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Interactions in powders and granules – a reappraisal

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Summary

Data and the subsequent conclusions made recently in studies of the interactions in powders and granules have been reappraised in the light of an incorrect definition of one of the terms in the original equations. Calculations have shown that although the actual values of the interaction parameters and adhesive interactions are different, the overall trends are unchanged. Hence, the conclusions drawn regarding the prediction of the likely interactions are not altered.

Introduction

In a series of recent papers (Rowe, 1988a–d, 1989a–c) attempts have been made at assessing and predicting the likely interactions in powders and granules using calculations of the relative magnitudes of the thermodynamic works of adhesion and cohesion based on a knowledge of either the partial cohesive/solubility parameters or surface free energies. In some of the calculations it was necessary to determine an interaction parameter (ϕ) for which Wu (1973) derived the equation:

$$\phi = 2\left[\frac{{}^{A}x_{d}\cdot{}^{B}x_{d}}{{}^{A}x_{d}\cdot g_{1}+{}^{B}x_{d}\cdot g_{2}}+\frac{{}^{A}x_{p}\cdot{}^{B}x_{p}}{{}^{A}x_{p}\cdot g_{1}+{}^{B}x_{p}\cdot g_{2}}\right] \quad (1)$$

where x_d and x_p represent the fractional non-polarity and polarity, respectively, of each material A and B in a binary system and g_1 and g_2 are constants for the system.

In his original paper, Wu (1973) incorrectly defined g_1 and g_2 in terms of the surface energies γ of the two materials, i.e.

$$g_1 = \frac{{}^{A}\gamma}{{}^{B}\gamma} \quad \text{and} \quad g_2 = \frac{{}^{B}\gamma}{{}^{A}\gamma} \quad (2)$$

when in fact they should be defined in terms of the square roots of the surface energies (Wu, 1982):

$$g_1 = \left[\frac{{}^{A}\gamma}{{}^{B}\gamma}\right]^{1/2} \quad \text{and} \quad g_2 = \left[\frac{{}^{B}\gamma}{{}^{A}\gamma}\right]^{1/2} \quad (3)$$

Unfortunately, Rowe (1988a) used the Wu (1973) definitions and hence the calculations involving the assessment of g_1 and g_2 from solubil-

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ity parameters (δ) and molar volumes (V) using the expression (Gardon, 1967)

$$\gamma = \frac{\delta^2 V^{1/3}}{K} \quad (4)$$

(where K is a constant) are incorrect.

In this paper, the results and subsequent conclusions made by Rowe in his studies of interactions in powder systems containing lubricants (Rowe, 1988b,c), in coloured powders (1989b) and in granules (1988d, 1989a,c) have been reappraised using the correct equations and formulae.

Results and Discussion

Interactions in powder systems containing lubricants

Table 1 lists the recalculated interaction parameters and the relative strengths of the adhesive (A-B) and cohesive (B-B) interactions for microcrystalline cellulose and anhydrous lactose lubricated with magnesium stearate, stearic acid and polytetrafluoroethylene (PTFE). Compared to the previous work (Rowe, 1988b), the calculated interaction parameters and consequent adhesive interactions are all larger but the rank order magnesium stearate > stearic acid > PTFE is the same. An interesting consequence of the new data is that for all three lubricants the adhesive interactions are now greater than the cohesive interactions within the lubricants, implying film formation over the excipient in all three cases, although the extent of film formation will be greatest for magnesium stearate and lowest for PTFE. The conclusions drawn are consistent with the experimental data referred to in the original paper (Rowe, 1988b).

The addition of colloidal silica to a binary mixture of microcrystalline cellulose and magnesium stearate is known to cause enrobement of the lubricant with a consequent change in the compaction properties of the mixture (Staniforth and Ahmed, 1986, 1987). Calculations of the interaction parameters and the adhesive and cohesive interactions in such a system (Table 2) confirm this. Again, the calculated values are different from those in the original paper (Rowe, 1988c) but the inferences drawn are the same.

TABLE 2

Interaction parameters (ϕ), and adhesive and cohesive interactions in ternary systems

	Interaction parameter (ϕ)	Strength of interaction (MPa)
Adhesive		
MCC-MS	0.68	121.0
CS-MS	0.59	94.8
MCC-CS	0.88	306.9
Cohesive		
MCC-MCC	–	386.1
CS-CS	–	311.5
MS-MS	–	82.8

MCC, microcrystalline cellulose; MS, magnesium stearate; CS, colloidal silica.

TABLE 1

Interaction parameters (ϕ) and strengths of the adhesive (A-B) and cohesive (B-B) interactions for microcrystalline cellulose and anhydrous lactose lubricated with magnesium stearate, stearic acid and polytetrafluoroethylene (PTFE)

Excipient A	Lubricant B	ϕ	Strength of interaction (MPa)	
			Adhesive (A-B)	Cohesive (B-B)
Microcrystalline cellulose	magnesium stearate	0.68	121.0	82.8
Microcrystalline cellulose	stearic acid	0.58	100.2	77.4
Microcrystalline cellulose	PTFE	0.42	58.2	49.0
Anhydrous lactose	magnesium stearate	0.67	121.2	82.8
Anhydrous lactose	stearic acid	0.57	100.5	77.4
Anhydrous lactose	PTFE	0.41	58.0	49.0

Interactions in coloured powders

Calculated strengths of the adhesive and cohesive interactions for red iron oxide and carbon black mixed with various tablet ingredients are given in Table 3. As expected, there are differences in the actual values compared to those originally presented (Rowe, 1989b) but the three cases highlighted previously – i.e., one where the adhesive interaction within the system is lower than the cohesive interaction in the colour; one where the adhesive interaction within the system is lower than the cohesive interaction within the colour but higher than that within the other component and one where the adhesive interaction within the system is higher than the cohesive interaction within the colour but lower than that within the other component – can still be identified. The inferences and conclusions drawn from the data are the same as those originally made.

TABLE 3

Calculated strength of adhesive and cohesive interactions for red iron oxide and carbon black mixed with various tablet ingredients

Material	Strength of interaction (MPa)		
	Adhesive		Cohesive
	Red iron oxide	Carbon black	
Drugs			
Caffeine (anhydrous)	178.2	160.9	176.9
Theophylline (anhydrous)	193.6	173.5	204.5
Testosterone propionate	135.5	129.4	94.0
Fillers			
Microcrystalline cellulose	207.3	173.3	386.1
Lactose	206.8	172.2	398.0
Binders			
Hydroxypropyl methylcellulose	155.5	143.9	130.0
Methylcellulose	147.3	140.2	113.4
Polyvinyl pyrrolidone	147.9	144.5	112.4
Opacifiers			
Titanium dioxide	237.5	218.1	295.8
Lubricants			
Magnesium stearate	121.8	116.5	82.3
Stearic acid	107.9	106.6	77.4

Cohesive interactions in red iron oxide = 196.0 MPa; cohesive interactions in carbon black = 193.0 MPa.

TABLE 4

Predicted strengths of substrate-binder interactions

Substrate	Strength of interaction [a] (MPa)		
	HPMC	MC	PVP
Caffeine (anhydrous)	150.7	138.2	132.7
Theophylline (anhydrous)	157.2	145.3	143.0
Testosterone propionate	106.2	100.9	102.0
Microcrystalline cellulose	187.8	164.3	150.8
Lactose (anhydrous)	187.6	163.9	150.2
Polymethyl methacrylate	117.9	113.3	117.1
Polyvinyl chloride	105.5	102.9	108.5

[a] HPMC, hydroxypropyl methylcellulose; MC, methylcellulose; PVP, polyvinyl pyrrolidone.

Binder-substrate interactions in granules

Binder-substrate interactions in granules have been considered in two previous papers (Rowe 1988d, 1989c). In the former, calculations of the interactions for various drugs and excipients granulated using hydroxypropyl methylcellulose, methylcellulose and polyvinyl pyrrolidone were presented as a table – an updated version of which is shown in Table 4. In the latter, the data were presented graphically, showing a parabolic relationship between the reduced spreading coefficient (λ) defined as the ratio of the adhesive interactions to the cohesive interactions within the binder of the form:

$$\lambda = c + ax + bx^2 \tag{5}$$

where c, a and b are constants and x is the fractional polarity of the substrate. Updated versions of the graphs for the three binders are shown in Fig. 1 and the results of quadratic curve fitting in Table 5. In all cases, the trends are the same as those reported previously, i.e. for optimum spreading and film formation there is no single universal binder and each substrate has to be taken individually. However, for substrates with a low polarity (< 0.5), polyvinyl pyrrolidone would appear to be the binder of choice while for substrates with a high polarity the cellulose derivatives would be recommended.

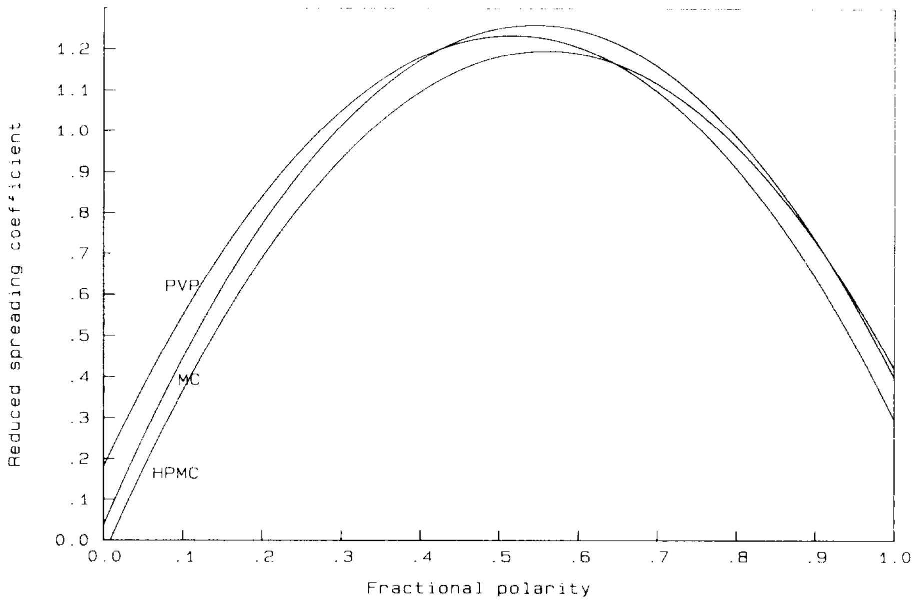

Fig. 1. Reduced and spreading coefficient vs fractional polarity for hydroxypropyl methylcellulose (HPMC), methylcellulose (MC) and polyvinyl pyrrolidone (PVP).

TABLE 5

Results of quadratic curve fitting of data shown in Fig. 1 to Eqn 5 (n = 8)

Binder	Derived values			Correlation coefficient	Standard error	Polarity for $\lambda = 1$	Data at max	
	c	a	b				λ	x_p
HPMC	−0.0364	4.422	−3.965	0.9054	0.0968	0.34–0.78	1.196	0.56
MC	0.0374	4.496	−4.135	0.8982	0.0973	0.30–0.79	1.260	0.54
PVP	0.1806	4.093	−3.976	0.8721	0.0890	0.27–0.75	1.233	0.52

Conclusion

Recalculation of the interaction parameters and the adhesive interactions using the correct formulae does not affect the inferences and conclusions drawn in previous work. In many cases, the actual values do not differ significantly. This was not unexpected since, in many of the systems studied, g_1 is close to unity. The largest differences between the values occurred for microcrystalline cellulose and lactose and it may be that the literature values of the solubility parameters and/or (more likely) the molar volumes used for these materials are suspect.

It must be emphasized that the approach is somewhat crude and oversimplified and hence the data generated can do nothing more than give indications of the likely trends. However, the predictions are in general agreement with accepted findings in practice. The ability to predict trends clearly has potential use in the optimisation of both formulation and processing in product development, especially in construction of computer expert systems in these areas.

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