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Application of conical screen mills in controlled particle size reduction of various pharmaceutical excipients

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INTRODUCTION

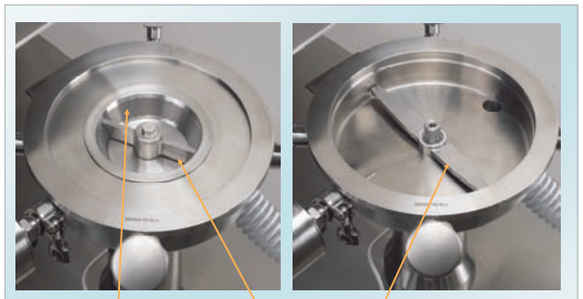
There is great interest in fine grinding of drugs and excipients in the pharmaceutical industry, especially towards controlling the resultant particle size and particle size distribution (PSD). These properties are important as they govern blend homogeneity, compaction properties and dissolution rate of the finished product. Various milling methods have been employed for particle size reductions including atomizer, pin, impact and most recently, conical screen milling. A new development is the use of conical screen milling with fine grinding capabilities for targeted particle size reduction in the 5–150 µm size range.

OBJECTIVES

1.To investigate fine grind conical screen milling as a means of controlled particle size reduction of common pharmaceutical excipients.

2. To compare the performance of conical screen milling against other milling methods.

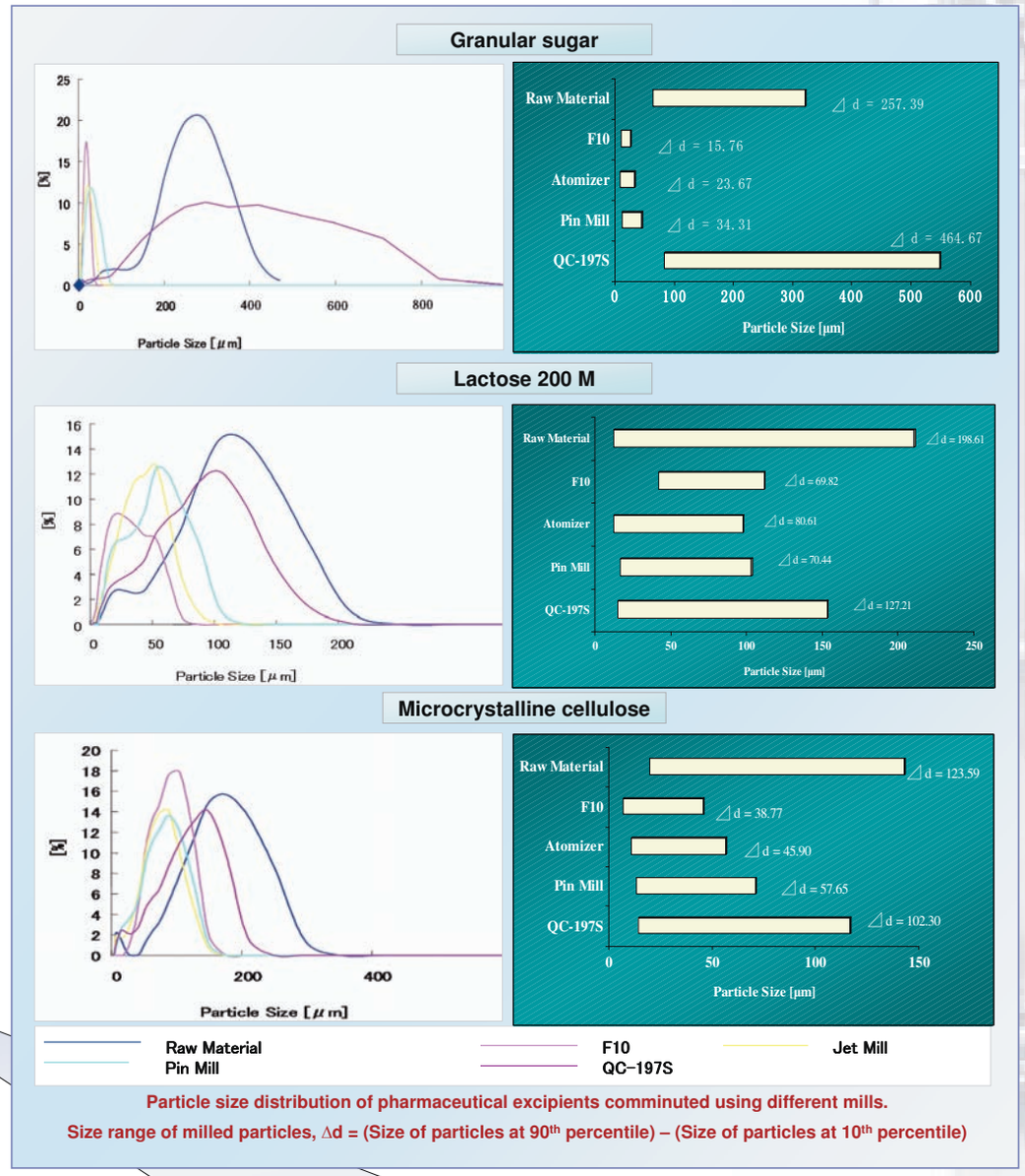
METHODOLOGY



L – R: First (conical screen) and second chamber of F10 Fine Grind mill

- Atomizer, pin, and conical screen milling with (F10; Quadro Fine Grind F10) and without (QC-197S; Quadro Comil 197S) fine grinding capabilities were used to comminute granular sugar, lactose 200M and microcrystalline cellulose (MCC).
- PSD of the raw materials and milled products were obtained using an in-line particle sizer.
- Size range, determined as the size difference between 90th and 10th percentile, was evaluated.
- Efficiency of comminution was measured as percent particle size reduction i.e. the percentage size ratio of the milled product over the raw material.

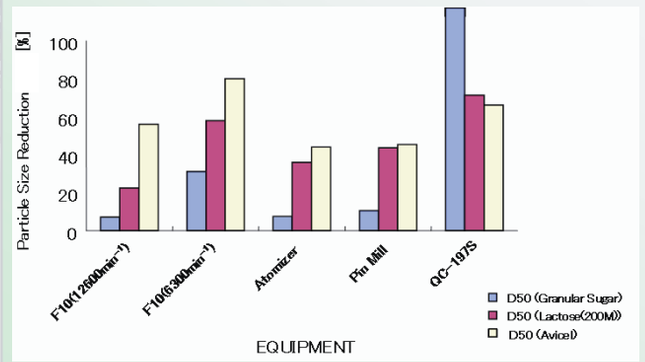
RESULTS AND DISCUSSION



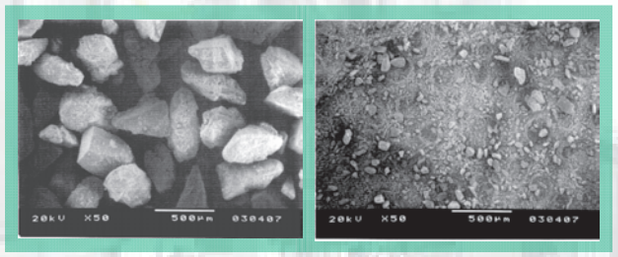
Particle size distribution of pharmaceutical excipients comminuted using different mills.

Size range of milled particles, Δd = (Size of particles at 90th percentile) – (Size of particles at 10th percentile)

Conical screen mills utilize the generation of **vortex flow** within the conical screen chamber by a rotating impeller resulting in size reduction at the screen surfaces itself. In the F10, an additional lower chamber with a second impeller is present leading to more consistent size reduction by means of inter-particulate acceleration. Size reduction occurs via the **impact attrition mechanism**.



Size reduction efficiency determined by percent particle size reduction



SEM photo of lactose before (L) and after (R) fine grinding with F10

- F10 produced particles of **narrower, unimodal PSDs** compared to those produced by other mills studied.
- Normal conical screen milling using the QC-197S was less successful for milling all three materials tested, producing larger mean sizes and broader size distributions. Thus, it was considered more suitable for coarse grinding purposes.
- Atomizer and pin milling had almost similar size reduction efficiencies.
- The presence of a **cooling jacket** maintained the temperature of the milling chamber below 50 °C, preventing the melting of sugar during comminution.
- Both conical screen mills also resulted in the lowest dust and noise production levels.

CONCLUSION

Use of conical screen milling with fine grinding capabilities resulted in more precise particle sizes with narrower size distributions for the materials tested. The technique is versatile for crystalline material such as granular sugar, as well as light-weighted amorphous material such as lactose.