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The dispersive component of the surface free energy of powders assessed using inverse gas chromatography and contact angle measurements

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Abstract

The nonpolar parameter of solid surface free energy γ_s^d has been determined for some pharmaceutical powders by means of contact angle measurement (Wilhelmy plate method) and inverse phase gas chromatography (IGC). For most samples, a good correlation between the results of the two methods was found. Additionally it was found that to get comparable results with the IGC method, contact angles obtained with totally nonpolar liquid should be used for calculating γ_s^d. Comparison of our results with those from the literature showed that the correlation depends on the method used for contact angle determination and the properties of the liquids used for contact angle measurements. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Contact angle; Wilhelmy plate method; Inverse gas chromatography; Surface free energy

1. Introduction

Most pharmaceutical substances are powders, and surface energetics play an important role in controlling their behavior. Different methods for surface free energy assessment are available. The traditional method is to measure a liquid contact angle on solid samples. Usually compacted powders are prepared to give plates with a suitable geometry. Contact angles have to be measured with several liquids to assess the surface free energy of a powder. In the method of Wu (1973) two liquids of known polar (γ_l^p) and dispersion (γ_l^d) components are used for measurement. The solid surface free energy is the sum of nonpolar (γ_s^d) and polar (γ_s^p) components and is calculated according to the Eq. (1) (Wu, 1973):

$$\gamma_l^d(1+\cos\theta) = \gamma_s + \gamma_l - \frac{4(\gamma_s^d \times \gamma_l^d)}{\gamma_s^d + \gamma_l^d} - \frac{4(\gamma_s^p \times \gamma_l^p)}{\gamma_s^p + \gamma_l^p} \quad (1)$$

In the method of Good and van Oss the contact angle of three separate liquids with known nonpolar (γ^{LW}), acid (electron acceptor-γ^+) and base (electron donor-γ^-) components have to be measured (Van Oss et al., 1988). The solid surface free

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energy is the sum of nonpolar (LW, Lifshitz-van der Waals) and polar (AB, acid-base) components given by Eq. (2) and Eq. (3) (Van Oss et al., 1988):

$$\gamma_i^{AB} = 2\sqrt{\gamma_i^+\gamma_i^-} \tag{2}$$

$$(1+\cos\theta)\gamma_l^{TOT} = 2\left(\sqrt{\gamma_s^{LW}\gamma_l^{LW}} + \sqrt{\gamma_s^+\gamma_l^-} + \sqrt{\gamma_s^-\gamma_l^+}\right) \tag{3}$$

From the theoretical point of view the solid surface free energy is not dependent on the liquids used for its calculation. In practice this is not the case. The problem of solvent choice has been approached statistically in some papers (Dalal, 1987; Della Volpe and Sibioni, 1997). A difference in liquid contact of 1°, influences solid surface free energy value by different amount, depending on the choice of combination of liquids. For two components approach (Wu's method), a combination of water and diiodomethane, the polar and nonpolar liquids with the highest possible surface tension, extents minimum influence on the result. For the three component approach (Good and van Oss method), water/glycerol/bromonaphthalene and water/glycerol/diiodomethane are favorable and optimal combinations for solid surface free energy calculations (Dalal, 1987; Della Volpe and Sibioni, 1997).

Solid surface free energy can also be assessed by means of inverse gas chromatography (IGC). The powder to be investigated is packed into a column and known gas is passed over its surface. By injecting a series of alkanes of known γ_l^d (which is identical to γ_l because of their nonpolarity) at infinite dilution, it is possible to obtain the dispersion component of the solid surface free energy γ_s^d. The retention volume V_n is calculated from Eq. (4) (Schultz et al., 1987) and the dispersion component of the solid surface free energy γ_s^d from Eq. (5) (Schultz et al., 1987; Schultz and Lavielle, 1989).

$$V_n = JF(t_r - t_0) \tag{4}$$

$$RT \ln V_n = 2N\sqrt{\gamma_s^d}a\sqrt{\gamma_l^d} + K \text{ (intercept)} \tag{5}$$

where, F is the carrier gas flow; J, James and Martin compressibility correction factor (James and Martin, 1951) due to pressure differences; t_r, retention time of the probe; t_0, retention time of non-interacting standard (methane); a, molecular area of the adsorbed molecule; R, gas constant; T, absolute temperature; K, intercept; N, Avogadro's number.

This γ_s^d parameter can be compared with the dispersion component obtained from contact angle measurements on compacted solid samples. Ticehurst et al. (1994) stated that results of the two methods cannot be identical, because the theoretical approaches are different. Further, IGC at infinite dilution measures only a small portion of the powder surface; with a heterogeneous surface, adsorbates would tend to interact first of all with the more energetic surface sites. However, Dove et al. (1996) compared nonpolar parameters of theophylline and caffeine surface free energy obtained from two contact angle methods (Wilhelmy plate and glass slide methods) and IGC and found some agreement.

Electron donor and acceptor properties of a solid can be determined by IGC using polar liquids in the vapor phase (toluene, acetonitrile, tetrahydrofuran, xylene etc.). For adsorbates other than *n*-alkanes, i.e. polar liquids, the overall interaction with the sample (adsorbent) contains contribution due to nonspecific (nonpolar) and specific (polar) interactions. The magnitude of the nonspecific component can be evaluated by use of a dispersion interaction reference state based on n-alkanes. The magnitude of specific component can be measured by additional use of polar liquid's vapor. Strong interaction of the solid with the vapor will develop only between acid and a base. Polar liquids used for IGC measurements are characterized by donor (DN) and acceptor number (AN) (Schultz et al., 1987; Schultz and Lavielle, 1989):

1. the donor number DN, expressing the basicity or electron-donor ability, is the molar enthalpy value for the reaction of the electron donor with a reference acceptor $SbCl_5$.
2. the acceptor number AN expressing the acidity or electron acceptor ability, is defined on the following basis: it is the ^{31}P NMR chemical shift observed when $(C_2H_5)_3PO$ reacts with the acceptor (Schultz et al., 1987).

It is expected that acid and base properties of solid obtained from IGC measurements by use of polar liquids are consistent with results obtained from contact angle measurements.

The aim of this work was to compare only the dispersion components (γ_s^d) of surface free energy of model substances (polyvinylpyrrolidone (PVP), hydroxypropylmethylcellulose (HPMC), lactose monohydrate and acyclovir) obtained by contact angle measurement with those obtained by means gas chromatography.

2. Materials and methods

The model powders used were polyvinylpyrrolidone (PVP, BASF, Germany), hydroxypropylmethylcellulose (HPMC, Syntypharm, Germany), lactose monohydrate (DMV International, Netherlands) and acyclovir (LEK Ljubljana, Slovenia). Methane (Messer, Slovenia), *n*-pentane and *n*-hexane (Kemika, Croatia), *n*-heptane and *n*-octane (Riedel-de Haën AG, Germany) were used for IGC measurements. Liquids used for contact angle measurement were bidistilled water, glycerol, ethyleneglycol and 1-bromonaphthalene (Riedel-de Haën AG, Germany), diiodomethane and formamide (Sigma, Germany).

2.1. Contact angle measurements

Compacts of the powders (200 mg) were prepared in a rectangular stainless steel punch and die assembly (25 × 10 mm) in a Specac hydraulic press (Kent, England) with a 10 s dwell time at a pressure of 2×10^8 Pa. The exact perimeter of the sample plates was measured using a micrometer. The plate was attached to the balance loop of the microbalance in a Krüss Tensiometer K12 (Germany). The temperature of the liquid used for contact angle measurements was controlled at 20 ± 0.5°C, by flowing water from a circulator (Haake, Germany). The test liquid was placed in a special glass dish and raised by means of a motorized platform to contact the powder plate. The platform was raised by means of a motorized platform to contact the powder plate. The platform was raised with the speed of 1.2 mm/min. From the force measurements, the contact angle was obtained using the Krüss tensiometer software (Krüss GmbH, 1996). At least five plates of same powder were used for measurements with every liquid.

2.2. Inverse gas chromatography

Inverse gas chromatography was carried out using a Hewlett-Packard 5870 Gas Chromatograph. The carrier gas, nitrogen, was maintained at a constant pressure and it flow rate was measured using a bubble flowmeter.

Approximately 2.5 g of the powder was packed in a glass chromatographic column (0.6 m long, 4 mm i.d.) that was cold silanized before use in order to prevent interaction with the adsorbate (Mohhamad and Fell, 1982). The powder was dried at 30°C for 15-h prior the measurement to remove surface moisture. Sample probe molecules (pentane, hexane, heptane and octane) were injected into the nitrogen flow, passed through the column and detected with a flame ionization detector. Methane was used as non-adsorbing standard.

3. Results and discussion

The problem for solid surface free energy measurement arises from the drawbacks of the technique for contact angle measurement and from the calculation method used. For these reasons, it is advisable to obtain this solid surface property from an independent method such as IGC. In Table 1, the surface tension parameters of liquids used for contact angle measurement are listed.

Table 1
Surface tension parameters of some liquids (mN/m, Van Oss et al., 1997)

	γ_1	γ^{LW}	γ^+	γ^-
Water	72.8	21.8	25.5	25.5
Glycerol	64.0	34.0	3.92	57.4
Diiodomethane	50.8	50.8	0	0
Ethyleneglycol	48.0	29.0	1.92	47.0
Formamide	58.0	39.0	2.38	39.6
Bromonaphthalene	44.6	44.6	0	0

Table 2
Nonpolar component of model substances calculated from contact angle according to Good and van Oss method (mN/m)

Powder sample	Liquid combination	γ^{LW}
PVP	Diiodomethane in any combination	40
HPMC	Water/ethyleneglycol/formamide	12
HPMC	Diiodomethane in any combination	38
HPMC	Water/ethyleneglycol/formamide	1
HPMC	Water/formamide/glycerol	23
Lactose monohydtrate	Diiodomethane in any combination	44
Lactose monohydtrate	Bromonaphthalene in any combination	43
Lactose monohydtrate	Water/ethyleneglycol/formamide	27
Lactose monohydtrate	Water/formamide/glycerol	7
Lactose monohydtrate	Ethyleneglycol/formamide/glycerol	13
Acyclovir	Diiodomethane in any combination	43
Acyclovir	Bromonaphthalene in any combination	43
Acyclovir	Water/formamide/glycerol	56
Caffeine[a]	Water/ethyleneglycol/formamide	44
Caffeine[a]	Diiodomethane in any combination	35
Theophylline[a]	Water/ethyleneglycol/formamide	44.5
Theophylline[a]	Diiodomethane in any combination	30

[a] Dove et al. (1996).

They all have high surface tension (above 40 mN/m) (Van Oss et al., 1997) but they differ in polarity. The use of different liquid combinations for solid surface free energies, calculated according to the method of Good and van Oss method led to different results (Table 2). Contact angles were measured with six liquids on each solid. The use of six liquids allows ten different combinations, each with three liquids. Some combinations give no result with certain solids and are not listed in Table 2 (for example water–glycerol–formamide for PVP). An equation system without solution is called ill-conditioned (Della Volpe and Sibioni, 1997). It can result from the use of solvents whose polarities are too similar, or from the use of liquids with too low surface tension for contact angle measurements (Della Volpe and Sibioni, 1997; Dalal, 1987). Our results (Table 2) confirm that different liquid combinations lead to different values of solid surface free energy.

In spite of the fact that it was statistically proved in the literature that some liquid combinations should be better than others for solid surface free energy calculations (Della Volpe and Sibioni, 1997), it is still not clear if their use results in true information about the nature of the surface. For this reason, IGC provides additional and important information about the investigated surface properties.

The dispersion parameter of solid surface free energy can be calculated directly using Eq. (6) from measurements of the contact angle of totally nonpolar liquid (van Oss et al., 1988). From this equation it can be seen that, to achieve a contact angle greater than 0°, the surface tension of nonpolar liquid must be greater than the dispersion component of the solid surface free energy. In practice, only a few nonpolar liquid have sufficiently high surface tension, such as diiodomethane $\gamma_l = 50.8$ mN/m and bromonaphthalene $\gamma_l = 44.6$ mN/m.

$$1 + \cos\theta = 2\sqrt{\frac{\gamma_s^{LW}}{\gamma_l^{LW}}} \tag{6}$$

To determine, which liquid combination should be used for solid surface free energy calculation, the obtained nonpolar parameter γ_s^d of model powders were compared with those obtained using inverse gas chromatography. It was found that best agreement was achieved when the contact angle with diiodomethane or bromonaphthalene was used (Tables 2 and 3). Contact angle of bromonaphthalene on PVP was not measurable. If it is taken as 0°, the γ_s^d value would, from Eq. (6) be 44.6 mN/m, which is closer to the value of 48 mN/m measured by IGC than that result obtained with diiodomethane. These results suggest that, for calculation of the nonpolar component of solid surface free energy, the contact angle should be always measured with several totally nonpolar liquid (for example diiodomethane, bromonaphthalene, hexadecane…). Using a nonpolar liquid in contact angle measurement usually leads to the highest value of γ_s^d compared with other liquid combinations. Literature value of γ_s^d

Table 3
Dispersion parameter of solid surface free energy of the test probes calculated with contact angles (Good and Van Oss method) and by means of IGC (mN/m) with standard deviation in parenthesis

Powder sample	Diiodomethane contact angle	Bromonaphthalene contact angle	IGC
PVP	39.7(0.9)	nm[a]	48.0(1.2)
HPMC	37.9(0.9)	37.4(1.0)	39.2(1.1)
Lactose monohydtrate	43.6(0.8)	42.8(0.8)	41.4(1.1)
Acyclovir	42.8(0.8)	42.5(0.8)	47.8(1.5)

[a] nm, not measurable.

determined by means of IGC lead to the similar conclusion as contact angle measurements (Table 4): values of the γ_s^d parameter are usually greater than 40 mN/m. This could be mainly due to the fact that pharmaceutical substances consist of carbon, oxygen and hydrogen. However, the use of diiodomethane in combination with polar liquids for contact angle measurements usually indicates a lower polarity of the surface, which can lead to a wrong conclusion about the nature of the surface.

Ahfat et al. (2000) determined the nonpolar parameter of some pharmaceutical powders and found the same ranking orders for contact angle and IGC measurements (Table 5). The higher values determined by IGC were attributed to high-energy spots on the powders interacting preferentially with the vapor of used liquid. Comparison of our results obtained from contact angle measurements of diiodomethane and bromonaphthalene on lactose with those from the literature (Table 3 and Table 4, Ahfat et al., 2000) shows differences on values of γ_s^d. They could be attributed to the method for contact angle on surface, where powder particles coated the slides using a camera instead of the smooth surface that is obtained from a powder press for the Wilhelmy plate method. Our results show the similar trend when γ_s^d obtained from contact angle measurements and IGC are compared with the exception of PVP (Table 3). Differences between lactose and acyclovir are small and are in the standard deviation (S.D.). Similar conclusion can be made when γ_s^d obtained from both method are compared only in the case of HPMC and lactose. Higher γ_s^d values obtained with IGC than with contact angle measurements (PVP, acyclovir) can be result of energetically nonhomogenous samples and need further investigation. Ticehurst et al. (1994) also stated that differences in the nonpolar parameter values assessed from contact angle measurements and IGC arise from high-energy spots on the solid surface. It is expected that a better correlation between results of contact angle measurements and inverse gas chromatography would be achieved, if sample surface is energetically homogeneous.

As already mentioned γ_s^d can be calculated directly from nonpolar liquid contact angle. Diiodomethane belongs to nonpolar liquid with high surface tension. In comparison with other nonpolar liquids, it forms highest possible contact angle on a certain surface. For this reason, it is together with bromonaphthalene generally accepted as nonpolar liquid of choice for contact angle measurements. Values of contact angle of diiodomethane on PVP and HPMC obtained from

Table 4
Dispersion parameter of solid surface free energy of some powders determined by means of IGC (mN/m)

Powder	γ_s^d
Theophylline[a]	50.1
Caffeine[a]	39.9
Lactose monohydrate (four different batches)[b]	40–44
Propranolol hydrochloride[c]	45 (unmilled), 61 (milled)
Salbutamol sulphate (two different batches)[d]	38 (batch1), 83 (batch2)

[a] Dove et al. (1996).
[b] Ticehurst et al. (1996).
[c] York et al. (1998).
[d] Ticehurst et al. (1994).

Table 5
Comparison of dispersion parameter of solid surface free energy of some powders determined by contact angle measurements and IGC (mN/m)(Ahfat et al., 2000)

Powder	γ_s^d (bromonaphthalene contact angle)	γ_s^d (IGC)
Zamifenacin	30.4	46.8
Spray dried lactose	29.5	41.4
Anhydrous lactose	28.2	41.3
Starch	27.2	39.8
Lactose monohydrate	24.6	39.3

wetting measurements (Buckton, 1993) lead to values of γ_s^d similar to those obtained in our laboratory. About 40° on PVP and 49° on HPMC determined by means of Wilhelmy plate and sessile drop techniques give 40.2 and 35.9 mN/m, respectively. This confirms reasonabless for use of diiodomethane in contact angle measurements.

Further research should be carried out to obtain polar components of solid surface free energy from IGC measurements. Acid and base parameters of powders obtained in this way are not comparable to those from contact angle measurements, because they are defined on a different basis. Anyway, these results may be valuable and used to compare solid acid and base properties calculated from both methods.

4. Conclusion

The dispersion component of solid surface free energy was determined for some pharmaceuticals assessed by means of contact angle measurement and by inverse gas chromatography (IGC). The best correlation for all model substances, between the results of these two methods was found when contact angle with diiodomethane or bromonaphthalene were used for calculating nonpolar component of solid surface free energy. It was confirmed that inverse gas chromatography is a useful additional method for solid surface characterization.

References

Ahfat, N.M., Buckton, G., Burrows, R., Ticehurst, M.D., 2000. An exploration of inter-relationships between contact angle, inverse phase gas chromatography and triboelectric data. Eur. J. Pharmacol. Sci. 9, 271–276.

Buckton, G., 1993. Assessment of the wettability of pharmaceutical powders. J. Adhesion Sci. Technol. 3, 205–219.

Dalel, E.N., 1987. Calculation of solid surface tensions. Langmuir 3, 1009–1015.

Della Volpe, C., Sibioni, S., 1997. Some reflection on acid-base solid surface free energy theories. J. Coll. Interf. Sci. 195, 121–136.

Dove, J.W., Buckton, G., Doherty, C., 1996. A comparison of two angle measurement methods and inverse gas chromatography to assess the surface energies of theophylline and caffeine. Int. J. Pharm. 138, 199–206.

James, A.T., Martin, A.T.P., 1951. Gas-liquid partition chromatography: the separation and micro-estimation of volatile fatty acids from formic to dodecanoic acid. Biochem. J. 15, 679–690.

K121 Contact angle and adsorption measuring system, Kruss GmbH, Hamburg, Germany 1996, Information material.

Mohhamad, H.A.H., Fell, J.T., 1982. Contact angles of powder mixtures consisting of spherical particles. Int. J. Pharm. 11, 149–154.

Schultz, J., Lavielle, L., 1989. Interfacial properties of carbon fibre-epoxy matrix composites. In: Lloyd, D.R., Ward, T.C., Schreiber, H.P. (Eds.), Inverse Gas Chromatography of Polymers and Other Materials, ACS Symp. Ser. 391. American Chemical Society, Whasington DC, pp. 185–202.

Schultz, J., Lavielle, L., Martin, C., 1987. The role of the interface in carbon fibre-epoxy composites. J. Adhesion 23, 45–60.

Ticehurst, M.D., Rowe, R.C., York, P., 1994. Determination of the surface properties of two batches of salbutamol sulphate by inverse gas chromatography. Int. J. Pharm. 111, 241–249.

Ticehurst, M.D., York, P., Rowe, R.C., Dwivedi, S.K., 1996. Characterization of the surface properties of α-lactose monohydrate with inverse gas chromatography, used to detect batch variation. Int. J. Pharm. 141, 93–99.

Van Oss, C.J., Good, R.J., Chaudhury, M.K., 1988. Additive and nonadditive surface tension components and the interpretation of contact angles. Langmuir 4, 884–891.

Van Oss, C.J., Giese, R.F, Wu, W., 1997. On the predominant electron donicity of polar surface. J. Adhesion 63, 71–88.

Wu, S., 1973. Polar and nonpolar interactions in adhesion. J. Adhes. 5, 39–55.

York, P., Ticehurst, M.D., Osborn, J.C., Roberts, R.J., Rowe, R.C., 1998. Characterisation of the surface energies of milled di-propranolol hydrochloride using inverse gas chromatography and molecular modeling. Int. J. Pharm. 174, 179–186.