A versatile approach to the production of nano-particles

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Introduction

The comminution of coarse particles down to sub-micron levels is widely applied in industry [1]. This includes methods such as media milling, high pressure homogenisation and micro-fluidisation. Problems associated with these techniques include dealing with materials having extreme mechanical properties such as hard-abrasive substances through to soft-viscoelastic materials. This study therefore describes the use of a versatile system which is able to reduce effectively the particle size of a range of materials with different mechanical properties down to sub-micron levels.

Experimental Methods

- Nano-particles of the range of compounds in Table 1 were produced by recirculation of aqueous suspensions of different concentration (2% w/w and 15% w/w) through the DM-100 size reduction system (Dena Technology Ltd, UK) [2].

Table-1 Mechanical property indices of compounds

Compounds	Melting point (deg)	Yield stress (MPa)	Hardness (MPa)	Brittleness indices ($\mu m^{-1/2}$)
Aspirin	136°	73	87	0.56
Adipic acid	152°	NA	123	0.88
Paracetamol	170°	102	421	3.65
Glibenclamide	172°	NA	NA	NA
Emcompress	Dehydrates at 100°	252	752	NA

- This system comprises a size reduction chamber, in which grinding media sit within indents in a narrow gap between a conical rotor and conical polymeric sleeve (figure 1).

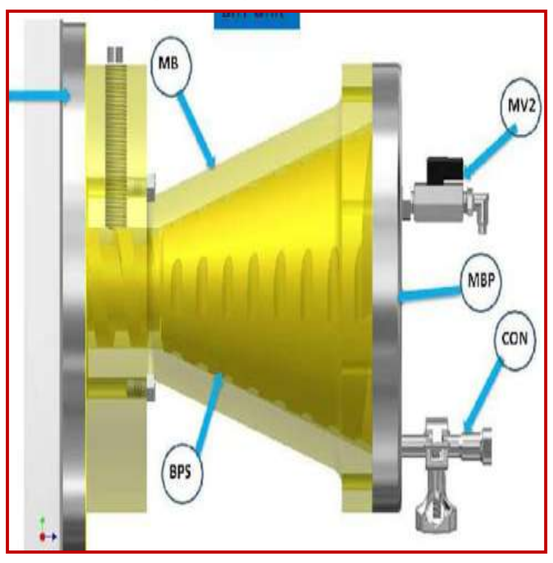
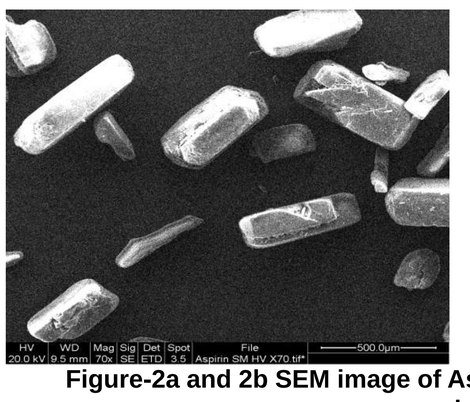


Figure-1 Diagram of the processor unit of Lena DM-100 rig

- The high energy, turbulence and shear forces associated with agitation of grinding media causes size reduction to nano-particulate levels.
- Compounds were processed at solids loads of 2%w/w to 15%w/w in aqueous suspension for 60 to 120 minutes. At-line measurements of particle size (PS) and polydispersity index (PDI) were undertaken using dynamic light scattering (DLS).
- Starting materials and processed samples were characterized by scanning electron microscopy (SEM), transmission electron microscope (TEM), differential scanning calorimetry (DSC) and X-ray powder diffraction (XRPD).

Results and discussions

- Figures 2a to 5b shows the SEM images for the starting material and the size reduced suspensions of Aspirin, Paracetamol, Glibenclamide and Emcompress (Dibasic Calcium Phosphate Dihydrate).



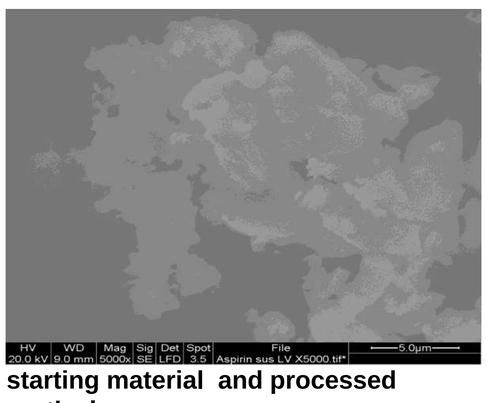
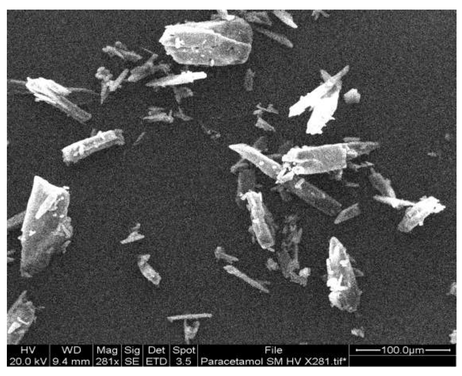


Figure-2a and 2b SEM image of Aspirin starting material and processed suspension respectively



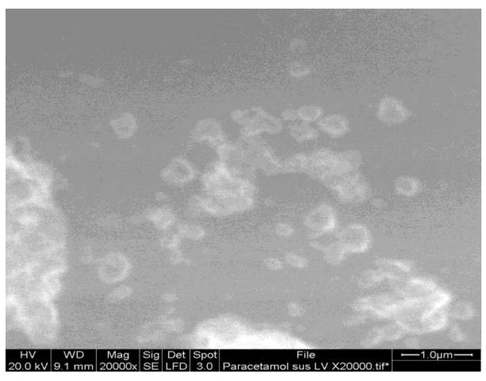
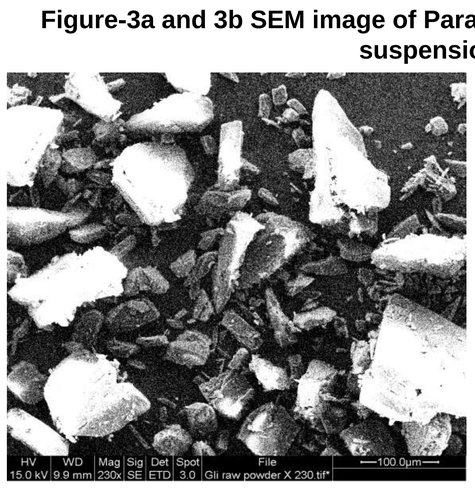


Figure-3a and 3b SEM image of Paracetamol starting material and processed suspension respectively



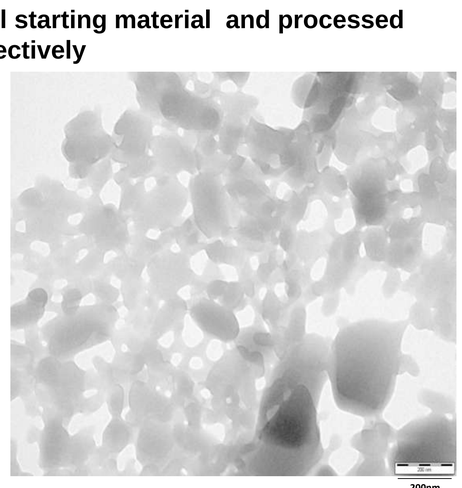
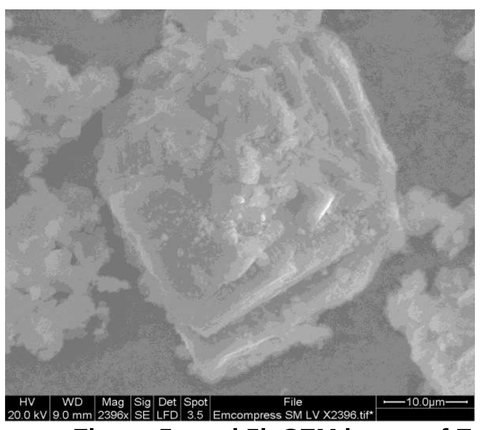


Figure-4a and 4b SEM image of Glibenclamide starting material and TEM image for processed suspension respectively

- Although the size reduction system was able to process the Emcompress samples (see Figure 5a), the aqueous suspension media was insufficient to stabilise the sub-micron particles formed (see Figure 5b) such that low density porous aggregates were quickly produced, which were retained in the machine, preventing formation of a homogeneous suspension.
- Adipic acid however, appeared to be excessively soluble in the dispersion media and so no size reduction of solubilised particles was possible.
- The results however indicate that all other compounds were rapidly reduced to sub-micron levels.



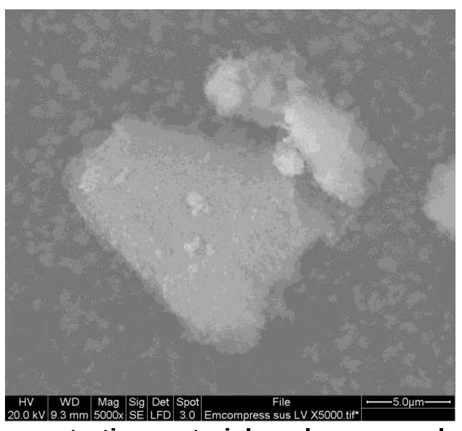


Figure-5a and 5b SEM image of Emcompress starting material and processed suspension respectively

- Figures 6, 7 and 8 show the reduction in average particle size (PS) and polydispersity index (PDI) versus time for Aspirin, Paracetamol and Glibenclamide respectively.

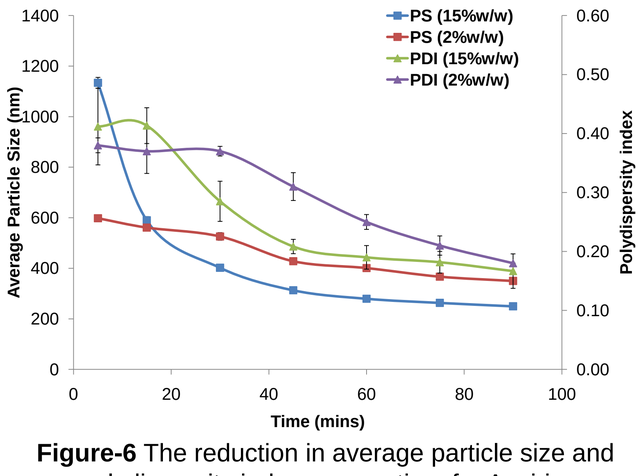


Figure-6 The reduction in average particle size and polydispersity index versus time for Aspirin.

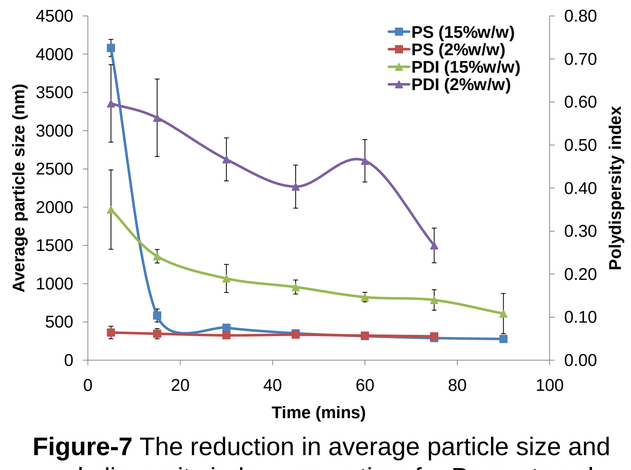


Figure-7 The reduction in average particle size and polydispersity index versus time for Paracetamol

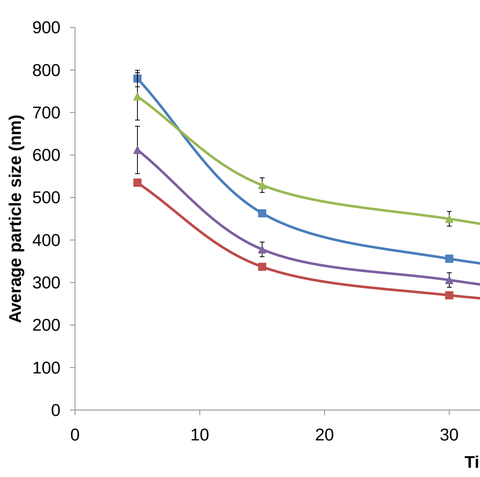


Figure-8 The reduction in average particle size and polydispersity index versus time for Glibenclamide

- Some differences in the rate of size reduction were observed between different materials. Particle size reduction appeared to be achieved more quickly over the first 15 minutes for the more brittle Paracetamol sample (2% w/w) than for the Aspirin (2% w/w) which is probably related to the smaller size of the Paracetamol feedstock. The mechanical properties of each substance appear to have limited impact on the rate of size reduction.

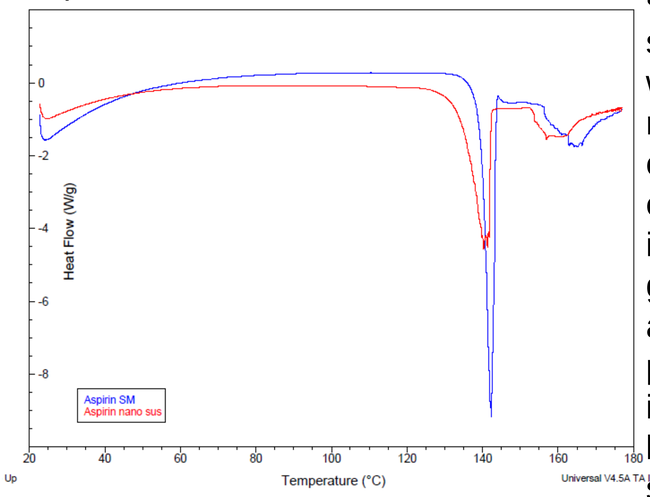


Figure-9 DSC chromatogram for Aspirin starting material and the nano-suspension

- DSC (figures 9 to 11) and XRPD showed that the crystal form of samples was maintained. There was slight reduction in melting temperature, with a concomitant slight reduction in the enthalpy of fusion suggesting some impact on the crystal lattice in the order glibenclamide > aspirin > paracetamol although differences were negligible for paracetamol. These data suggest that influences on crystal properties could be linked to mechanical behaviour with samples showing greatest brittleness demonstrating least impact.

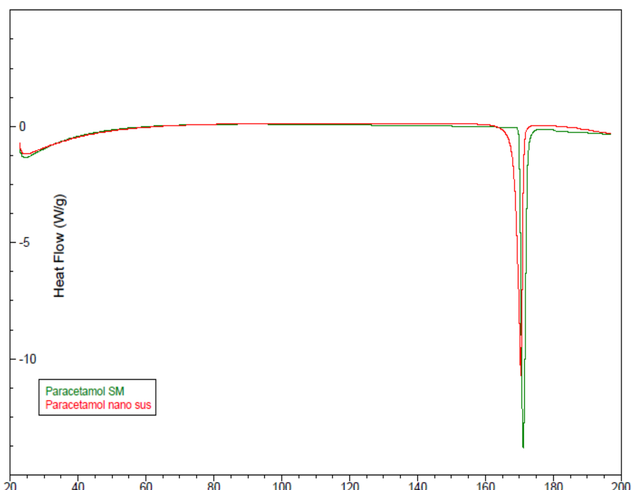


Figure-10 DSC chromatogram for Paracetamol starting material and the nano-suspension

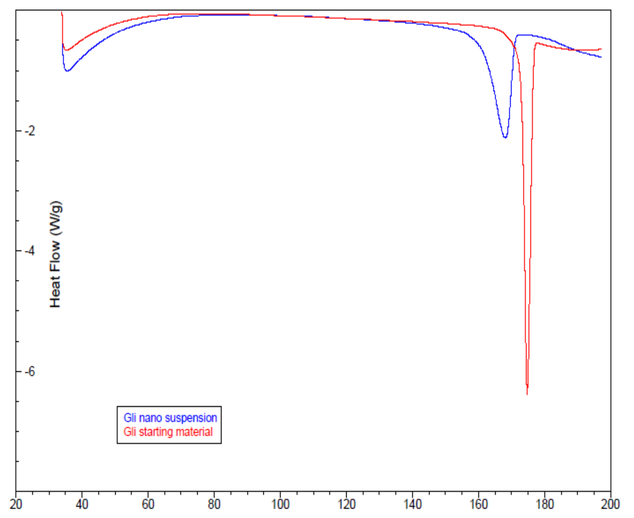


Figure-11 DSC chromatogram for glibenclamide starting material and nano-suspension

Conclusion

The studies have shown that sub-micron sized crystalline particles of compounds with a range of mechanical properties can be produced rapidly using a new comminution technology. For the compounds tested, the mechanical properties do not appear to markedly influence the initial rate of size reduction, although the susceptibility to small effects on the crystal lattice could be dependent on these factors.

References

[1] R. Bawa. NanoBiotech 2008: Exploring global advances in nanomedicine. Nanomedicine: nanotechnology, biology and medicine. 5(1) (2009) 5-7.
[2] “The Milling System”, Sulaiman, Brian, Patent no.:WO/2007/020407.

Acknowledgements

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For further information

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