International Journal of Pharmaceutics, 41 (1988) 223–226
Elsevier

IJP 01395

Interaction of lubricants with microcrystalline cellulose and anhydrous lactose — a solubility parameter approach

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(Received 7 May 1987)
(Accepted 30 July 1987)

Key words: Lubricant; Microcrystalline cellulose; Anhydrous lactose; Solubility parameter

Summary

Based on a model involving the integrating of the Lennard–Jones pair potential function to predict the properties of a single and two component system it has been possible to predict the intensity of the molecular interactions between the excipients microcrystalline cellulose and anhydrous lactose and the lubricants magnesium stearate, stearic acid and polytetrafluoroethylene using literature values of their partial solubility parameters. In the case of magnesium stearate the lubricant–excipient interactions are higher than those of lubricant–lubricant while in the case of polytetrafluoroethylene the reverse is true. This is consistent with the generally held belief that magnesium stearate forms a monomolecular film around the excipient causing a decrease in tablet strength.

Introduction

Lubricants are, in most cases, essential components in tablet formulations. However, their presence may cause undesirable changes in properties, notably a decrease in tablet strength (Alpar et al., 1969; Jarosz and Parrott, 1984). This decrease in strength has been attributed to weaker bonds resulting after compression between lubricant–lubricant molecules rather than the stronger excipient–excipient bonds (De Boer et al., 1978). If it is assumed that the bond strengths are due entirely to the summation of the interactions of the intermolecular bonding forces then it is possible to predict these interactions using values for the cohesive energy densities or solubility parameters of the lubricant and excipient.

Theoretical Considerations

In a binary system involving an excipient (A) and a lubricant (B) there will be 3 interactions: excipient–excipient (A–A), lubricant–lubricant (B–B) and excipient–lubricant (A–B). While the first two can be regarded as cohesive, the third is adhesive in nature. If it is assumed that all materials are separated by a plane of thickness corresponding to the equilibrium distance at zero potential energy and that each site of one surface interacts with a continuum of sites on another then it is possible, based on the Lennard–Jones pair potential function, to predict the relative strengths of the interaction (σ) to the solubility

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parameter (δ), expressed in units of $\mathrm{MPa}^{1/2}$, of the two surfaces (Gardon, 1977), i.e.,

$$\sigma_{AA} = 0.25\,{}^{A}\delta^{2} \tag{1}$$

$$\sigma_{BB} = 0.25\,{}^{B}\delta^{2} \tag{2}$$

$$\sigma_{AB} = 0.25\phi\,{}^{A}\delta\,{}^{B}\delta \tag{3}$$

where ϕ is the interaction parameter (Girifalco and Good, 1957). Although several equations exist for the estimation of the interaction parameter (Wu, 1973; Gardon, 1977) the one derived by Wu (1973) using the so-called harmonic mean equation would appear to be the most appropriate for the low energy systems encountered in tablets, i.e.,

$$\phi = 2\left[\frac{{}^{A}x_{d}\cdot{}^{B}x_{d}}{{}^{A}x_{d}\cdot g_{1} + {}^{B}x_{d}\cdot g_{2}} + \frac{{}^{A}x_{p}\cdot{}^{B}x_{p}}{{}^{A}x_{p}\cdot g_{1} + {}^{B}x_{p}\cdot g_{2}}\right] \tag{4}$$

where x_d and x_p are the fractional non-polarity and polarity, respectively, for each material defined by the expressions:

$$x_{d} = \left[\frac{\delta_{d}}{\delta}\right]^{2} \tag{5}$$

and

$$x_{p} = 1 - \left[\frac{\delta_{d}}{\delta}\right]^{2} \tag{6}$$

where δ_d is the dispersion or non-polar component of the Hansen 3-dimensional solubility parameter (Hansen, 1967). The parameters g_1 and g_2 can also be defined in terms of the solubility parameters of the materials (Rowe, 1987).

$$g_{1} = \frac{{}^{A}\delta^{2}\cdot{}^{A}V^{1/3}}{{}^{B}\delta^{2}\cdot{}^{B}V^{1/3}} \tag{7}$$

$$g_{2} = \frac{1}{g_{1}} = \frac{{}^{B}\delta^{2}\cdot{}^{B}V^{1/3}}{{}^{A}\delta^{2}\cdot{}^{A}V^{1/3}} \tag{8}$$

where V is the molar volume of the material, i.e. its molecular weight divided by its density.

It should be noted that although Hansen defined his partial solubility parameters by the equation:

$$\delta^{2} = \delta_{d}^{2} + \delta_{p}^{2} + \delta_{h}^{2} \tag{9}$$

where δ_p and δ_h are the polar (dipole/dipole interaction) and hydrogen bonding components respectively, the fractional polarity x_p cannot be calculated using δ_p alone, since this would ignore any additive effect of hydrogen bonding.

Discussion

Values for the Hansen partial solubility parameters for materials considered in this study are shown in Table 1. The solubility parameters for magnesium stearate (assumed to be pure) were taken as being identical to those measured by Panzer (1973) for lithium stearate. This assumption is reasonable in the light of the data generated for a variety of the metal stearates by Little (1966). Table 2 shows data for the interaction parameter and strengths of both the adhesive and cohesive interactions within the lubricant for the various excipient/lubricant systems studied. The values for the cohesive interactions within the excipients were 386.1 MPa and 398.0 MPa for the microcrystalline cellulose and anhydrous lactose, respectively. An important point to note is the relationship between the cohesive interactions and the fractional polarities, the larger the fractional polarity the higher the value for the cohesive interactions. In the case of polytetrafluoroethylene the cohesive interactions are due entirely to dispersion forces.

For both the excipients, the values for the adhesive interaction between excipient and lubricant decrease in the order magnesium stearate > stearic acid > polytetrafluoroethylene. However, it is not just the adhesive interactions that are important but the ratio of these to the cohesive interactions. In the case of magnesium stearate the adhesive interactions are higher than the cohesive interactions while in the case of stearic acid the adhesive interactions are only 80% of the cohesive interactions. For polytetrafluoroethylene the ad-

TABLE 1

Molar volumes, Hansen solubility parameters and fractional polarities for the materials used in this study

Material	V (cm^2 mol^{-1})	δ	δ_d (MPa$^{1/2}$)	δ_p	δ_h	x_p	Reference
Microcrystalline cellulose	216.0	39.3	19.4	12.7	31.3	0.76	Phuoc et al. (1987)
Anhydrous lactose	236.8	39.9	19.6	26.2	23.1	0.76	Phuoc et al. (1986)
Magnesium stearate [1]	542.0	18.2	15.7	8.3	3.9	0.26	Panzer (1973)
Stearic acid	326.0	17.6	16.4	3.3	5.5	0.13	Hansen and Beerbower (1967)
Polytetrafluoroethylene (PTFE)	50.0	14.0	14.0	0	0	0.00	Koenhen and Smolders (1975)

[1] Solubility parameters were taken to be identical to those of lithium stearate; the molar volume was calculated assuming the material to be pure magnesium stearate.

hesive interactions are less than half the cohesive interactions. The relevance of these findings to tabletting can now be seen. When microcrystalline cellulose or anhydrous lactose is compacted with magnesium stearate as a lubricant, the strong adhesive interactions will cause a film to be formed over the excipient. This film will be extensive since continued shearing of the system will cause the magnesium stearate to spread further until a monomolecular film is formed. This will decrease the number of the strong cohesive interactions between the excipient particles causing a decrease in tablet strength. On the other hand, when polytetrafluoroethylene is used as a lubricant the low adhesive interactions coupled with the much stronger cohesive interactions indicate that this lubricant will tend to concentrate in the interstitial pores between the excipient particles. This will not significantly decrease the excipient–excipient interactions and hence there will be little decrease in tablet strength. Stearic acid will have properties somewhere between the two extremes but nearer magnesium stearate than polytetrafluoroethylene. This is consistent with the experimental data of Jarosz and Parrott (1984) who studied the effect of magnesium stearate and stearic acid on the tensile strengths of tablets prepared from microcrystalline cellulose and anhydrous lactose and Alpar et al. (1969) who studied the effect of magnesium stearate and polytetrafluoroethylene on the strengths of tablets prepared from spray-dried lactose.

Although it must be realised that the model used in the derivation of the equations is somewhat crude and oversimplified and hence the equations can do nothing more than predict trends, the data presented clearly illustrated the potential of this type of approach. Unfortunately, before it can be applied further, more data on the partial solubility parameters of other excipients are required. The method used by Phuoc et al. (1986, 1987) based on gas-solid chromatography

TABLE 2

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 [adhesive (A–B)]	Interaction (MPa) [cohesive (B–B)]
Microcrystalline cellulose	magnesium stearate	0.48	85.8	82.8
Microcrystalline cellulose	stearic acid	0.40	69.2	77.4
Microcrystalline cellulose	PTFE	0.16	22.0	49.0
Anhydrous lactose	magnesium stearate	0.48	87.1	82.8
Anhydrous lactose	stearic acid	0.38	65.7	77.4
Anhydrous lactose	PTFE	0.14	19.6	49.0

would appear to provide the best means of generating these data.

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