POSTER 71

Understanding Drying Effects on Active Pharmaceutical Ingredient Particle Properties

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Methodlogy

100uL drop of paracetamol & Patent Blue V dye solution in methanol added to bed of gl

Solvent left to evaporate in a fume hood

Dry sample sieved to measure extent of agglomeration and agglomerate brittleness index (ABI)

Solvents
- Methanol
- Water

Paracetamol concentration (g/ml)
- 0.01 – 0.001

Glass beads (um)
- 40-70
- 90-150
- 150-250
- 300-400
- 400-600

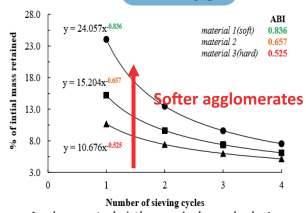
Characterization

Extent of Agglomeration

Initial transfer | After 4x 1min sieving

1mm sieve retains agglomerated material (1 lump) non-agglomerated material collected in receiver

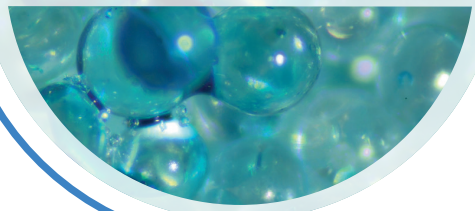
ABI Index



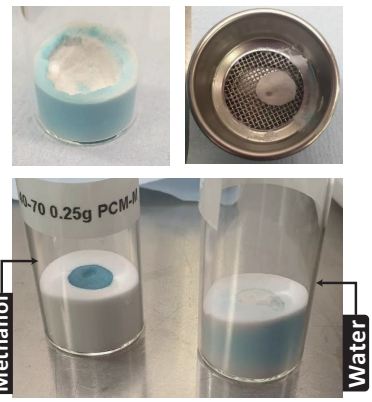
Agglomerate brittleness index calculation of a model compound*.

*Birch, M. and Marziano, I. (2013) 'Understanding and Avoidance of Agglomeration During Drying Processes: A Case Study'. doi: 10.1021/op4000972.

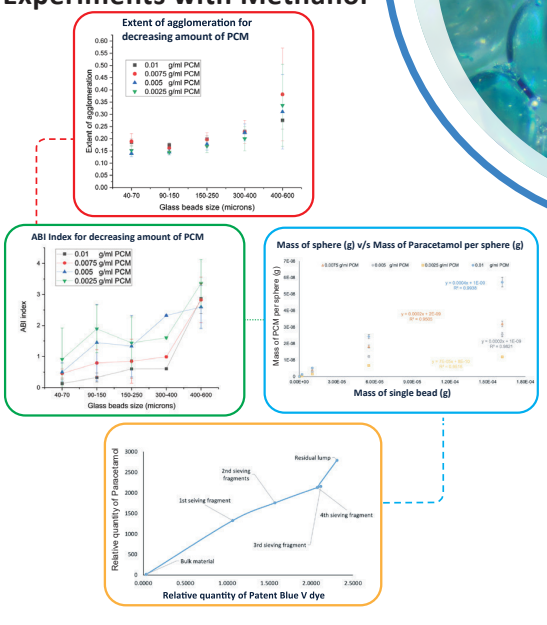
The anticipated impact of the research will be to deliver strategies to mitigate undesired granule formation (lumping) and particle breakage which routinely occur during drying and to develop these into a workflow. The main objective of this work is to quantify the amount of deposited material which can cause lump formation. This has been addressed using glass spheres of different sizes and paracetamol (PCM) solutions of different concentrations.



Experiments with water



Experiments with Methanol



Conclusions

This initial work was performed to quantify the amount and concentration of residual mother liquor which can cause lump formation. The transport mechanism of residual solvent and solute in particle beds during static drying was also investigated.

- Concerning agglomeration, the results show that as the particle size increases, the lumps become larger and softer.
- Robustness of lumps reduces with reduced solute concentration (paracetamol) as the strength of particle bridges reduces.
- Analyses to track the transport of solution indicates that the highest concentration of PCM and dye were in the residual lump remaining after four sieving cycles.
- The final result indicating the minimum mass of paracetamol needed to form an agglomerate is useful information to support design of filter cake washing processes to avoid agglomeration.

Future work

- Quantification of granule formation by using Water as a solvent.
- Transport of residual moisture during drying by using Water as a solvent.
  - ▶ Role of contact angle (Washburn Method)
  - ▶ Role of different solvent compositions
  - ▶ Role of Capillary forces
  - ▶ Behavior of different solutes with water as a solvent
- Implication of methodology developed by glass beads on actual API
  - ▶ Paracetamol
  - ▶ Spherical agglomerates of benzoic acid
- Alternative ways to calculate ABI INDEX
- Evaluate particle breakage as a function of agitation and drier loading

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