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Research paper

Asymmetric distribution in twin screw granulation

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ABSTRACT

Positron Emission Particle Tracking (PEPT) was successfully employed to validate measured transverse asymmetry in material distribution in the conveying zones of a Twin Screw Granulator (TSG). Flow asymmetry was established to be a property of the granulator geometry and dependent on fill level. The liquid distribution of granules as a function of fill level was determined. High flow asymmetry at low fill level negatively affects granule nucleation leading to high variance in final uniformity. Wetting of material during nucleation was identified as a critical parameter in determining final granule uniformity and fill level is highlighted as a crucial control factor in achieving this. Flow asymmetry of dry material in conveying zones upstream of binder fluid injection leads to poor non-uniform wetting at nucleation and results in heterogeneous final product. The granule formation mechanism of 60 °F kneading blocks is suggested to be primarily breakage of agglomerates formed during nucleation. Optimisation of screw configuration would be required to provide secondary growth. This work shows how fill dependent flow regimes affect granulation mechanisms.

1. Introduction

Granulation is a size enlargement process wherein particles are brought together to form permanent agglomerates to improve their handling and mechanical properties. Twin screw granulation (TSG) is a new method of continuous wet granulation developing considerable interest within the pharmaceutical industry. Granulation has traditionally been employed as a batch operation within pharmaceutical processes. Recently development has shifted in focus towards continuous production due to the perceived achievable benefits in control and efficiency [1]. A twin screw granulator consists of two co-rotating screws confined in a barrel. Screws are modular and consist of conveying and mixing elements. Powder is fed into the base of the barrel and transported by conveying elements. Liquid is added to bind particles together and mixing zones typically consisting of blocks of broad kneading elements provide the intensive mixing and densification required for granulation to take place.

In the past two decades the depth of research into TSG has increased considerably. Research has looked into the response to process parameters including the following: screw speed [2–4], material feed rate [2,5–7] and liquid to solid ratio [4,8–10]. Despite this the mechanisms of TSG are still not well understood, and the modular nature of the screws and differences in granulator size and geometry makes drawing comparison between different granulators difficult. Visualisation of the flow inside the granulator is inherently difficult due to the requirement of running within an enclosed barrel. Granulation mechanisms must usually be inferred from final granule properties. Dhenge et al. [11] examined the steps in granule growth by stopping an actively running process and extracting samples of granules from the different regions of the granulator. El Hagrasy and Litster [12] used three dimensional shape characterisation to develop concepts for the dominant granulation rate mechanisms in the mixing zones of a twin screw granulator. Kumar et al. [13] employed near infrared chemical imaging in order to determine residence time distribution (RTD) and infer the degree of axial mixing with changes in process parameters. Visualisation of the flow of material inside an actively running granulator was achieved by Lee et al. [14] who employed Positron Emission Particle Tracking (PEPT) to determine RTD and fill level occupancy across individual screw elements.

There remains a need to understand processes occurring within the granulator. This work examines fundamentals of material flow within conveying zones of the granulator and their dependence on fill level. Liquid distribution is examined and the importance of nucleation in determining granule properties is highlighted. Finally the conveying zone mixing efficiency is examined and typical granulation formation mechanisms are suggested.

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Table 1
Screw configurations explored in liquid distribution study.

Local fill level	Material feed rate (kg/h)	Screw speed (rpm)	Screw configuration
Unmodified	2	400	18× 1D **C**//4× 0.25D **K** 60 °F//6× 1D **C**
Low	2	400	7× 1D **C**//3× 1D **C** (0.25D Pitch)//8× 1D **C**//4× 0.25D **K** 60 °F//6× 1D **C**
Medium	2	400	7× 1D **C**//4× 0.25D **K** 60 °F//10× 1D **C**//4× 0.25D **K** 60 °F//6× 1D **C**
High	2	400	7× 1D **C**//4× 0.25D **K** 90°//10× 1D **C**//4× 0.25D **K** 60 °F//6× 1D **C**
Overall fill level			
Low	1	200	18× 1D **C**//4× 0.25D **K** 60 °F//6× 1D **C**
High	4	200	18× 1D **C**//4× 0.25D **K** 60 °F//6× 1D **C**

2. Experimental method

2.1. Preparation of powder formulation

For granulation experiments a formulation consisting of 75% alpha lactose monohydrate (316/FAST-FLO®, Foremost Farms, USA), 20% Microcrystalline Cellulose (Avicel PH101, FMC BioPolymer, Ireland) and 5% Hydroxypropyl Cellulose (Klucel EXF, Ashland Inc, USA) was used. The formulation was blended in a Pascal Lab Mixer for 25 min to ensure homogenous mixing. Median particle size was determined to be ∼125 μm through image size analysis (Sympatec QICPIC).

2.2. Granulation process

Granulation was performed using a lab scale co-rotating Twin Screw Extruder (TSE) (Haake, Thermo Scientific, Germany) with screw diameter of 16 mm and length to diameter ratio of 25:1. Granulation was performed based around screw configurations consisting of a single 60° forwarding kneading block, assigned the notation [18× 1D **C**//4× 0.25D **K** 60 °F//6× 1D **C**] where D represents the screw diameter, **C** conveying elements and **K** kneading elements. Thus from the base the configuration consists of 18 conveying elements each 1 diameter in length, 4 kneading elements each 0.25 diameters in length offset at an angle of 60° in the forwarding direction and finally 6 conveying elements each 1 diameter in length. Powder was fed into the barrel at the base of the screws via a volumetric twin screw feeder (T20, K-Tron Soder). Granulation liquid (distilled water) was added through a single injection port positioned above the screws approximately 9 diameters length from the base and provided by an 8 roller peristaltic pump (REGLO Digital, Ismatec, Switzerland).

2.3. Determination of transverse distribution in conveying zones as a function of fill

In order to determine the mass load conveyed by each screw the Haake TSE was fitted with screws consisting of only conveying elements (25× 1D **C**). The dry formulation was fed through the granulator and the fill level varied through material feed rate (1–7 kg/h) at set screw speed (100 and 400 rpm). A stainless steel sheet was positioned at the outlet aligned with the centreline to physically separate the material as it was discharged from each screw into separate vessels. The mass of material collected in each container at steady state was measured. The distribution of material at the discharge is believed to be representative of the transverse distribution of material across the entire conveying section.

2.4. Size selective segregation

The extent of size segregation in conveying zones was examined by feeding a bimodal mixture of spherical MCC pellets through the long conveying section of the Haake extruder. The mixture consisted of a 50/50% (w/w) blend of 1000 μm and 100 μm pellets (Cellets 1000 & Cellets 100, Pharmatrans Sanaq AG, Switzerland). No granulation liquid was added to ensure the surface forces between particles and the screws was the same and segregation was as a result of differences in particle volume only. Material was separated at the discharge as described above and the size distribution determined by the mass fraction of material which could be passed through a 500 μm aperture sieve.

2.5. Positron Emission Particle Tracking (PEPT)

PEPT was employed in order to determine the transverse distribution of material in the conveying zones of an actively running twin screw granulator. The experimental set-up for PEPT was that of Lee et al. [14] and the data was reprocessed in order to determine the transverse distribution of material in conveying zones. PEPT is a technique which allows for the tracking of a radioactive tracer particle in three dimensions within an actively running process. The tracers used in the experiments were 100 μm ion exchange resin particles labelled with Fluorine-18 through an ion exchange technique. ^{18}F was selected as the tracer radionuclide as it undergoes beta decay, has a short half-life and degrades to water. As the tracer undergoes beta decay it releases a positron which very quickly collides with a local electron and is annihilated to release two "back to back" 511 keV gamma rays. PEPT cameras are used to detect the γ-rays and the position of the tracer is determined from the intersection of multiple pairs. PEPT visualisation was performed on a specially modified twin screw granulator provided by GEA Niro, UK. The granulator barrel was machined down to a low thickness to minimise the attenuation of gamma rays and maximise tracer detection. The screws of the granulator were 19 mm in diameter with a length to diameter ratio of 10:1.

The tracer was fed through the granulator a minimum of 100 times. For each pass through the granulator the time spent by the tracer on either screw in conveying zones was determined, which is representative of the distribution of material. Due to the short residence time of material in conveying zones, the final transverse distribution was determined from the summation of the time spent by the tracer in all passes.

2.6. Liquid distribution

The effect of fill level on nucleation and final liquid distribution was investigated in this study. Granules were produced using the Haake TSE, and local fill level was controlled by including elements with longer residence times immediately upstream of the point of liquid injection. Long residence time elements have correspondingly high local material fill levels. Overall fill level was controlled through material feed rate at set screw speed. The screw configurations used to achieve desired fill level distributions are shown in Table 1. Fill levels were not measured directly and 'high' and 'low' fill levels are qualitative relative descriptions. Granulation was performed at 400 rpm screw speed and 2 kg/h mass feed rate. Liquid distribution was first determined gravimetrically through