Chemical Engineering Science 86 (2013) 9–18

Contents lists available at SciVerse ScienceDirect

Chemical Engineering Science

journal homepage: www.elsevier.com/locate/ces

The effects of lubrication on roll compaction, ribbon milling and tabletting

Shen Yu [a], Michael Adams [a], Bindhu Gururajan [b], Gavin Reynolds [b], Ron Roberts [b], Chuan-Yu Wu [a,*]

[a] School of Chemical Engineering, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK
[b] Pharmaceutical Development, AstraZeneca, Macclesfield, Cheshire SK10 2NA, UK

ARTICLE INFO

Article history:
Received 3 November 2011
Received in revised form
30 January 2012
Accepted 18 February 2012
Available online 12 March 2012

Keywords:
Dry granulation
Roll compaction
Milling
Tabletting
Lubrication
Magnesium stearate

ABSTRACT

Lubricants are commonly used in the pharmaceutical industry to prevent adhesion and improve the efficiency of roll compaction and tabletting. The aim of the current work is to develop an improved understanding of the mechanisms involved. Two commonly used pharmaceutical excipients, microcrystalline cellulose (MCC) and di-calcium phosphate dihydrate (DCPD), were selected as the model feed powders with magnesium stearate (MgSt) as the lubricant. An instrumented roll compactor was used, the ribbons were milled using an oscillating mill and the granules were compressed into tablets. The wall and internal friction angles of the feed powders were measured and related to the performance of the roll compaction that was characterised by the nip angle and maximum pressure. The milling performance was related to the fracture energy of the ribbons. The tabletting was assessed by the density and strength of the tablets. A qualitative interpretation of the data was developed and the practical implications of the work are considered. It was also shown that the bulk lubrication results in the reduction in internal friction for MCC but not for DCPD. The wall friction of DCPD is reduced by both bulk and wall lubrication unlike MCC for which the friction coefficient is essentially unchanged. The behaviour of the powders in roll compaction can be ascribed to the variation of the frictional properties due to lubrication. It is found that wall lubrication does not affect either the nip angle or the maximum roll pressure during roll compaction of MCC, but for DCPD the nip angle and maximum pressure are reduced with wall lubrication. In addition, the nip angle and the maximum pressure during roll compaction of MCC and DCPD are reduced with bulk lubrication. Furthermore, bulk lubrication causes reduction in the bonding properties and hence the tensile strength for MCC, but not for DCPD.

1. Introduction

In the pharmaceutical industry, especially for drug development with formulations that are sensitive to heat and moisture, dry granulation is preferred to wet size enlargement processes that require solution or melt binders. Dry granulation generally involves roll compaction in which the feed powders are compressed between counter-rotating rolls to form a coherent ribbon; granules are obtained by milling the ribbons. For most cohesive feed powders, a lubricant is generally required to improve flowability and to prevent adherence to the roll surfaces. Magnesium stearate (MgSt) is widely used as the lubricant for this purpose. It is a common boundary lubricant and such materials reduce solid–solid friction by providing a film with an interfacial shear strength that is smaller than that of the underlying surfaces. The distribution of the lubricant on the surfaces of the particles is a critical factor in controlling the effectiveness when used for powders. A number of mechanisms have been proposed on this basis (Bolhuis et al., 1975, 1980; Pintye-Hodi et al., 1981; Tawashi, 1963a, b) as summarised in Table 1. The most commonly accepted mechanism is the formation of Langmuir–Blodgett monolayer of MgSt and the filling of cavities by MgSt (Roblot-Treupel and Puisieux, 1986), especially with prolonged mixing time (Johansson and Nicklasson, 1986). It is probable that the large variations in particle sizes and surface topographies for different feed powders will result in a considerable variation in the performance of the lubricant.

There have been a number of studies of roll compaction with MgSt as the lubricant (He et al., 2007; Miguélez-Morán et al., 2008; von Eggelkraut-Gottanka et al., 2002). von Eggelkraut-Gottanka et al. (2002) compacted two different batches of dry herbal extract using a gap width and force controlled roll compactor and investigated the influence of processing parameters and the amount of magnesium stearate using multilinear stepwise regression analysis. It was reported that the disintegration time of the tablets increased with the concentration of MgSt due to an increase in hydrophobicity. They also argued that incorporation of MgSt into the granules (in the internal phase of the tablet) minimised the increase in disintegration time, while preserving its functionality as a lubricant.

* Corresponding author. Tel.: +44121 4145365; fax: +44121 4145324.
E-mail address: C.Y.Wu@bham.ac.uk (C.-Y. Wu).

0009-2509/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.ces.2012.02.026

Table 1
Proposed mechanisms for the lubrication of MgSt based on the nature of the surface coverage.

Mechanisms	References
Monomolecular film formation such that the inter-particle surfaces are separated by several molecular layers	Bolhuis et al. (1975)
Uniform mono-particulate continuous layers with the separation between the particles involving a few MgSt particles	Tawashi (1963a, b)
The cavities on the host particle surfaces filled by MgSt to form smooth surfaces	Bolhuis et al. (1980)
Non-uniform distribution of MgSt on the host particle surfaces	Pintye-Hodi et al. (1981)

He et al. (2007) roll-compacted MCC (grade Avicel PH 102, 44–75 μm sieve fraction) without lubricant and with 0.5% (w/w) MgSt. Heckel analysis, tablet tensile strength and dynamic indentation measurements were performed in order to evaluate the mechanisms for the loss of re-workability of the feed powder after roll compaction, especially with the addition of MgSt. They concluded that work-hardening occurred in the process, and that over-lubrication due to the presence of MgSt appeared to be the major cause for the decrease in mechanical strength of the tablets. Miguélez-Morán et al. (2008) investigated roll compaction with MCC (grade Avicel PH 102) under three conditions: (1) unlubricated, (2) lubricated roll surfaces and (3) lubricated powders, and showed that the most uniform feeding of the powders and the most uniform density of the compacted ribbons were obtained when the powder was lubricated internally with MgSt, while a reduction in the maximum pressure during roll compaction was observed. Their work clearly demonstrated that MgSt can affect the roll compaction of MCC.

Despite the previous studies, the relationships between the performance of roll compaction, and the downstream processes of milling and tabletting, and the lubrication mechanisms have not been established. In particular, the influence of the lubricant on the milling behaviour, and the properties of the granules and tablets are not well understood. These were the aims of the current work, in which MCC and DCPD were chosen as the feed powders. They are both commonly used pharmaceutical excipients but with distinctive particle sizes, surface topographies and sensitivities to lubrication with MgSt; it has been reported that the lubrication of DCPD with MgSt is very insensitive to the mixing conditions (Vromans et al., 1988), unlike MCC (Zuurman et al., 1999).

2. Materials

MgSt is a white odourless flake-like powder (see Fig. 1). Calipharm D grade DCPD (Rhodia, France) is a brittle crystalline powder with shale-like particles (Fig. 2a). MCC (Avicel grade PH 102, FMC Biopolymer, USA) is a crystalline powder (crystallinity $>78\%$) with needle-shaped particles (see Fig. 2b) that exhibits greater plastic deformation than DCPD, which is relatively brittle. The true densities for MCC and DCPD were measured using a helium pycnometer (AccuPycII 1340, Micromeritics, USA) and are 1569 kg/m^3 and 2582 kg/m^3, respectively. The mean particle sizes for the two materials are 96.3 μm and 8.1 μm, respectively, measured using a particle size analyser (Model Helos, SympaTec, Germany).

Various amounts of MgSt (w/w 0.15–1.5%) were mixed with the two powders using a double-cone blender. Preliminary studies (not presented here) revealed that the frictional and flow properties of the powders did not change for mixing times longer than 5 min, which was the time period finally selected for all the experiments reported here. The surface morphologies of the powders lubricated with 0.75% (w/w) MgSt are shown in Fig. 2c and d.

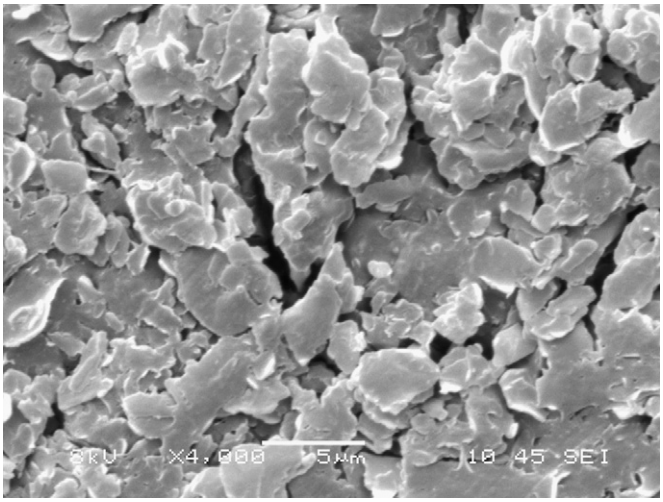

Fig. 1. Scanning electron micrograph of magnesium stearate.

3. Experimental

3.1. Ring shear cell tests

The effective angle of internal friction of the feed powders and milled granules was measured using an RST-XS ring shear cell tester (Dietmar Schulze, Germany) with normal stresses in the range of 4–10 kPa. This instrument was also used to measure the angles of wall friction against a smooth stainless steel plate (surface roughness Ra $\sim$0.3 μm) with normal stresses in the range of 1.1–20 kPa. The morphologies of the powders before and after the wall friction measurements were attained using a Scanning electronic microscopy (6060, JEOL, Japan) and are shown in Fig. 2e and f.

3.2. Roll compaction

The powders were compacted using a laboratory scale instrumented roll compactor developed at the University of Birmingham (Bindhumadhavan et al., 2005; Miguélez-Morán et al., 2008; Patel et al., 2010). It consists of two stainless steel rolls of 46 mm in width and 100 mm in radius. Gravity powder feeding was employed, which involved an initial constant volume of powder in a hopper with a rectangular cross-section that was filled manually, and the excess was levelled gently. In the current study, the minimum roll gap, S, and the roll speed, u, were fixed at 1.0 mm and 1 rpm, respectively. The angular position, θ, was measured from the minimum roll gap, and the corresponding radial roll pressure, p was measured using a piezoelectric pressure sensor (PCB 105C33, Techni-Measure, Studley, UK), which fitted in the centre of one roll, allowed the roll pressure distributions to be obtained. The influence of bulk and wall lubrication was investigated. In the case of wall lubrication, the metal roll surfaces were lubricated with ethanol suspensions of MgSt having concentrations of 0.25% and 1%.

The dimensions (*i.e.* length, width and thickness) of the ribbons were measured using a digital calliper (Mitutoyo, Hampshire, UK) to determine their volumes, from which the bulk densities were obtained. The fracture energies of the ribbons were measured by 3-point bending configuration using a universal mechanical testing machine (Instron, High Wycombe, UK). This involved integrating the force–displacement data to determine the total work to fracture. The fracture energy was obtained as the ratio of the work and the area of the fracture surface.