mini-tablets of ciprofloxacin and found that stronger ribbons generated larger granules. Recent studies have revealed that the strength of compressed pharmaceutical compacts primarily depends on their relative densities, i.e., solid fraction (Tye et al., 2005; Wu et al., 2005, 2006). Hence, the properties of the granules will be predominantly determined by the density distributions of the ribbons.

Although ribbons with homogeneous density distribution are desirable in pharmaceutical processing, it is a challenge to produce such ribbons. Zinchuk et al. (2004) compared the ribbons produced using a lab-scale compactor with the tablets produced by uniaxial compression with a compactor simulator. They found that the ribbons presented much larger variations in tensile strength and solid fraction values than the tablets, which was due to the non-uniform stress distribution across the length and the width induced during the roller compaction process. Guigon and Simon (2000, 2003) examined the heterogeneity of the ribbons by mixing coal into a lactose monohydrate blend. They found that the number of fragmented coal particles was higher at those regions subjected to higher stresses. Consequently, those regions appeared darker in the photographic images and their lateral positions on the strip varied in a sinusoidal way. They also used an array of pressure transducers to obtain the stress profiles at the roller surface as the feeding screw rotated and observed a variation pattern whose periodicity corresponded to the screw rotation. They, hence, attributed the sinusoidal pattern to the period fluctuation of the powder feed as the feeding screw rotated. The density variation in roller compacted ribbons was also investigated by Perera (2005) and Busies (2006). Perera (2005) found a higher density in the central part of the ribbon than that at the edges using a gravity fed compactor with sealing plates at the compaction zone. Busies (2006) examined the density of ribbons produced with a screw fed compactor and showed that the fluctuation of solid fraction distribution along the ribbon width apparently depended on whether the compaction zone is sealed using rims that rotate with the roller at the same speed or sealing plates that are stationary.

Clearly, feeding which is non-uniform in time and/or space will result in ribbons with non-uniform density distributions. As in most powder flow problems, both internal and wall friction is implicated. The objective of the present study was to determine whether ribbons with more uniform density distributions can be produced with the aid of lubrication. Both internal (powder) lubrication and wall (boundary) lubrication has been investigated.

2. Materials and methods

A widely used pharmaceutical excipient, microcrystalline cellulose (MCC) of Avicel grade PH102 (FMC Biopolymer, USA), was used for all experiments reported here. Magnesium stearate (MgSt) (Liga MF-2-V, Saville Whittle, UK) was employed as the lubricant. The roller compaction experiments were performed using a laboratory scale instrumented roller compactor (see Fig. 2) developed at the University of Birmingham (Bindhumadhavan et al., 2005). The roll is 45 mm wide and 200 mm in diameter. The powders were fed into the compaction zone under gravity through a feeding hopper. For all

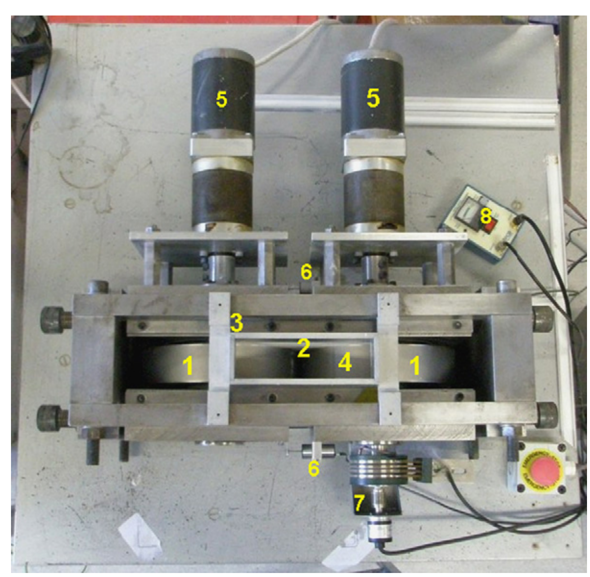

Fig. 2. The instrumented roller compacter used in this study. (1) Rollers, (2) cheek side plates, (3) hopper, (4) pressure transducer, (5) stepper motors, (6) displacement transducers, (7) encoder and (8) signal amplifier.