Evaluation of particle size evolution during high-shear wet granulation using twin-screw granulator

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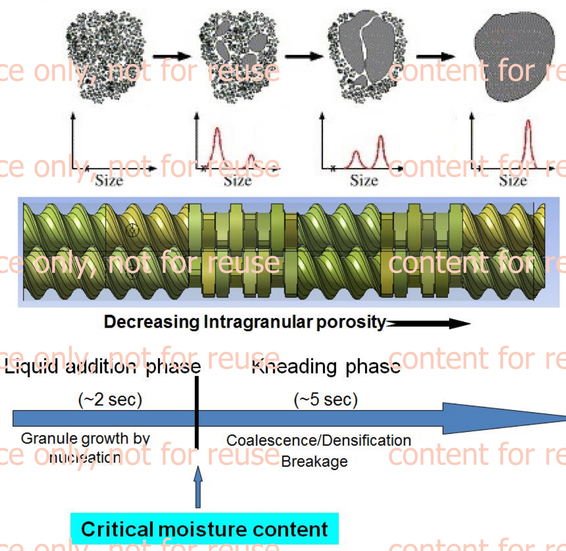
Introduction

- In pharmaceutical solid dosage manufacturing, many physical and chemical properties related to product quality (e.g. tablet final finish, drug content uniformity etc.) depend on the granules' shape and size distribution used.
- In a twin-screw granulator (TSG) the arrangement of transport and kneading element modules causes mixing and impacts distribution.
- The primary shaping mechanisms behind this distribution during wet-granulation are not well understood due to the opacity of the multiphase system.
- This study experimentally characterises the change in granule size distribution (GSD) along the TSG length in order to understand the function of individual screw modules and their interaction in the TSG.

Continuous high shear wet granulator

Working principle



Experimental Plan

Continuous twin-screw C1 granulator (25 mm diameter), ConsiGma™ (GEA Pharma Systems nv., Wommelgem, Belgium).

Formulation of granules

Lactose/PVP (97.5/2.5) was granulated with a 0.01% cochenille red aqueous solution. After granulation, wet granules were collected and tray dried.

Experimental design

Factors:
kneading elements (2, 4, 6 and 12)
screw speed (500-900 rpm)
powder feed rate (10-25 kg/h)
liquid content (4.58-6.72 % (w/w))

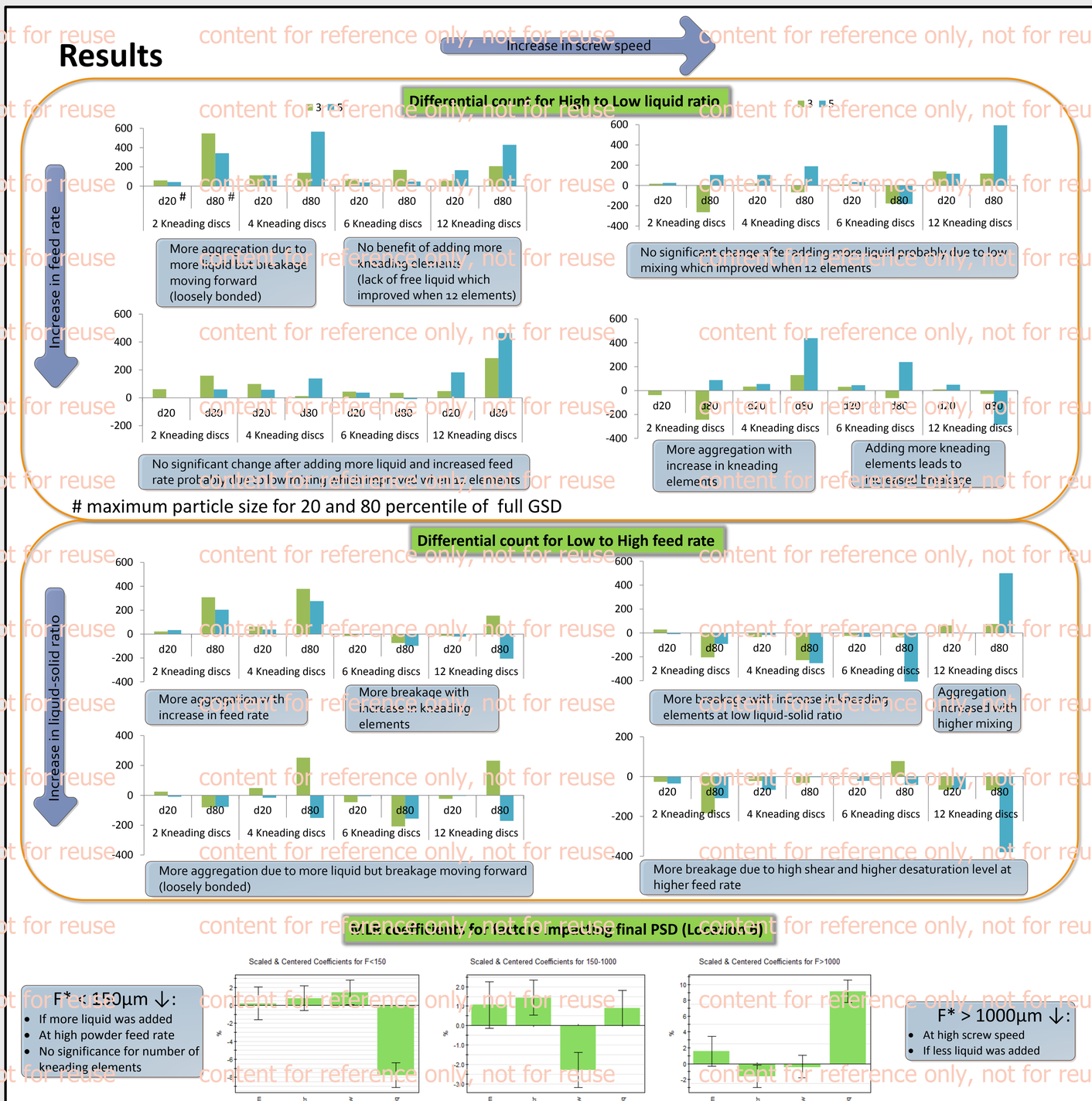
Responses:
GSD via laser microscopy

Full factorial design, 4 × 2 × 2 × 2 = 32 runs, 3 center points.

Sampling Approach

Comparative study done for samples from location 3 and 5 to see the effect of changes in parameters on the granules at "mixing-critical" points

Results



Conclusions:

- The study provides an understanding of the effectiveness of various equipment parameters with respect to process parameter changes during granulation in a TSG.
- High liquid-solid ratio along with high mixing (i.e. increasing the number of kneading elements) leads to higher granulation yield.
- The second kneading zone in the granulator is mostly involved in reshaping the PSD formed through the first kneading zone by breakage and shear-squeeze the over wet granules to provide more liquid for further granulation.
- Experimental data are of key importance for better understanding the mechanisms involved in wet-granulation using TSG and are a prerequisite for mechanistic process modelling which can further improve the available knowledge and control of the granulation process.

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