



## Surface Energetic Heterogeneity Profiles by iGC Surface Energy Analyzer

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***Surface energy is a useful parameter describing the energetic properties of the surface of a solid sample. Inverse gas chromatography (IGC) is an established and versatile tool in determining the surface free energy of solids by adsorption of vapours with known properties. This application note describes measurement of surface energetic heterogeneity of D-mannitol samples, with and without surface methylation. Second generation IGC instrument: iGC SEA is proven to be a fast and accurate energy mapping technique, generating highly reproducible surface energy data.***

### Introduction

Inverse gas chromatography (IGC) has been widely used to determine the surface free energy of particulate and fibrous solids. Current IGC methodology is generally conducted at very low solute concentration, and limited to providing a single numerical value of surface free energy [1,2, 3].

Since real solid surfaces are fundamentally inhomogeneous, a single value of surface free energy is not necessarily representative of the entire surface. Real solids in fact exhibit a range of lower and higher energy sites on their surfaces due to presence of different types of surface functional groups, surface topographies, surface irregularities or impurities [4].

Surface energetic heterogeneity profile can be represented by an energy distribution function, which can provide more comprehensive information on the nature and population of different surface sites. A heterogeneity profile constitutes an energy “map” of the material surface and also allows prediction of product

properties, in particular in the formulation of blends, composites or coatings.

Despite the potential importance of heterogeneity profiles, until now, there has been little emphasis on the characterisation of the surface energy distribution of organic solids. Recent advances of IGC surface energy methodology allow for the determination of surface energy distribution [2, 3], from the adsorption isotherms of a series of *n*-alkanes at finite concentrations (Figure 1).

Second generation IGC instrument: iGC SEA adopts this new approach and is equipped with the state-of-the-art injection technology which allows the precise control of the injection size. If a series of concentration (mole, *n*) of dispersive and polar probe vapours are injected at the same surface coverage ( $n/n_m$ )<sup>1</sup>, the surface energy and free energy at that particular surface coverage can be determined. Consequently, the injections of probe vapour at different surface coverages will

<sup>1</sup>  $n_m$  refers to the monolayer capacity of a probe molecule.  $n_m$  for each probe is different and can be determined from the test sample's BET specific surface area and the effective area occupied by each probe molecule.



result in a distribution of surface energy as a function of surface coverage, which is referred to as a surface energy profile. The determination of surface energy heterogeneity by iGC SEA can, therefore, be described as a mapping technique.

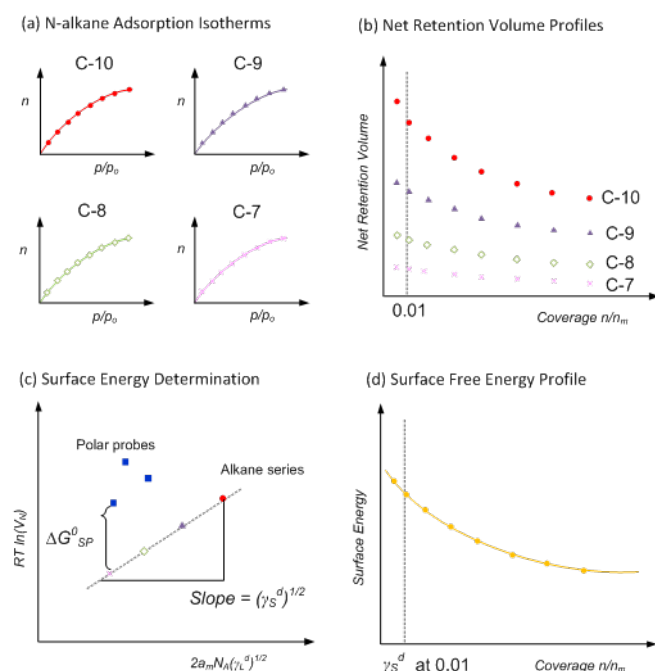


Figure 1. Schematic diagram of iGC experimental method for determining the distribution profiles [3].

In this study, detailed surface energetics of a model pharmaceutical excipient: D-mannitol, with and without surface methylation was determined using iGC SEA. D-mannitol is a particularly interesting example since it is known to have, energetically, a high level of inhomogeneous surface on the native mannitol crystal [5].

## Method

### Material – D-mannitol

D-mannitol ( $C_6H_{14}O_6$ ) was used as received (M4125  $\geq 98\%$ ; Sigma Aldrich). D-mannitol is a crystalline pharmaceutical excipient. It is commonly used in a wide range of formulations for oral and chewable tablets, powder granules and moisture sensitive active pharmaceutical ingredients [6].

### Surface Modification - Methylation

A 5% solution of dichlorodimethylsilane in 1,1,2-trichloroethylene was used to promote surface methylation [7]. The solution was mixed with D-mannitol particles at 80°C for three hours under constant reflux. During the course of the reaction, the mixture was agitated continuously to ensure good dispersion.

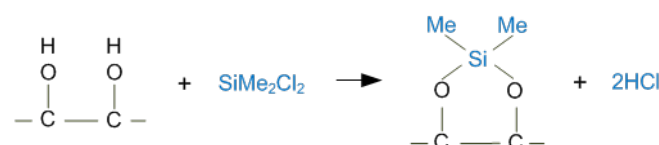


Figure 2. Chemical reaction scheme for methylation of hydroxyl groups on D-mannitol surfaces.

The methylation reaction (Figure 2) occurred at the surface of D-mannitol where dichlorodimethylsilane condensates the surface hydroxyl groups, with a concomitant evolution of hydrogen chloride. The liquid was decanted off after reaction and the samples were dried in a vacuum oven at 80°C for two hours. This treatment ensured that a large portion of the surface hydroxyl groups were methylated and that all the solvent was evaporated. Subsequently both silanised and untreated D-mannitol were sieved to 75-180µm particle size fraction.

### Surface Energy Heterogeneity

All analyses were carried out using iGC Surface Energy Analyzer (SMS, Alpert, UK) and the data were analysed using both standard and advanced SEA Analysis Software. The samples were labelled as Silanised D-mannitol and AR D-mannitol (as received/untreated). For all experiments, about 2g of samples were packed into individual iGC glass column (300mm long by 4mm inner diameter) using the SMS Column Packing Accessory.

Samples were run at a series of surface coverages with alkanes and polar probe molecules to determine the dispersive surface energy distribution as well as the specific (acid-base) surface energy distribution. For the analysis, Dorris and Gray was employed for

dispersive component [8]. Specific contribution was determined by first measuring the free energy of desorption of a pair of mono-functional acidic and basic probe molecules, based on the polarisation approach [9] and Della Volpe scale [10]. Each column was pre-conditioned for two hours at 30°C and 0%RH with helium carrier gas. All experiments were conducted at 30°C with 10sccm total flow rate of helium, using methane for dead volume corrections.

## Results

### Surface Energy Heterogeneity

Dispersive,  $\gamma_s^D$  and specific (acid-base),  $\gamma_s^{AB}$  surface energy profiles obtained directly from the iGC SEA for silanised and AR samples are shown in Figure 3 and Figure 4, respectively.

It can be clearly observed that AR D-mannitol is energetically more active and more heterogeneous, meaning the surface energy changes as a function of surface coverage. There is a notable difference between maximum and minimum  $\gamma_s^D$  values, ranging from about 37.50 and up to 53.00 mJ/m<sup>2</sup>.

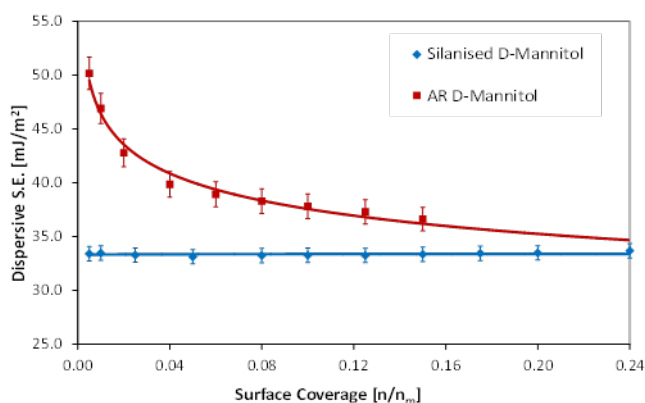


Figure 3. Dispersive surface energy profiles (as a function of surface coverage).

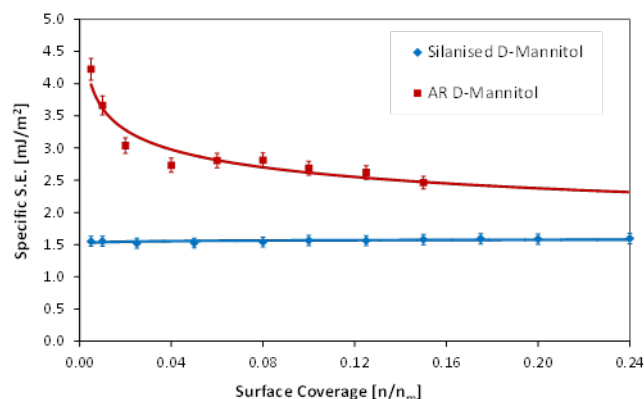


Figure 4. Specific (acid-base) surface energy profiles.

It is known that there is abundance of hydroxyl surface groups on AR D-mannitol, and these hydroxyl groups were substituted with  $-\text{Si}(\text{CH}_3)_2$  groups after the methylation reaction. Therefore as expected, silanised surfaces became energetically more homogeneous and hydrophobic (Figure 4), with significantly smaller  $\gamma_s^{AB}$ .

Surface energy profile results presented here also coincide with previous report of contact angle measurement on a native mannitol macroscopic crystal, which has shown a high level of surface heterogeneity [5].

In order to represent the heterogeneity of the samples in more reader- friendly way, the surface energy distributions are obtained by a point-by-point integration of the surface energy profiles, resulting in plot of dispersive and specific surface energy versus percentage of surface (area increment), as shown in Figure 5 and Figure 6.

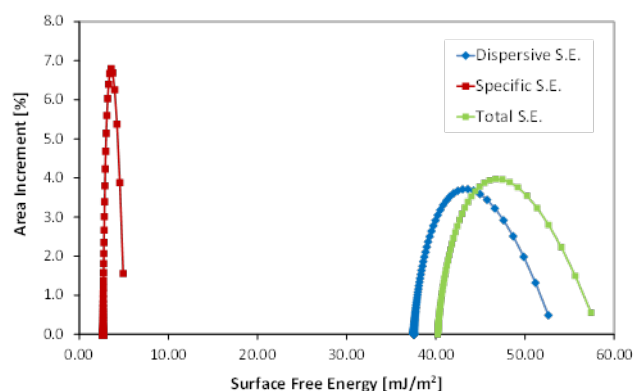


Figure 5. Surface energy distributions of AR D-mannitol.

Evidently shown here, AR D-mannitol has much wider distributions of  $\gamma_S^D$ , with a mean value  $\gamma_{S50}^D$  of 40.34 mJ/m<sup>2</sup>, comparing to silanised D-mannitol's at 34.10 mJ/m<sup>2</sup>. Meanwhile for specific contribution, AR D-mannitol possesses a  $\gamma_{S50}^{AB}$  of 3.09 mJ/m<sup>2</sup>, nearly two times more than that of silanised D-mannitol ( $\gamma_{S50}^{AB}$  at 1.60 mJ/m<sup>2</sup>).

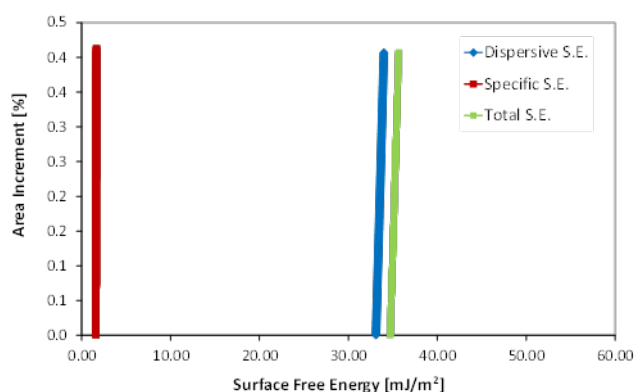


Figure 6. Surface energy distributions of silanised D-mannitol.

This study has shown that iGC SEA is able to determine detailed surface energetics of D-mannitol samples directly and accurately, reflecting the changes in surface chemical environment. This is in particular important to differentiate any subtle differences in surface physical and/or chemical conditions of a wide range of solid materials.

### Reproducibility of Heterogeneity Data

In the current study, reproducibility of iGC SEA instrument was investigated. Silanised and AR D-mannitol have been routinely used as the representative materials on SMS iGC instruments. The aim of this work is to demonstrate the unrivalled performance of iGC SEA, as well as the effect of instrument-to-instrument, experiment-to-experiment and column-to-column variability on the surface energy distribution results measured.

Figure 7 and Figure 8 show the  $\gamma_S^D$  profiles measured using different iGC SEA instruments, and conducted on the same column of silanised D-mannitol and AR D-mannitol, respectively.

Relative standard deviation (%RSD) for both silanised and AR D-mannitol columns are very low and highly reproducible. Results also show that materials with homogenous surface properties have relatively better %RSD, than materials which are energetically heterogeneous and more active.

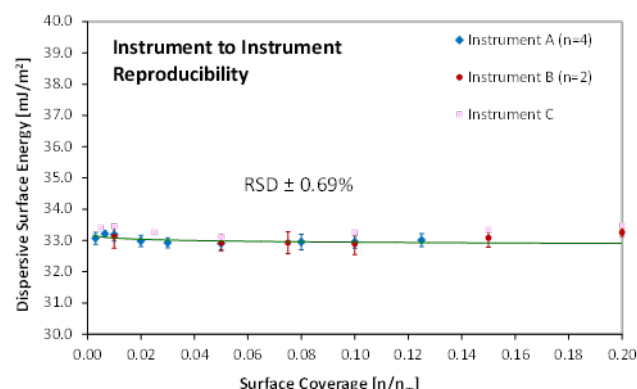


Figure 7. Instrument-to-instrument reproducibility of dispersive surface energy profiles using the same silanised D-mannitol column.

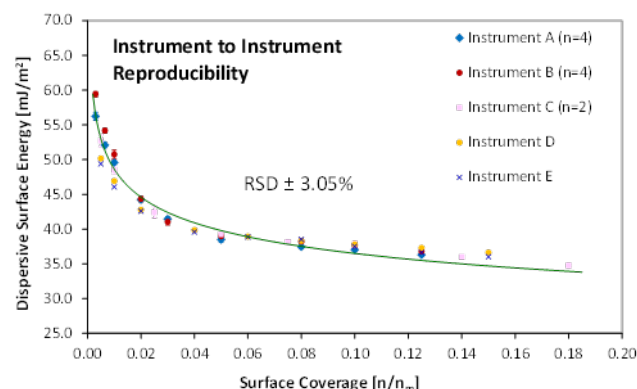


Figure 8. Instrument-to-instrument reproducibility of dispersive surface energy profiles using the same AR D-mannitol column.

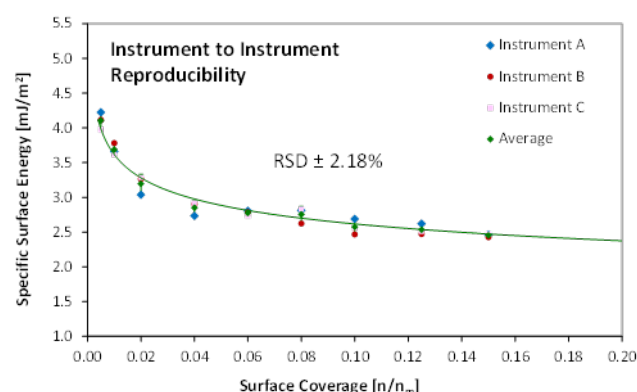
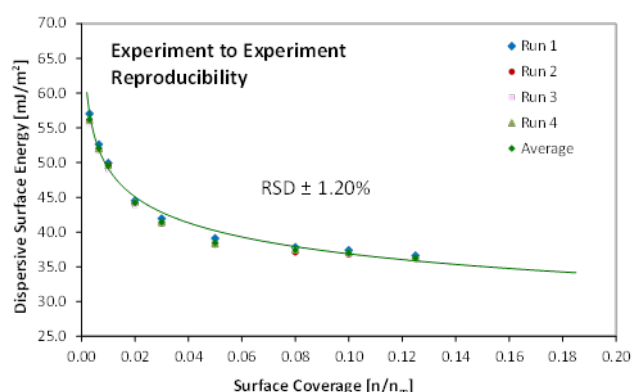


Figure 9. Instrument-to-instrument reproducibility of specific (acid-base) surface energy profiles using the same AR D-mannitol column.

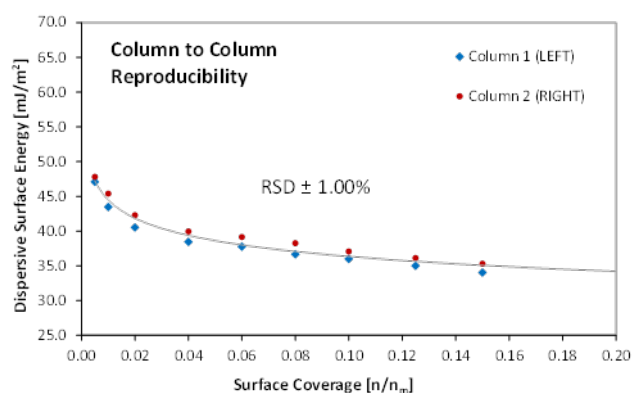
Figure 10 depicts  $\gamma_s^D$  profiles of four successive measurements carried out on one column of AR D-mannitol. Again, it demonstrates the excellent reproducibility of iGC SEA instrument, with an average RSD as low as 1.20%, for an energetically heterogeneous sample.

In addition, Figure 11 show very good reproducibility of column-to-column (referring to the left and right side of the column oven), using the same AR D-mannitol column.

This is made possible by the very accurate mass flow controller system, the state-of-the-art injection technology, automated temperature control of the column oven and solvent reservoirs within the iGC SEA instrument.



*Figure 10. Experiment-to-experiment reproducibility of dispersive surface energy profiles using the same AR D-mannitol column.*



*Figure 11. Column-to-column reproducibility of dispersive surface energy profiles using the same AR D-mannitol column.*





## Conclusion

In summary, IGC was proven as a fast and sensitive technique for determining surface heterogeneity profiles. It is evident that energetic heterogeneity and homogeneity of bulk powders, reflecting the surface chemical environment, can be easily distinguished using the iGC SEA instrument.

This study also demonstrates the excellent reproducibility of iGC SEA instrument. The average relative standard deviation of dispersive surface energy profiles for instrument-to-instrument reproducibility is merely ~ 3% or less, even for materials with large variations of surface sites, i.e. AR D-mannitol.

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