International Journal of Pharmaceutics 462 (2014) 108–114

Contents lists available at ScienceDirect

International Journal of Pharmaceutics

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

Energy-based analysis of cone milling process for the comminution of roller compacted flakes

Asim Kumar Samanta, Likun Wang, Ka Yun Ng, Paul Wan Sia Heng*

GEA-NUS Pharmaceutical Processing Research Laboratory, Department of Pharmacy, National University of Singapore, 18 Science Drive 4, Singapore 117543, Singapore

ARTICLE INFO

Article history:
Received 23 September 2013
Received in revised form 2 December 2013
Accepted 19 December 2013
Available online 27 December 2013

Keywords:
Roller compaction
Flakes
Cone milling
Effective specific energy
Milling rate

ABSTRACT

Cone mill is commonly used for the milling of wet and dry agglomerates in the pharmaceutical industry as it is capable of producing milled granules with desired size characteristics. The aim of this study was to evaluate the various cone mill process parameters in terms of milling rate and energy consumption for the comminution of roller compacted flakes. A placebo formulation containing microcrystalline cellulose, lactose and magnesium stearate was used to evaluate the milling performance. Results of this study showed that higher milling rate was obtained with the combination of higher impeller speed, teethed round sidearm impeller and grater screen surface profile. Either one of the later two parameters when present in any mill setting was found to be capable of shortening the residence time of flakes inside the milling chamber, thus resulting in a higher milling rate. On the other hand, selection of appropriate screen surface profile and impeller speed was very important at lowering the effective specific energy consumption during milling. Grater screen surface profile and impeller speed between 2000 and 2400 rpm were found to act synergistically as the best combination for an energy sparing process. Impeller sidearm shape was found to have no significant effect on energy consumption.

1. Introduction

Size reduction is an important unit operation in pharmaceutical granulation process to produce granules of suitable size, size distribution and amount of fines which may affect subsequent operations such as flow and compaction, and in turn, content uniformity and dissolution characteristics of final dosage form. In particular, the milling step is even more crucial in dry granulation process due to relatively poorer binder distribution in roller compacted granules compared to wet or spray dried granules (Seager et al., 1979). Poor binder distribution in granulation may lead to production of granules with wider size distribution and more fines after milling. Manufacturing and product quality requirements for pharmaceutical products have become more stringent with time and specifications involving finer particles, mean particle size or size cut-off are increasingly being applied.

In a previous study, controlled comminution of roller compacted flakes was achieved by investigating various cone mill process parameters aimed at minimizing fines (Samanta et al., 2012). However, the energy efficiency of the different process parameters is one of the major aspects in the size reduction process especially with rising energy costs. In the mineral industry, the theory of grinding has mainly been developed as a response to needs for maximizing production capacity and minimizing energy use for low value added products (Prasher, 1987). In trying to reduce the manufacturing carbon footprint, the rather extremely inefficient size reduction unit operation in the entire pharmaceutical production chain should be a focal area to investigate on how to save energy, from the economic view point.

Energy consumption during milling of flakes depends on the mill type and process parameters such as impeller speed, impeller type, screen type and screen aperture size. Mechanical characteristics of flakes such as hardness and thickness will also have their effects. The improper selection of equipment and milling parameters may lead to undesirable changes in the milled material including softening and melting of low melting point materials, polymorphic transformation, increased rate of drug degradation and the build-up of static charges due to the use of excessive mill energy (Byers and Peck, 1990). Therefore, real-time measurement of energy consumption by the mill during the comminution process can provide not only information regarding the milling energy requirement during milling but also how granules of desired characteristics can be produced using a selected set of operational parameters. Properties of the flakes may be deduced from the amount of energy utilization by the mill, for a given set of mill settings.

* Corresponding author. Tel.: +65 6516 2930; fax: +65 67752265.
E-mail address: phapaulh@nus.edu.sg (P.W.S. Heng).

0378-5173/$ – see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.ijpharm.2013.12.042

An ideal milling condition should also enable a high milling rate to produce granules of the desirable quality by careful selection of milling parameters. Higher milling rate will correspond with shorter residence time of flakes inside the milling chamber and resultant granules are quickly transverse through the screen as appropriately sized granules. In contrast, lower milling rate prolonged residence of material inside the mill and tended to reduce flakes into smaller sized granules or fines due to increased time of attrition. Moreover, prolonged residence time may cause temperature rise inside the milling chamber with possible consequence of degradation of the drug or change in the polymorphic form. Hammer mills commonly used to breakdown the flakes tend to produce granules with wider size distribution alongside causing a dusty process. Thus, the more versatile, precise and economical process of cone milling of flakes was the subject of investigation in this study.

Much reported research work on the milling of wet and dry masses in wet granulation process had been on the effects of milling on granule characteristics. However, by comparison, relatively little research work had been undertaken on the comminution of roller compacted flakes. Vendola and Hancock (2008) investigated the milling efficiency of roller mill, oscillating granulator, hammer mill and cone mill on the comminution of roller compacted flakes. Samanta et al. (2012) evaluated the various cone milling process parameters for the milling of roller compacted flakes by adopting minimal fines approach. Reynolds (2010) modeled the size reduction process in a conical mill. Sakwanichol et al. (2012) compared different mills and commented about energy savings when using a roll mill. Only a few studies were conducted to examine the specific energy requirements of mills (Bitra et al., 2009; Mohapatra and Bal, 2007). However, no research report had been directed at the energy requirements during cone milling of roller compacted flakes. Therefore, it is imperative to study the effect of cone milling parameters on the energy consumption and milling rate for the optimization of roller compacted flake comminution process. The objective of the study was to evaluate the effect of different cone mill process parameters (impeller type, impeller speed and screen type) on the comminution of undulated roller compacted flakes by adopting minimal energy consumption and high milling rate approach.

2. Materials and methods

2.1. Materials

Commercially available α-lactose monohydrate (Pharmatose® 200M, DMV, Veghel, Netherlands), microcrystalline cellulose (MCC; Avicel® PH102, FMC, UK) and magnesium stearate (MgSt; Sigma–Aldrich, Germany) were used. Prior to experimentation, all the materials were passed through a 355 μm aperture size sieve to eliminate the presence of any loose aggregated lumps in the bulk powders, and sifted powders were stored in sealed bags for at least 48 h at 25 ± 2 °C and 50 ± 5% relative humidity (RH) prior to use.

2.2. Methods

2.2.1. Powder blending

Lactose, MCC and MgSt were blended in the final weight ratio of 49.5:49.5:1, respectively, in a double cone blender (AR 400, Erweka, Germany) rotated at 40 rpm for 50 min. MgSt was added after 45 min of blending lactose with MCC. The final powder blend was collected and used for the roller compaction. Batch size of each blending cycle was 2 kg.

2.2.2. Roller compaction of powder blend

The powder blend was roller compacted (Pharmapaktor® L200/30P, Hosokawa Bepex, Germany) with 20 cm diameter rolls and 3 cm width axially-corrugated roll surfaces at roll force (RF) of 50 kN and roll speed (RS) of 2.6 rpm. The roller compactor was operated in the automatic mode where the speed of vertical feeding screw was automatically controlled by a feedback system to maintain 50 kN RF at 2.6 rpm RS. The flakes produced were then subjected to sifting on a sieve shaker (KS 1000, Retsch, Germany) set at 70 shakes per min for 2 min for the removal of non-compacted powder by a 2 mm aperture size sieve. The flakes produced were then stored in sealed plastic bags at 25 ± 2 °C and 50 ± 5% RH for at least 3 days before cone milling.

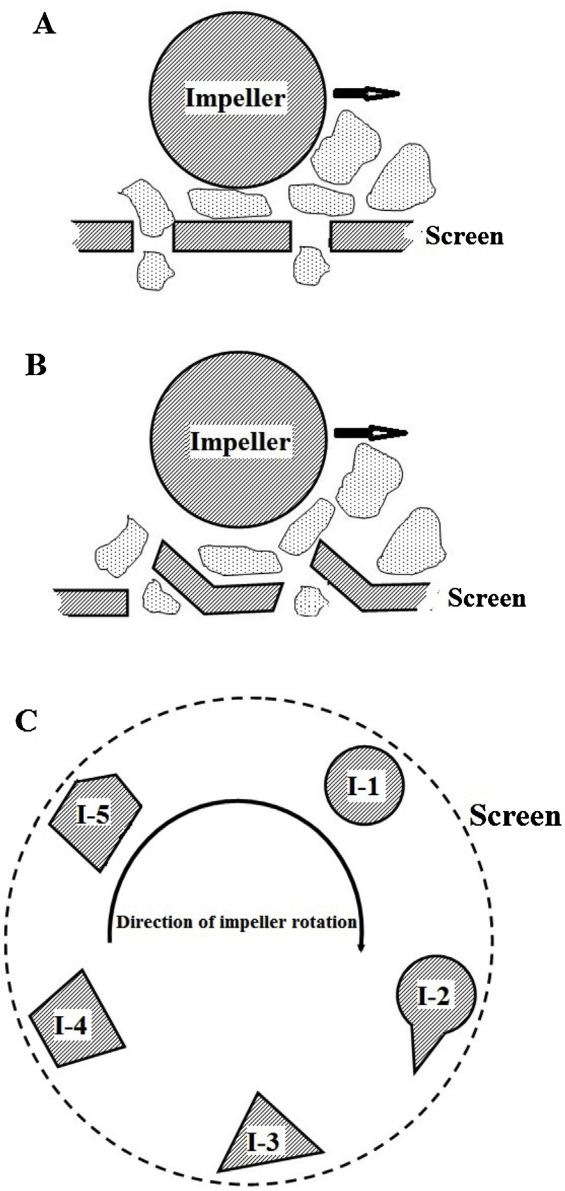

Fig. 1. Schematic diagram of screen surface profile [(A) smooth and (B) grater] and (C) impeller sidearm shape along with the position of the screen and the direction of impeller rotation.

2.2.3. Comminution of flakes

Flakes were cone milled (Comil® 197S, Quadro Engineering, Waterloo, Canada) to produce granules. Screens with two different types of surface profile (smooth (Fig. 1A) and grater (Fig. 1B)) of same aperture size (2388 μm) and impellers (Fig. 1C) with five different types of sidearm shape (round [I-1], round with teeth [I-2], triangular [I-3], pyramidal [I-4] and pyramidal with a leading