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Experimental investigation of granule size and shape dynamics in twin-screw granulation

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ABSTRACT

A twin-screw granulator (TSG), a promising equipment for continuous high shear wet granulation (HSWG), achieves the desired level of mixing by a combination of the appropriate screw configuration and a suitable set of process settings (e.g. feed rate, screw speed, etc.), thus producing a certain granule size and shape distribution (GSSD). However, the primary sizing and shaping mechanism behind the resulting distribution is not well understood due to the opacity of the multiphase system in the granulator. This study experimentally characterised the GSSD dynamics along the TSG barrel length in order to understand the function of individual screw modules and process settings, as well as their interaction. Particle size analysis of granules collected at the outlet of the TSG suggested significant interaction between the process and screw configuration parameters influencing the heterogeneity in the GSSD. By characterising the samples collected along the screw length, a variable influence of the screw modules at different process conditions was observed. At low liquid-to-solid ratio (L/S), the first kneading module seemed to play a significant role in mixing, whereas the second kneading module was found to be more involved in reshaping the granules. At high L/S and high throughput, aggregation mainly took place in the second kneading module changing the GSSD. The results obtained from this study will be further used for the calibration and validation of a mechanistic model and, hence, support future development of a more detailed understanding of the HSWG process in a TSG.

1. Introduction

Granulation is a process aiming at enlarging powder particles, which can be advantageous for many reasons. The size enlargement results in gravity forces exceeding the van der Waals forces, thereby contributing to better flow properties required for improved processability and accurate dosing in further downstream processing. Especially in the pharmaceutical industry, where often highly potent drugs are processed, the amount of dust generated by powder handling is reduced by granulation, resulting in improved safety. Also, segregation (demixing) can be minimized along with the improved downstream processing characteristics of the granules. Therefore, wet granulation is an important process for the particle enlargement during the formulation of solid dosage forms in the pharmaceutical industry (Ennis, 2010). Vervaet and Remon (2005) extensively reviewed continuous granulation techniques. The high shear twin-screw granulation system has received most attention in the last decades due to its inherent benefits, including ease of use in continuous operation and the potential to integrate the TSG with other operations (Kumar et al., 2013). The high shear wet granulation (HSWG) process in the twin-screw granulator (TSG) can be divided into several stages (Fig. 1). A number of different mechanisms, including nucleation, growth, aggregation,

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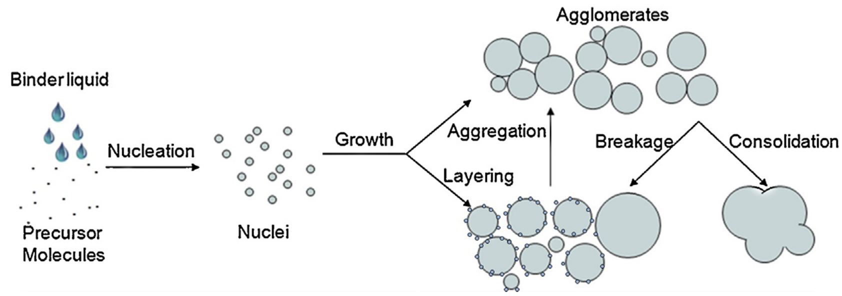

Fig. 1. Schematic presentation of the wet granulation process.

and breakage, which ultimately determine the characteristics of the produced granules, typically drive the dynamics of wet granulation. Although details about the precise sequence of growth and breakage mechanisms during TSG are not available from the literature, growth and breakage of granules are expected to occur simultaneously due to the inhomogeneous shear force distribution inside the TSG barrel (Dhenge et al., 2012).

Normally in batch HSWG the granulation time is in the order of minutes, while, in a TSG, it is limited to a few seconds (Kumar et al., 2014). The short granulation time is, although desirable from the productivity point of view, challenging for micro to meso scale rate processes in HSWG (Fig. 1). The rate processes of wet granulation are required to occur during the short granulation time before the material leaves the TSG. Thus, besides a homogeneous distribution of granulation liquid and powder, the wet mixing in a TSG is also required to be achieved within the shortest possible screw length and with minimum power input. To facilitate wet granulation, the TSG screw is composed of mainly two blocks (Fig. 2). The first and the larger component contains the inter-meshing conveying elements involved in transport of the dry and then wetted powder. The second component is the mixing section, which contains kneading discs staggered at a certain angle to cause restriction to the flow and hence provide the required mixing for wet granulation. These modules change the shear environment of the material being conveyed, which determines the final granule characteristic distribution, such as granule size and shape distribution (GSSD) and granule strength (Djuric et al., 2009). Besides the functional role of the screw configuration, performance of a TSG is also related to the applied process parameters. Along with the screw speed and the screw configuration, the feeding rate of the powder and the granulation liquid which together determine the liquid-to-solid ratio (L/S), and the fill ratio inside the barrel are the main process parameters. Therefore, they can be independently chosen to achieve the desired mixing levels of the powder and the granulation liquid, and influence the granulation yield at the outlet (Vercruysse et al., 2012, 2013).

However, there is very little understanding regarding the primary shaping mechanisms behind the particle size and shape distribution in the TSG during wet granulation, due to the opacity of the multiphase system (Dhenge et al., 2012; El Hagrasy and Litster, 2013). Most of the studies rely on the characterisation of the granules from the outlet of the TSG. Furthermore, the measured torque of the granulator drive is used as the steady state criterion in most studies using TSG. However, torque being a 0-dimensional measurement does not provide information linking the role of change in process parameters to the role of individual screw elements in the TSG.

This study extends the spatial dimension of knowledge regarding HSWG using TSG in order to understand the dynamic change in characteristics of the material while progressing in the TSG barrel. The purpose of this study was to experimentally characterise the change in GSSD along the TSG barrel in order to understand the function of individual screw modules and their interaction with other process parameters such as L/S, screw speed and filling degree in the TSG.

2. Materials and methods

2.1. Pharmaceutical model formulation

In this study, a premix of α-Lactose monohydrate (Pharmatose 200M, Caldic, Hemiksem, Belgium) and Polyvinylpyrrolidone (PVP) (Kollidon® 30, BASF, Ludwigshafen, Germany) (ratio: 97.5/2.5, w/w) was granulated with distilled water using the ConsiGma-1 continuous wet granulation system.

2.2. Continuous twin screw granulation

Granulation experiments were performed using a 25 mm diameter co-rotating TSG with option to open the barrel, which is the granulation module of the ConsiGma-1 unit (GEA Pharma Systems, Collette™, Wommelgem, Belgium). The granulator screws had a length-to-diameter ratio of 20:1 (Fig. 2). The screw configurations up to 6 kneading discs (Length = Diameter/4 for each kneading disc) were composed of one kneading block. For the screw configuration with 12 kneading discs, two kneading blocks each consisting of 6 kneading discs were used. Both kneading zones were separated by a conveying screw block (Length = 1.5 Diameter). The stagger angle of the kneading elements was fixed at 60°. An extra conveying element (Length = 1.5 Diameter) was implemented after the second kneading block together with 2 narrow kneading discs (Length = Diameter/6 for each kneading disc) in order to reduce the amount of oversized agglomerates, as reported by Van Melkebeke et al. (2008). The barrel jacket temperature was set at 25 °C. The TSG barrel had a feed segment, where the powder entered the barrel and was transported through the conveying zone to the work segment, where the granulation liquid was added to the powder (Fig. 2) (Fonteyne et al., 2012; Vercruysse et al., 2012). During processing, the powder premix was gravimetrically fed into granulator by using a twin concave screw feeder with agitator (DDW-MD2-DDSR20, Brabender, Duisburg, Germany). Distilled water as granulation liquid was pumped into the screw chamber using a peristaltic pump (Watson Marlow, Comwall, UK) using silicon tubings connected to 1.6 mm nozzles. The granulation liquid was added before the first kneading disc by dripping through two liquid feed ports, each port located just above each screw in the barrel. The wetted, but not yet mixed powder was forced to follow a granulation track composed of the two co-rotating screws with a number of transport and mixing modules based on screw configuration. As the wet powder progresses along the length of the granulator, the distribution of particle characteristics changes.