

Micro-Manipulation Studies of Drug Particles and Granulating Solutions

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The selection of an appropriate polymeric binder to be used to agglomerate drug with excipients is a critical issue for development of pharmaceutical tablet systems. Bulk powder measurements tend to be used to enhance this selection, which may miss subtle interactions between particles during wet granulation. The aim of this study was to see if a novel micro-force balance (MFB), developed at UCL, could be used to distinguish between the interactions of binder solutions with individual drug crystals. The MFB was used to obtain images of the separation sequence of an axially strained binder-liquid bridge formed between either two paracetamol crystals or between a micro-pipette and a single paracetamol crystal. Simultaneous measurement was made, using the MFB, of the force exerted by the bridge.

The MFB approach distinguished between the ability of HPMC and PVP solutions to wet and bind paracetamol crystals in spite of the diversity of particle sizes and shapes employed:

1. 4% HPMC gave a lower contact angle on paracetamol than 4% PVP.
2. Upon removal of a paracetamol crystal from 4% PVP, the liquid essentially dewetted the crystal. In contrast, a significant amount of liquid was retained for 4% HPMC.
3. Greater forces were required to break liquid bridges of 4% HPMC than 4% PVP.

Rowe (1990) measured lower granule friability, lower tablet capping index and higher tablet strength when paracetamol was granulated with hydroxypropyl methylcellulose (HPMC) rather than with polyvinylpyrrolidone (PVP). Rowe noted that these results were in line with the spreading coefficients. Rowe (1989) also showed that predictions of spreading coefficient of a binder depend on the surface polarity of the drug concerned. Through this approach, measurements of surface polarity, derived from contact angles on drug-coated slides, have been used to develop successful formulations within MRL. However the approach does not consider the effect of the solvent that is usually added. The MFB measurements suggest another possible mechanism for HPMC giving improved granule and tablet properties with paracetamol over PVP: its solutions spread better over the drug, allowing more liquid bridges to form before drying to the solid binder.

Rowe, RC (1989) *Int. J. Pharmaceutics*, 56, 117-124

Rowe, RC (1990) *Int. J. Pharmaceutics*, 58, 209-213