PRELIMINARY COMPARISON OF INTERPARTICULATE ADHESION MEASURED BY ATOMIC FORCE MICROSCOPY & CALCULATED FROM HANSEN SOLUBILITY PARAMETERS MEASURED BY INVERSE GAS CHROMATOGRAPHY

Matthew D. Jones*, Simon Gaisford & Graham Buckton.
Department of Pharmaceutics, The School of Pharmacy, University of London, 29-39 Brunswick Square, London, WC1N 1AX, UK.
**** Corresponding author: matthew.jones@pharmacy.ac.uk; +44 (0)20 7753 5800 x 4870.***

1. Introduction

– The relationship between particle-particle interactions & dry powder inhaler (DPI) fine particle fraction (FPF) has been the subject of much recent research.
– One approach that has proved successful is the measurement of cohesive-adhesive balance (CAB) ratios between drugs & excipients using atomic force microscopy (AFM) (1, 2, 3).
– A CAB ratio describes the cohesion between the particles of one material relative to its adhesion to another material. Such ratios have demonstrated a consistent relationship with DPI FPF (3).
– Another technique that has been widely studied is inverse gas chromatography (IGC). In the majority of this work, dispersive surface energy was measured, with mixed results.
– Tong *et al*. employed another IGC approach, by measuring Hansen solubility parameters, from which the strength of the various adhesive & cohesive interactions within in a formulation could be calculated (4).
– Subsequently, these data were found to relate to the *in vitro* performance of DPI formulations (4).
– The aim of this study was to compare the data produced by these two techniques, which, in theory, should follow the same trends.

2. Atomic force microscopy

– The CAB ratios between five model micronised drugs & three model 63-90 µm sieved excipients were measured using the standard CAB technique (1, 2).

Table 1: AFM CAB ratios for the interaction of each drug with each excipient. $R^2 > 0.91$ in each case.

	Erythritol	Lactose	Mannitol
Beclometasone dipropionate (BDP)	0.51 ± 0.05	0.74 ± 0.04	0.69 ± 0.05
Budesonide	1.38 ± 0.01	0.91 ± 0.03	0.95 ± 0.03
Salbutamol sulphate	1.03 ± 0.05	0.72 ± 0.02	1.04 ± 0.03
Terbutaline sulphate	1.09 ± 0.03	0.72 ± 0.03	0.98 ± 0.03
Triamcinolone acetonide	1.15 ± 0.03	0.89 ± 0.03	0.96 ± 0.02

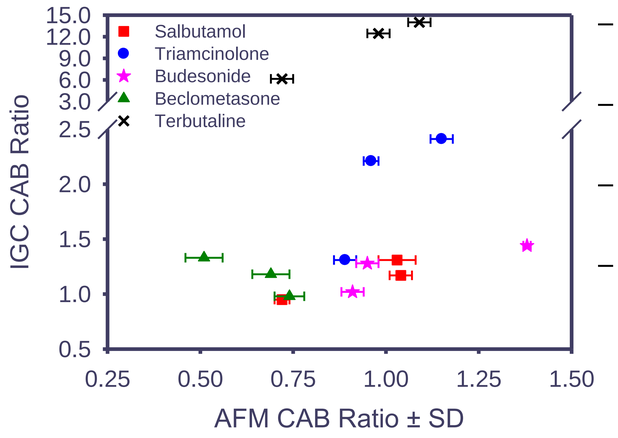
3. Inverse gas chromatography

– Hansen solubility parameters determined by IGC following the method described by Tong *et al*. (4).
– Adhesive & cohesive interactions between the materials calculated from their solubility parameters using the calculations described by Rowe (5). These were used to calculate IGC CAB ratios.

Table 2: Theoretical IGC CAB ratios for the interaction of each drug with each excipient.

	Erythritol	Lactose	Mannitol
Beclometasone dipropionate (BDP)	1.33	0.98	1.18
Budesonide	1.44	1.02	1.28
Salbutamol sulphate	1.31	0.95	1.17
Terbutaline sulphate	14.00	6.14	12.45
Triamcinolone acetonide	2.41	1.31	2.21

4. Comparison of AFM & IGC CAB ratios



– Considering all the data, there was no correlation between the two sets of CAB ratios.
– If each drug is considered separately, there was stronger correlation ($R^2 \geq 0.67$ in each case).
– However, the BDP line of best fit had a negative gradient.
– Therefore, the IGC technique may be able to produce CAB ratios of the same rank order as AFM for certain drugs.

5. Further work

– A study of the *in vitro* performance of carrier-based DPI formulations produced using the study materials will examine which technique (AFM or IGC) is most predictive of FPF.
– The reason for the negative AFM-IGC CAB ratio relationship for BDP will be investigated.

6. References

1: Begat *et al*. (2004). *Pharm. Res.* 21(9), pp. 1591-1597. **2:** Jones *et al*. (2008). *Pharm. Res.* 25(2), pp. 337-348. **3:** Jones *et al.* (2008). *Eur. J. Pharm. Biopharm.* DOI: 10.1016/j.ejpb.2007.11.019. **4:** Tong *et al*. (2006). *J. Pharm. Sci.* 95(1), pp. 228-233. **5:** Rowe. (1988). *Int. J. Pharm.* 41(3), pp. 223-226.

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