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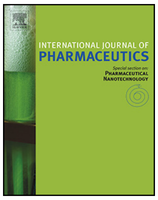

Twin screw wet granulation: Binder delivery

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ABSTRACT

The effects of three ways of binder delivery into the twin screw granulator (TSG) on the residence time, torque, properties of granules (size, shape, strength) and binder distribution were studied. The binder distribution was visualised through the transparent barrel using high speed imaging as well as quantified using offline technique. Furthermore, the effect of binder delivery and the change of screw configuration (conveying elements only and conveying elements with kneading elements) on the surface velocity of granules across the screw channel were investigated using particle image velocimetry (PIV). The binder was delivered in three ways; all solid binder incorporated with powder mixture, 50% of solid binder mixed with powder mixture and 50% mixed with water, all the solid binder dissolved in water. Incorporation of all solid binder with powder mixture resulted in the relatively longer residence time and higher torque, narrower granule size distribution, more spherical granules, weaker big-sized granules, stronger small-sized granules and better binder distribution compared to that in other two ways. The surface velocity of granules showed variation from one screw to another as a result of uneven liquid distribution as well as shown a reduction while introducing the kneading elements into the screw configuration.

1. Introduction

Granulation is a size enlargement process in which the particles are brought into contact with each other to form aggregates called granules (Dhenge et al., 2010). Granulation aims to improve the flow of materials as well as enhancing their compaction/homogeneity, reduce the production of dust, increase the bulk density and prevent the segregation of downstream blend of materials. Therefore, the application of granulation is used by a wide range of industries, such as pharmaceutical, food, chemical, detergents, fertilizers, and ceramics (Chen et al., 2009; Dhenge et al., 2012a; Djuric et al., 2009). Granulation is generally categorized into two classes; dry and wet.

The twin screw granulator (TSG) has recently become an equipment of choice for the continuous wet granulation in the pharmaceutical industry. TSG offers several advantages such as fewer or no scale up steps; continuous production at higher throughput; less space requirement etc., compared to the batch wise wet granulation equipment such as high shear granulator (HSG) and fluidised bed granulator (FBG) (Dhenge et al., 2010; Vercruysse et al., 2012). The wet granulation process depends on the use of liquid (water alone or with binder), to act as an adhesive to form a wet mass from the powder while being mixed mechanically. The particles are brought together by the usage of the combination of capillary and viscous forces in the wet state, rather than the usage of compaction forces only. The wet mass is dried, where the permanent bonds are formed to give agglomerates (Agrawal, 2011; Dhenge et al., 2010).

In twin screw granulation, the effect of process and formulation variables on the granule properties have been studied by various researches (Dhenge et al., 2010; El Hagrasy et al., 2013; Keleb et al., 2004; Lee et al., 2012). However, there is limited information available on the effect of the binder delivery on the granulation behaviour and the granule properties (El Hagrasy et al., 2013). Such a parameter has been studied in HSG and FBG (Osborne et al., 2011; Tan et al., 2014; Tan and Hapgood, 2011). Osborne et al. (2011), studied the effect of delivering the solid binder in 'wet' and 'dry' state, where they found that in HSG the dry binder addition method generated slightly larger granule size than wet binder addition method. However, in FBG the wet binder addition method generated significantly larger granules than the dry binder addition method.

In the twin screw granulation, El Hagrasy et al. (2013) studied the influence of different ways of binder addition into the

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granulator on the size distribution of granule produced. They added the solid binder as dry (with powder mixture), wet (in a solution with distilled water) and in both phases in ratio of 50:50. In the study, three different grades of lactose were used to investigate the effect of binder delivery method on overall size distribution and the results show limited effect.

Though, the effect of binder delivery on the properties of granules has been studied, further work is required to enhance the understanding of the mechanisms taken place during twin screw granulation. Therefore, in this paper a more detailed study was conducted to investigate the effects of changing the solid binder delivery into the TSG. This included online monitoring of the binder distribution along the barrel length using a specially built transparent barrel and the measurement of the granules surface velocity difference using particle image velocimetry (PIV). This is aimed to further the understanding of the effect and gain a greater insight of the process taken place inside the granulator. Furthermore, the effects of binder delivery on the granule properties (size distribution, strength and shape of the granules), residence time, torque and offline binder distribution was also examined. The binder was delivered in three ways (dry, 1:1 and wet), where the magnitudes of processing conditions were lowered (e.g. screw speed and feed rate) to help minimizing the shear and compaction forces imparted. The effect of the screw configurations (i.e. conveying and kneading elements), on the granules velocity and size distribution, was also studied.

2. Material and methods

2.1. Materials

The components in the powder mixture were (brand name and median particle size); α-lactose monohydrate (Pharmatose 200M, DMV-Fonterra Excipient GmbH and Co., Goch, Germany, 55 μm), microcrystalline cellulose (Avicel PH 101, FMC Biopolymer, Cork, Ireland, 57 μm) and crosscarmellose sodium (Ac-di-Sol FMC Biopolymer, Cork, Ireland, 58 μm). The solid binder used was hydroxypropylmethyl cellulose (HPMC) (Hypromellose 2910, Pharmacoat 603 Shin-Etsu Chemical Co., Ltd., Japan, 83 μm). The composition of each component was changed according to the experiment as it is shown in Table 1.

2.2. Methods

2.2.1. Experimental plan

The effects of three ways of solid binder delivery on the residence time, torque, granule properties (size, shape, strength), binder distribution and surface velocity of granules across the screw channel were investigated using the following approach;

Set 1 – all solid binder is mixed with the powder mixture.

Set 2 – 50% of the solid binder in powder mixture and 50% in the granulation liquid media (water).

Set 3 – all solid binder in granulation liquid (water).

Formulations composition and process conditions used in the three sets are shown in Table 1.

The viscosity was determined experimentally with a rheometer (Kinexus, Malvern Instruments, UK) using the cone and plate geometry (1°/50 mm) at shear rate of 1 s^{-1} and temperature of 25 °C. All three fluids displayed Newtonian behaviour.

2.2.2. Binder spreading and penetration on a static bed

The droplet was formed using 30-gauge needle and ejected from a height of 5 mm above the surface of the compress bed. At least, 10 compressed beds for each powder mixture in Sets 1–3 (Table 1), were produced, using a Zwick/Roell 0.5 materials testing machine (Zwick GmbH and Co., Ulm, Germany). The powder mixture (0.3 g) was carefully placed in a die of 10 mm diameter and 10 mm height. A maximum compression force of 500 N was applied, with upper punch-speed of 10 mm/min. A high speed camera, (Photron Fastcam 1024 PCI, Itronx Imaging Technologies, CA) was used to capture the spreading and penetration of the droplet through the compressed bed. The captured images were then analysed using First Ten Angstrom software (FTA32 version) to determine the size of the original spherical droplet (D_0) and maximum spreading of the droplet on the surface of the compressed bed (d_{max}); which is indicated by the biggest diameter of the droplet on the surface of the bed. The penetration time was also recorded.

2.2.3. Preparation of granules

Prior to the production of granules the powder components were mixed in a high-shear mixer (Romaco Roto Junior) for 5 min at impeller speed of 300 rpm and then conditioned to the constant humidity (40 %RH) and temperature (25 °C) using an environmental humidity chamber (Binder KMF 240 climatic chamber, Binder, UK) to avoid a change in the moisture content of the powder mixture.

All the granulation experiments were performed using a co-rotating twin screw granulator (16 mm Prism Eurolab. TSG, Thermo Fisher Scientific, Karlsruhe, Germany) having length to diameter ratio (L/D) of 25:1. The formulation was fed into the screws using a gravimetric, loss-in-weight twin screw feeder (K-PH-CL-24-KT20, K-Tron Soder, Niederlenz, Switzerland). The granulation liquid was pumped into the granulator using a peristaltic pump (101U, Watson Marlow, Cornwall, UK). The feed rate was 1 kg/h and screw speed was 100 rpm, where two different screw configuration were used; one with conveying elements only (Fig. 1a) and another with conveying element and one zone consisting four kneading elements (Fig. 1b). The description of the screw elements used in the screw configurations is given in Table 2.

2.2.4. Analysis of granules

2.2.4.1. Measurement of mean residence time and torque. Impulse-response technique was used to determine the residence time distribution (Nikitine et al., 2009), where the red dye, erythrosine B

Table 1
Formulation composition and process conditions used in three sets.

	Powder feed rate (kg/h)	Lactose (w/w %)	MCC (w/w %)	Crosscarmellose sodium (w/w %)	HPMC in powder mixture (w/w %)	Liquid feed rate (kg/h)	Water in granulation liquid (w/w %)	HPMC in granulation liquid (w/w %)	Granulation liquid viscosity (Pa.s)
Set 1	1	73.5	20	1.5	5	0.4	100	0	0.001
Set 2	1	75.43	20.53	1.54	2.5	0.4	93.75	6.25	0.022
Set 3	1	77.37	21.05	1.58	0	0.4	87.5	12.5	0.22

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