



Citation for published version:

Jones, MD & Buckton, G 2016, 'Comparison of the cohesion-adhesion balance approach to colloidal probe atomic force microscopy and the measurement of Hansen partial solubility parameters by inverse gas chromatography for the prediction of dry powder inhalation performance', *International Journal of Pharmaceutics*, vol. 509, no. 1-2, IJP-D-16-00632R1, pp. 419-430.

<https://doi.org/10.1016/j.ijpharm.2016.06.002>, <https://doi.org/10.1016/j.ijpharm.2016.06.002>

DOI:

[10.1016/j.ijpharm.2016.06.002](https://doi.org/10.1016/j.ijpharm.2016.06.002)

[10.1016/j.ijpharm.2016.06.002](https://doi.org/10.1016/j.ijpharm.2016.06.002)

Publication date:

2016

Document Version

Peer reviewed version

[Link to publication](#)

Publisher Rights

CC BY-NC-ND

University of Bath

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Table 1: Molar volume (V) and Hansen partial solubility parameters (δ_D^E , δ_P^E and δ_H^E) of the various potential elutants forming the domain from which the experimental elutants were selected [36-38].

Elutant number	Elutant	V ($\text{m}^3 \cdot \text{mol}^{-1}$)	δ_D^E ($\text{MPa}^{1/2}$)	δ_P^E ($\text{MPa}^{1/2}$)	δ_H^E ($\text{MPa}^{1/2}$)
1	Hexane	1.32×10^{-4}	14.81	0.0	0.0
2	Heptane	1.47×10^{-4}	15.18	0.0	0.0
3	Octane	1.64×10^{-4}	15.45	0.0	0.0
4	Nonane	1.80×10^{-4}	15.65	0.0	0.0
5	Decane	1.96×10^{-4}	15.80	0.0	0.0
6	Cyclohexane	1.09×10^{-4}	16.74	0.0	0.0
7	1,4-dioxane	8.60×10^{-5}	19.03	1.8	7.4
8	Acetone	7.40×10^{-5}	15.51	10.4	7.0
9	Acetonitrile	5.26×10^{-5}	15.35	18.0	6.1
10	Chloroform	8.10×10^{-5}	17.70	3.1	5.7
11	Ethyl acetate	9.80×10^{-5}	15.22	5.3	9.2
12	Toluene	1.07×10^{-4}	18.01	1.4	2.1

Table 2: Summary particle size statistics (n = 5) and true densities (n = 10) of the study materials.

	d₁₀ ($\mu\text{m} \pm \text{SD}$)	d₅₀ ($\mu\text{m} \pm \text{SD}$)	d₉₀ ($\mu\text{m} \pm \text{SD}$)	True density ($\text{g}\cdot\text{cm}^{-3} \pm \text{SD}$)
Beclometasone dipropionate	0.63 \pm 0.00	1.25 \pm 0.02	2.63 \pm 0.05	1.357 \pm 0.011
Budesonide	0.67 \pm 0.00	1.59 \pm 0.01	4.04 \pm 0.04	1.292 \pm 0.006
Salbutamol sulphate	0.67 \pm 0.00	1.50 \pm 0.01	3.31 \pm 0.01	1.334 \pm 0.002
Terbutaline sulphate	0.71 \pm 0.00	1.98 \pm 0.02	5.50 \pm 0.03	1.346 \pm 0.002
Triamcinolone acetonide	1.16 \pm 0.04	3.29 \pm 0.13	6.59 \pm 0.22	1.333 \pm 0.072
Erythritol	9.82 \pm 0.28	79.33 \pm 0.78	128.55 \pm 2.12	1.446 \pm 0.001
Lactose monohydrate	52.36 \pm 0.96	97.12 \pm 0.89	152.21 \pm 1.36	1.541 \pm 0.027
Mannitol	6.97 \pm 0.23	74.48 \pm 1.53	138.16 \pm 2.95	1.490 \pm 0.001

Table 3: Probable polymorph and dominant face Miller index of extremely smooth crystal substrates used for colloidal probe AFM adhesion and cohesion measurements.

Material and Polymorph	Dominant Face
Beclometasone dipropionate anhydrate	{110}
Budesonide	{002}
Salbutamol sulphate	{200} or {002}
Terbutaline sulphate anhydrate (form B)	{001} or {011}
Triamcinolone acetonide (form I)	{110}, {120} or {210}
Erythritol	{020} or {200}
α -lactose monohydrate	{100}
D-mannitol (β polymorph)	{002}

Table 4: AFM CAB ratios \pm SD and respective coefficients of determination (R^2) for each drug-carrier interaction.

AFM CAB ratio \pm SD (R^2)	Erythritol	Lactose	Mannitol
Beclometasone dipropionate	0.51 \pm 0.05 (0.91)	0.74 \pm 0.04 (0.97)	0.69 \pm 0.05 (0.97)
Budesonide	1.38 \pm 0.01 (1.00)	0.91 \pm 0.03 (0.99)	0.95 \pm 0.03 (0.99)
Salbutamol sulphate	1.03 \pm 0.05 (0.95)	0.72 \pm 0.02 (0.99)	1.04 \pm 0.03 (0.99)
Terbutaline sulphate	1.09 \pm 0.03 (0.98)	0.72 \pm 0.03 (0.96)	0.98 \pm 0.03 (0.98)
Triamcinolone acetonide	1.15 \pm 0.03 (0.99)	0.89 \pm 0.03 (0.99)	0.96 \pm 0.02 (0.99)

Table 5: Results of matrix optimisation calculations used to determine the best combination of elutants to use for measurement of Hansen partial solubility parameters by IGC.

N	Elutants (numbers from Table 1)	D-optimality		Variance inflation factors		
		$ X'X $	$ M $	$f(\delta_D^{E_i})$	$f(\delta_P^{E_i})$	$f(\delta_H^{E_i})$
4	5, 6, 9 & 11	1.044×10^{16}	1.631×10^{14}	3.391	3.731	1.457
5	5, 6, 7, 9 & 11	2.225×10^{16}	1.780×10^{14}	2.927	2.706	1.319
6	1, 5, 6, 7, 9 & 11	3.729×10^{16}	1.726×10^{14}	2.591	2.632	1.375
7	1, 4, 5, 6, 7, 9 & 11	6.026×10^{16}	1.757×10^{14}	2.785	2.721	1.511
8	1, 4, 5, 6, 7, 8, 9 & 11	9.095×10^{16}	1.776×10^{14}	3.193	3.118	3.193
9	1, 4, 5, 6, 7, 8, 9, 10 & 11	1.203×10^{17}	1.651×10^{14}	2.978	2.764	1.625

Table 6: Hansen partial solubility parameters determined for the eight study materials and the correlation coefficient of the multiple linear regression analysis used to obtain these data.

	δ_D^S (MPa ^{1/2} ± SD)	δ_P^S (MPa ^{1/2} ± SD)	δ_H^S (MPa ^{1/2} ± SD)	Multiple correlation coefficient
Beclometasone dipropionate	18.2 ± 1.5	13.2 ± 2.6	8.1 ± 4.8	0.9985
Budesonide	18.9 ± 2.9	10.5 ± 5.0	13.0 ± 9.1	0.9950
Salbutamol sulphate	17.6 ± 2.5	11.1 ± 4.4	11.0 ± 8.0	0.9415
Terbutaline sulphate	21.9 ± 10.3	13.8 ± 18.0	55.0 ± 32.7	0.8823
Triamcinolone acetonide	18.5 ± 1.2	3.0 ± 4.5	25.6 ± 4.7	0.9832
Erythritol	12.9 ± 2.3	7.7 ± 4.1	16.9 ± 7.4	0.9486
Lactose	14.3 ± 2.9	12.6 ± 5.0	18.8 ± 9.0	0.9554
Mannitol	17.1 ± 3.6	3.6 ± 6.2	14.4 ± 11.3	0.8465

Table 7: Relative strength of interparticulate interactions between each model drug and either itself (cohesion) or each of the model carrier excipients, as calculated from their Hansen partial solubility parameters (MPa).

	Drug cohesion	Erythritol	Lactose monohydrate	Mannitol
Beclometasone dipropionate	142.9	107.5	145.7	120.9
Budesonide	158.9	110.7	155.9	123.9
Salbutamol sulphate	138.1	106.1	145.1	118.1
Terbutaline sulphate	924.1	55.5	127.4	62.7
Triamcinolone acetonide	251.5	104.7	192.3	113.9

Table 8: IGC CAB ratios for each drug-carrier interaction, as calculated from Hansen partial solubility parameters.

	Erythritol	Lactose	Mannitol
Beclometasone dipropionate	1.33	0.98	1.18
Budesonide	1.44	1.02	1.28
Salbutamol sulphate	1.30	0.95	1.17
Terbutaline sulphate	16.65	7.25	14.74
Triamcinolone acetonide	2.40	1.31	2.21