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Impact of screw configuration on the particle size distribution of granules produced by twin screw granulation

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ABSTRACT

Twin screw granulation (TSG) has been reported by different research groups as an attractive technology for continuous wet granulation. However, in contrast to fluidized bed granulation, granules produced via this technique typically have a wide and multimodal particle size distribution (PSD), resulting in suboptimal flow properties. The aim of the current study was to evaluate the impact of granulator screw configuration on the PSD of granules produced by TSG.

Experiments were performed using a 25 mm co-rotating twin screw granulator, being part of the ConsiGma™-25 system (a fully continuous from-powder-to-tablet manufacturing line from GEA Pharma Systems). Besides the screw elements conventionally used for TSG (conveying and kneading elements), alternative designs of screw elements (tooth-mixing-elements (TME), screw mixing elements (SME) and cutters) were investigated using an α-lactose monohydrate formulation granulated with distilled water.

Granulation with only conveying elements resulted in wide and multimodal PSD. Using kneading elements, the width of the PSD could be partially narrowed and the liquid distribution was more homogeneous. However, still a significant fraction of oversized agglomerates was obtained. Implementing additional kneading elements or cutters in the final section of the screw configuration was not beneficial. Furthermore, granulation with only TME or SME had limited impact on the width of the PSD. Promising results were obtained by combining kneading elements with SME, as for these configurations the PSD was narrower and shifted to the size fractions suitable for tableting.

1. Introduction

Twin screw granulation (TSG) is an attractive technology for the continuous production of pharmaceuticals as it provides the optimum throughput for pharmaceutical manufacturing combined with the advantages of a continuous operating mode (Djuric and Kleinebudde, 2010; Vervaet and Remon, 2005). During the last decade, several research groups described the importance of the granulator screw configuration on machinery performance and granule and tablet quality (Djuric and Kleinebudde, 2010; El Hagrasy et al., 2012; Keleb et al., 2004; Shah, 2005; Thompson and Sun, 2010; Van Melkebeke et al., 2008; Vercruysse et al., 2012). Due to the modular set-up of the granulator screws inside a TSG, endless combinations of different types of screw elements are possible. Whereas this renders enormous flexibility, only limited fundamental knowledge is available about the screw configuration. The screw elements which are commonly used for TSG (conveying and kneading elements, Fig. 1a and b) were originally developed to convey and mix molten polymers during hot melt extrusion. However, it is important to evaluate if these elements remain useful for a wet granulation process.

Compared to Keleb et al. (2004),Van Melkebeke et al. (2008) shortened the length of the granulation zone in order to reduce possible degradation by mechanical stress or increase of temperature. By doing this, no negative effects on granule or tablet properties were detected. However, an extra conveying element after the kneading block was essential to improve the granulation yield based on a reduction of the oversized

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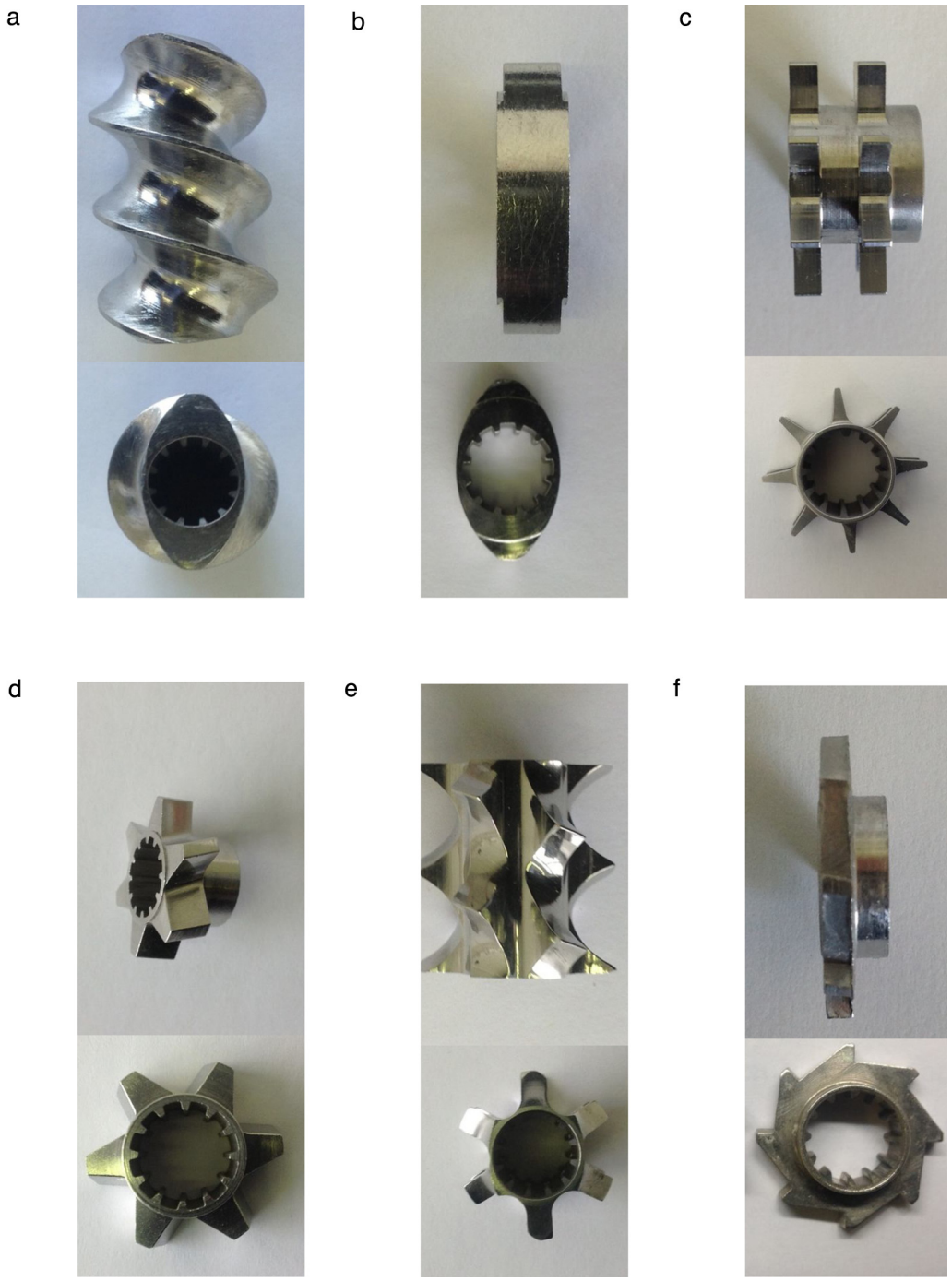

Fig. 1. Representation of the screw elements used in this study: conveying element (a), kneading element (b), narrow tooth-mixing-element (c), wide tooth-mixing-element (d), screw mixing element (e), and cutter (f).

agglomerates. Djuric and Kleinebudde (2008) concluded that the use of kneading elements resulted in an almost complete agglomeration of lactose, whereas conveying and combing mixer elements yielded smaller granules. Thompson and Sun (2010) stated that energy-intensive mixing elements such as kneading and combing mixer elements induced substantial particle growth over a single element. Vercruysse et al. (2012) reported that the powder was more intensively mixed with the granulation liquid using kneading elements, yielding less fines and more oversized agglomerates.