



The Determination of Acid-Base Parameters by Inverse Gas Chromatography

Majid Naderi and Daniel Burnett | Surface Measurement Systems Ltd.

The surface energy can be divided into a dispersive and specific component. Specific interactions consist mostly out of Lewis acid-base contributions. The latter are a useful descriptor for the acceptor and donor properties of surfaces. IGC SEA is a very sensitive and accurate way of determining dispersive and specific interactions and has several benefits over common wettability techniques. In this study two different concepts (van Oss and Gutmann) have been applied to study the acid-base properties of three different kinds of microcrystalline cellulose.

Introduction

Surface energy measurements are widely used parameters to gain a fundamental understanding of the energetic situation on the surface of a material. For this reason surface energies can be related to material performance, processing issues and stability [1]. The surface energy can be divided into a dispersive and specific component. The dispersive contribution is equal to the Lifshitz-van der Waals interactions, which take London, Dybe and Kessom forces into account while the specific contribution comprises Lewis acid-base interactions (with hydrogen bonding as a subclass) [2].

The acid-base contributions are commonly described by different concepts, including van Oss [3], Gutmann [4], Drago [5], Fowkes [6] and others. Most IGC SEA work published in the literature is based on a description of the acid-base parameters by the Gutmann theory. Although the Gutmann concept gives an extremely useful reflection of the acid-base chemistry of the investigated surface its numbers

are dimensionless and it is not possible to calculate the specific contribution of the surface energy based on these values. An attractive alternative is the van Oss concept which provides acid and base numbers as well as the specific surface energy in the same units as the dispersive surface energy [7].

In the current study the acid-base properties of different microcrystalline cellulose (MCC) samples have been investigated. This study describes the utilization of the Gutmann and van Oss methods and discusses the advantages and disadvantages of the two theories.

Theory

Traditionally, surface energies are measured by liquid wetting techniques. Most of these methods involving the measurement of a contact angle. However, these are difficult to implement reproducibly on free flowing powders since they usually involve a compression of the powder, which can change its surface characteristics. An alternative wetting technique, based on the Washburn equation has also been reported but has been shown to be strongly affected by



packing of the capillary, particle size and pore geometry.

Moreover, only a limited number of probe molecules can be used by either wettability method since the formation of a contact angle is required and many potentially interesting probe molecules spread on the relative highly energetic surfaces of micronised pharmaceutical materials. Another problem of wettability methods is the absorption of liquid in the bulk which would lead to an overestimation of the surface energy.

As an alternative, Inverse Gas Chromatography was shown in the literature to be a versatile and extremely sensitive technique for the determination of surface thermodynamic properties such as the surface energy [8]. This approach inverts the conventional relationship between mobile and stationary phase found in analytical chromatography. The stronger the interaction, the more energetic the surface and the longer the retention time. For this reason thermodynamic parameters can be derived from the retention behaviour. In contrast to wetting methods this technique involves neither liquid wetting nor compression of particles.

IGC SEA measurements are usually carried out under infinite dilution conditions. In this low concentration range only a few probe molecules interact with the high-energy sites on the surface of a solid. Parameters obtained under these conditions are highly sensitive and can reflect small changes on the surface. For this reason IGC SEA was successfully applied for batch-to-batch studies [9].

To obtain the dispersive as well as specific surface energies different polar and non-polar vapour phase probe molecules are injected under defined conditions. Their retention behaviour is expressed by the retention volume (Equation 1):

$$V_R^0 = j / m \cdot F \cdot (t_R - t_0) \cdot \frac{T}{273.15} \quad (1),$$

where T is the column temperature, m the sample mass, F the exit flow rate at 1 atm and 273.15K; t_R is the retention time for the adsorbing probe and t_0 is the mobile phase hold-up time (dead-time). j is the James-Martin correction, which

corrects the retention time for the pressure drop in the column bed.

The retention volume is related to the dispersive surface energy, γ_s^D by Equation 2.

$$RT \ln V_R^0 = 2N_A (\gamma_s^D)^{1/2} a (\gamma_L^D)^{1/2} + const. \quad (2).$$

N is the Avogadro constant and R the gas constant. If a series of alkanes is injected the dispersive surface energy can be derived from the slope of the alkane line in a plot of $RT \ln V$ versus $a(\gamma_L^D)^{1/2}$ (see Figure 1).

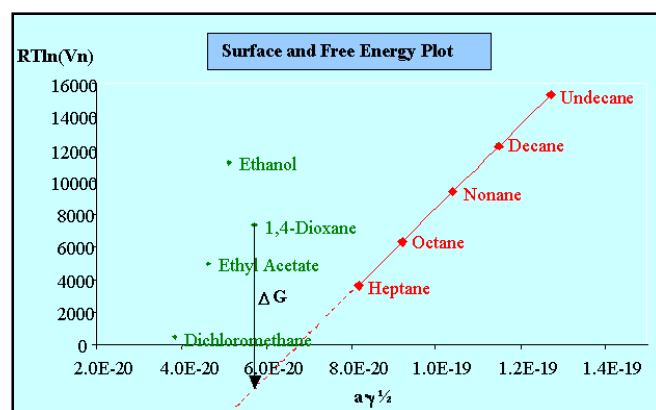


Figure 1. Dispersive surface energy plot (in red) and specific free energy of desorption for several polar probe molecules (in green) eluted through a column packed with excipient. 0% RH, 30°C, 0.03P/P₀.

If polar probe molecules are also injected, then specific interactions can be measured. The experimental points for the polar probe molecules are located above the alkane straight line in the surface energy plot. The distance between each point and the straight line represents the specific contribution of the interaction, which is expressed as the specific free energy, ΔG (see Figure 1). A detailed description of these calculations can be found elsewhere [2]. Specific free energies reflect the properties of the surface and the vapour probe. They can be converted into acid-base parameters if acid-base concepts are applied. Several approaches have been suggested over the years, most of them based on the Lewis acid-base concept, where the base is the electron-donating part while the acid is accepting electrons. These concepts assume that certain orbitals are shared and interactions do not involve complete electron transfers. Two of the most used

The results for the dispersive contribution of the surface energy are graphically illustrated in Figure 2.

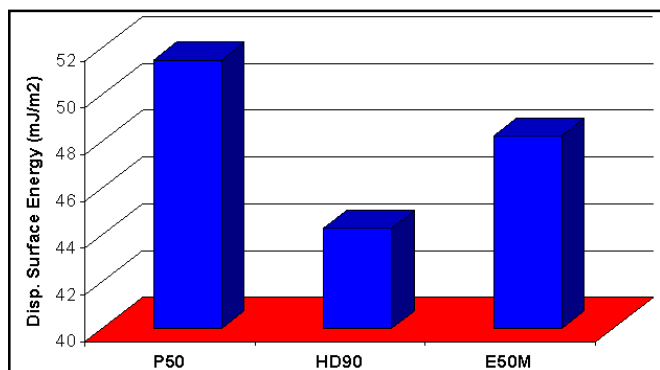


Figure 2. Dispersive surface energies of the three MCC samples studied (at 303 K).

There are significant differences in the dispersive surface energy between the microcrystalline cellulose samples, which are due to the differences in the surface properties. Specific free energies were measured for acetone, acetonitrile, ethyl acetate, dichloromethane, 1,4-dioxane, ethanol, THF and toluene. They are illustrated in Figure 3.

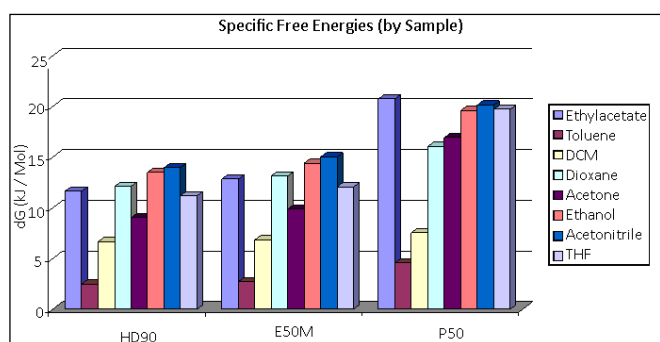


Figure 3. Specific free energies obtained with various polar probe molecules for each MCC sample at 303 K.

All probe molecules show the strongest interaction with P50 while HD90 and E50M appear to have similar specific interactions. As mentioned previously specific free energies can be converted into acid-base numbers by using the Gutmann or van Oss concept. This can be done in two different ways. If monopolar probe molecules are considered, acceptor and donor numbers can be obtained by using the specific

free energy of just one acidic and one basic probe molecule.

Alternatively, amphoteric probe molecules can be used, which comprise both donor and acceptor properties. A linearisation of the above mentioned equations allows then for a calculation of the acid-base parameters.

The latter method is usually more reliable since it is based on more datapoints. This is demonstrated by means of the Gutmann concept in Figure 4, based on the specific free energies of ethanol, ethyl acetate, acetone, acetonitrile and THF. The K_A number can be obtained from the slope and K_B from the intercept. The results are shown in Table 3.

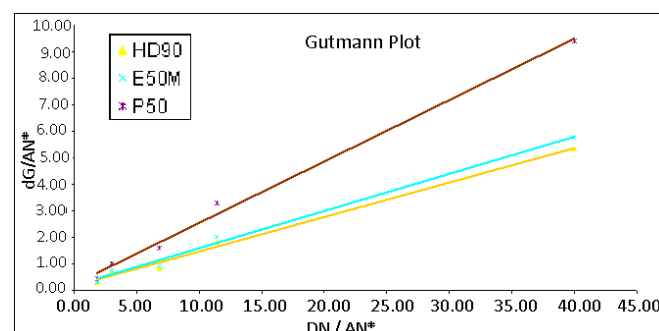


Figure 4. Gutmann plots based on the specific free energies of ethanol, ethyl acetate, acetone, acetonitrile and THF.

Unfortunately, there haven't been any amphoteric probes reported that are suitable for the gas phase and to be used with the van Oss concept. For this reason γ_s^+ and γ_s^- values have been obtained with the monopolar probe molecules dichloromethane and ethyl acetate. For comparison K_A and K_B numbers were calculated also with monopolar probe molecules using the Gutmann concept. Since ethyl acetate is amphoteric on the Gutmann scale, K_A and K_B numbers have been obtained with dichloromethane and 1,4-dioxane in this case. All results are summarised in Table 3.

Table 3. Acid and base numbers according to the Gutmann and van Oss concept.

	Method	Probe nature	E50M	HD90	P50
K_A [-]	Gutmann	Amphoteric	0.14	0.13	0.23
K_B [-]	Gutmann	Amphoteric	0.21	0.18	0.25
K_A [-]	Gutmann	Monopolar	0.21	0.20	0.26
K_B [-]	Gutmann	Monopolar	0.42	0.41	0.47
γ_S^+ [mJ/m ²]	Van Oss	Monopolar	54.24	44.73	141.75
γ_S^- [mJ/m ²]	Van Oss	Monopolar	102.82	97.55	125.53

biggest disadvantages of the van Oss approach and could be resolved by providing γ_S^+ and γ_S^- values for amphoteric probe molecules. However, these data are not easy to obtain.

Another well-known problem of the van Oss approach is the inaccuracy of the γ_L^+ and γ_L^- values. Van Oss selected water as a reference and defined $\gamma_S^+ = \gamma_S^- = 25 \text{ mJ/m}^2$ [3]. Della Volpe et al [8] showed that this assumption is not correct due to the slightly (Lewis) acidic character of water and suggested a corrected scale. Unfortunately, there are no Della Volpe numbers available for vapour phase probe molecules at this moment.

Comparing the values obtained from all three methods, the results suggest overall amphoteric surfaces. Overall absolute numbers are quite different when Gutmann results from amphoteric and monopolar probes are considered. This is due to the higher inaccuracy of the monopolar probe approach. If only trends are considered the numbers (including van Oss) are quite consistent for E50M and HD 90. These two substances seem to have a predominantly basic surface. For P50, however, results are inconsistent. While the values obtained from the Gutmann approach with amphoteric probe molecules suggest a fairly neutral surface the van Oss and Gutmann calculation using monopolar vapours identifies P50 as basic or acid, respectively.

These conflicting results from the van Oss and Gutmann approach are partially due to the different theoretical approaches, but as the comparison between monopolar and amphoteric probe molecules for the Gutmann approach shows, there is a high uncertainty in numbers obtained from just two monopolar probe molecules.

This finding is **not** a characteristic of the IGC SEA technique and should be observed with wetting techniques as well. The reason why this phenomenon is not frequently reported in contact angle literature is due to the limited choice of probe molecules so most researchers work with a standard set of wetting agents. This dependence of the results on the probe molecule is one of the



Conclusion

IGC SEA is a useful technique for the determination of acid and base numbers and provides several benefits over common wettability methods when powder samples are considered. For the calculation of acid-base properties, both the Gutmann and van Oss concepts can be applied. Despite its theoretical problems the van Oss concept has become extremely popular amongst researchers as it provides acid and base numbers in the same unit as the surface energy and therefore allows for direct comparison of dispersive and specific interactions. However, due to its shortcomings only acid with acid and base with base numbers can be compared. The Gutmann concept reflects very accurately the acid and base properties of the surface but as its numbers are dimensionless it is only semi-quantitative.

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Head Office:
Surface Measurement Systems, Ltd
5 Wharfside, Rosemont Road
London HA0 4PE, UK
Tel: +44 (0)20 8795 9400
Fax: +44 (0)20 8795 9401
Email: science@surfacemeasurementsystems.com

United States Office:
Surface Measurement Systems, Ltd, NA
2125 28th Street SW, Suite I
Allentown PA, 18103, USA
Tel: +1 610 798 8299
Fax: +1 610 798 0334

