Investigating the Effect of Process Parameters of the Dome-Ex Twin-Screw Granulator on Particle Size and Particle Size Distribution

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PURPOSE

As the pharmaceutical industry moves towards more continuous operations, twin-screw granulators are advantageous over typical high-shear batch granulators. Quality, consistency, and PAT implementation elevate twin-screw granulation over high shear operations. Many twin-screw processes typically result in bimodal particle size distributions (PSD), which include significant fractions of fines and agglomerates.[1] The varying elements of twin-screw systems dictate the differences in product quality and yield. The twin-screw system used in this study includes segments for blending, kneading, granulating, comminuting, and drying the material. The dome-die comminutor mills the wet massed product, which is followed by pneumatic conveyance through a spiral dryer. This unique process results in a narrow particle size distribution of the granules. The purpose of this study is to determine the response to various process inputs of both the d_v50 and the granule size distribution (GSD).

METHOD(S)

A model theophylline formulation was granulated with the Dome-Ex Granulator and DG-Dryer system (Dalton, Osaka, Japan). A screening test design investigated the correlation of Liquid/Solid (L/S) ratio with d_v50 and narrow PSD by exploring a range of L/S ratios under varying conditions of binder content and kneading screw configuration. The first condition, 0.12 (0), represents a stabilization period and was run for 30 minutes in each test. 2.5% and 5% binder content were tested in screening test 1 (ST1) and screening test 2 (ST2), respectively. Low, mid, and high shear kneading configurations were tested in ST2, screw configuration test 1 (SCT1) and screw configuration test 2 (SCT2), respectively. Analysis of granules was conducted with the Canty Solidsizer™ imaging system.

REFERENCE

1. Fonteyne, M., et. al. (2014). International Journal of Pharmaceutics, 462(1-2), 8-10.

ACKNOWLEDGEMENTS

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RESULT(S)

Test	d_v10	d_v50	d_v90
Raw	130	256	455
ST1	160	302	566
ST2	167	416	1098
SCT1	175	360	896
SCT2	234	613	1303

DISCUSSION

In the table above, “Raw” represents blended powder before liquid addition. The remaining rows represent each test. The focus of comparing ST1 and ST2 was to compare the relationship between L/S ratio and d_v50 under varying binder concentrations. The increase in d_v50 from ST1 to ST2 demonstrates the success of increasing binder content. Proper binder content is important since granule formation is crucial to establishing a relationship between L/S ratio and d_v50. The entire GSD is shifted towards larger granules rather than broadening the distribution, indicated by the increase in d_v10.

The screw configuration tests, SCT1 and SCT2, demonstrated the relationship between L/S ratio and d_v50 as well as evaluating the effect of shear. The decrease in d_v90 from ST2 to SCT1 indicates a narrower GSD. A narrow GSD helps to highlight the relationship between L/S ratio and d_v50 by reducing the effect of both fines and oversized granules. When comparing the d_v50 trend of ST1 and SCT2, the granulation occurring in SCT2 becomes more evident. By optimizing the conditions of binder content and shear forces, the effect of L/S ratio on d_v50 becomes apparent.

CONCLUSION(S)

- Product d_v50 is increased with increasing L/S ratio under appropriate conditions.
- Process optimization increases the volume fractions within the desired granule range (550-650 um).
- Sufficient binder content results in granule formation across a wider range of L/S ratios.
- Adequate shear forces in the twin screws were required to produce granulated product.

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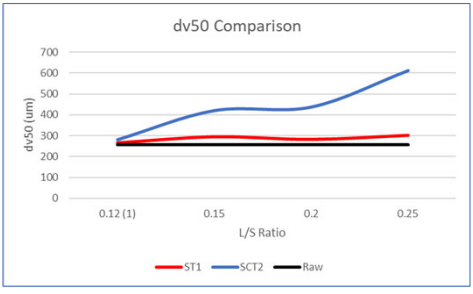
Liquid/Solid Ratio influences granule size in a continuous twin-screw granulator.

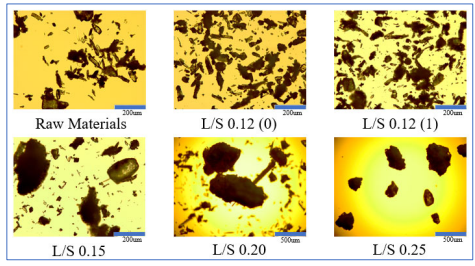
D_V50 TREND – ST1 VS SCT2

Plot shows granule formation in high shear condition (SCT2) compared to the initial low shear condition (ST1). A relationship between L/S ratio and d_v50 is visualized.



GRANULE IMAGES

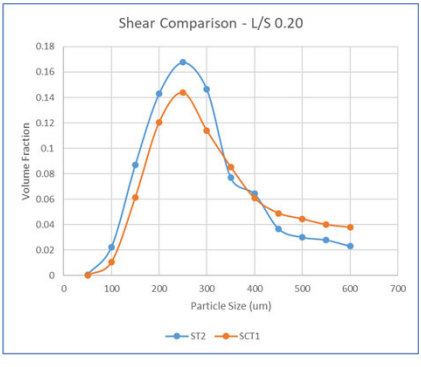
The micrographs demonstrate the formation and growth of granules with each successive L/S ratio increase. The scale change at L/S 0.20 is also an indicator that the granulated product is dissimilar from the raw materials.



EFFECT OF SHEAR AT L/S 0.20

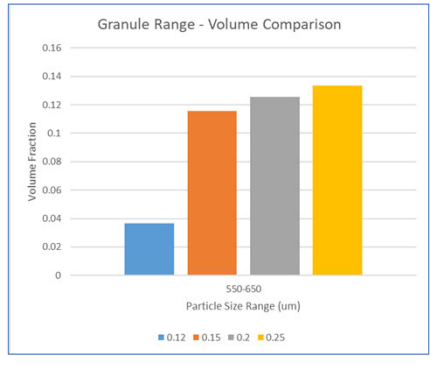
ST2 vs. SCT1 (Shear increase)

The decrease in volume fractions from ST2 to SCT1 exemplifies the effect of increased shear. By decreasing the volume fraction of fines (<300um), the volume fraction of granules is increased.



VOLUME FRACTION COMPARISON

Plot shows an increase in volume fraction for granule range, 550-650 um. It provides evidence that granulation is occurring once the L/S ratio is increased from 0.12 to 0.15, and that the yield of granules is increased with increased L/S ratio.



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