iGC SEA Case Study 611

Use of surface energy distributions to relate the effect of surface modification to powder flow properties

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Surface energy is a useful parameter describing the energetic properties of the surface of a solid sample. It can be determined in a fast and accurate way by iGC SEA. This paper describes measurement of surface energy heterogeneity of D-mannitol, relating surface chemical modification to flow properties of bulk particles.

Introduction

Surface energy is an important parameter for the characterisation of surface properties. It can provide a useful picture of the energetic situation on the surface and shows a strong dependency on various macroscopic properties, including the flow properties of bulk particles.

Energetic heterogeneity occurs with a wide distribution of various surface sites of different energetic levels. Such a heterogeneity profile can be represented by an energy distribution function, which can provide important information on surface property variation. A heterogeneity profile constitutes an energy "map" of the material surface and also allows prediction of product properties.

Flow behaviour is multidimensional, and in fact flowability is not an inherent material property. Given the importance of powder flow, most industries still rely heavily on flow properties that are poorly understood and applied. Various factors can change the rheological properties of powders, for examples, physical properties like particle size, shape, surface texture, hardness etc. Change in surface chemical environment however is often overlooked when determining the flowability of a particular powder.

In this study, detailed surface energetics of a model pharmaceutical excipient: D-mannitol was determined using iGC SEA, in an attempt to relate surface energy heterogeneity measurements to powder flow properties due to changes in surface chemistry.

The state-of-the-art injection technology of the iGC SEA allows the precise control of the injection size, therefore different amount (mole, n) of probe vapour can be chosen to pass through the sample column to achieve different surface coverages, n/n_m. If a series of probe vapours is

injected at the same surface coverage, the surface energy and free energy can be determined. Consequently, the injections of probe vapours at different surface coverages will result in a distribution of surface energy as a function of surface coverage, which is referred as a surface energy profile. The determination of surface energy heterogeneity by iGC SEA can, therefore, be described as a mapping technique.

Method

Material – D-mannitol

D-mannitol ($C_6H_{14}O_6$) was used as received (M4125 ≥98%; Sigma Aldrich). D-mannitol is a crystalline pharmaceutical excipient, commonly used in formulations for oral and chewable tablets, powder granules and moisture sensitive APIs [1]. Crystal habit is prismatic rod in shape, as shown in Fig. 1.

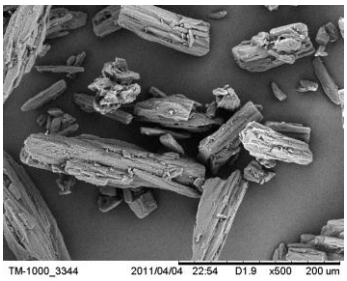

Fig. 1 SEM image of AR D-mannitol particles

Surface Modification - Methylation

A 5% solution of dichlorodimethylsilane in 1,1,2-trichlorethylene was used to promote surface methylation [2]. The solution was mixed with AR D-mannitol particles at 80°C for 3 hours under constant reflux. During the course of the reaction, the mixture was agitated continuously to ensure good dispersion.

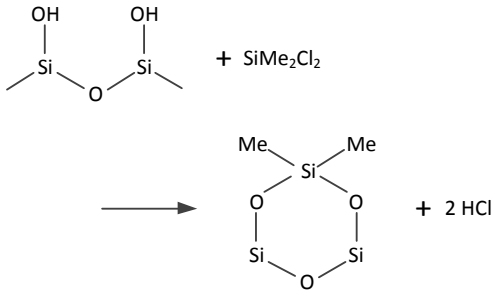

Fig. 2 Chemical reaction scheme for methylation of hydroxyl groups

The methylation reaction (Fig. 2) occurred at the surface of AR D-mannitol where dichloro-dimethylsilane 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 2 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 AR D-mannitol were sieved to 75-180µm particle size fraction.

Powder Flow Measurement

Flow tests were conducted using FT4 Powder Rheometer (Freeman Technology, Tewkesbury, UK). Both samples were first sieved at 500µm to remove any soft agglomerates. Each sample was then held in a glass jar in which it was tumbled prior to testing to put it into a homogeneous state with respect to segregation.

Fig. 2 FT4 Powder Rheometer (left) and dynamic flow test (right) ©Freeman Technology

All flow tests, including determination of dynamic, bulk and shear properties were carried out with a 23.5mm blade and a 25mm diameter vessel. All measurements were repeated twice to demonstrate the repeatability of the FT4 methodologies.

Surface Energy Heterogeneity

All analyses were carried out using iGC Surface Energy Analyzer (SMS, Alperton, UK) and the data were analysed using both standard and advanced SEA Analysis Software. For all experiments, about 2g of samples were packed into individual silanised 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, method of Dorris and Gray was employed for dispersive component [3]. Specific contribution was determined by first measuring the free energy of desorption based on the polarisation approach [4]. Each column was pre-conditioned for 2 hours at 30°C and 0%RH with helium carrier gas to remove any physisorbed water. All experiments were carried out at 30°C with 10sccm total flow rate of helium, using methane for dead volume corrections.

Results

Surface Energy Heterogeneity

Dispersive, γ_S^D and specific (acid-base), γ_S^{AB} surface energy profiles obtained directly from the iGC SEA for both samples are shown in Fig. 3 and Fig. 4, respectively.

It can be clearly observed that AR D-mannitol is energetically heterogeneous, meaning the surface energy changes as a function of surface coverage. There is a notable difference between maximum and minimum γ_S^D values, ranging from 37.51 to 52.63mJ/m^2.

This findings coincides with previous report of contact angle measurement and IGC finite concentrations on a native mannitol macroscopic crystal, which has shown a high level of surface heterogeneity [5].

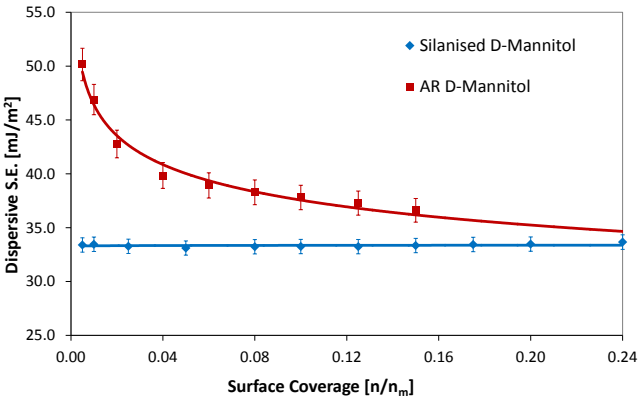

Fig. 3 Dispersive surface energy profiles (as a function of surface coverage).

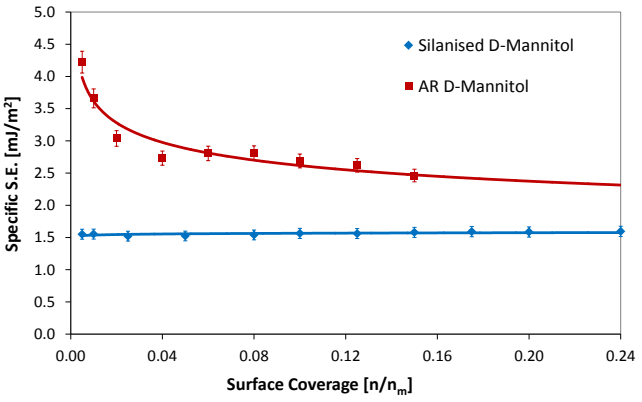

Fig. 4 Specific (acid-base) surface energy profiles.

It is known that there is abundance of -OH groups which can be found on surfaces of AR D-mannitol. These hydroxyl groups were substituted with –$Si(CH_3)_2$ groups after methylation reaction. Hence, silanised surfaces became energetically more homogeneous, with relatively small mean

γ_S^{AB} value of 1.60mJ/m^2 – implying an isotropic hydrophobic surface property (Fig. 5).

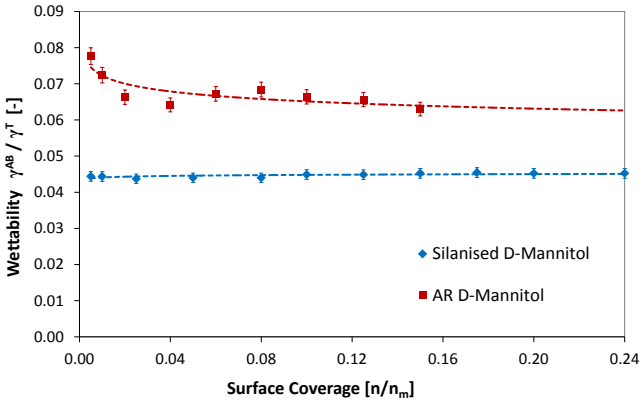

Fig. 5 Wettability, γ_S^{AB}/γ_S^T profiles (as a function of surface coverage).

Powder Flow Characteristics

Results indicate clear rheological differences between AR D-mannitol and silanised D-mannitol. Key flow characteristics of the samples are summarised in Table 1. AR D-mannitol exhibited unstable flow behaviour, in particular in the aeration test[1], showing dramatic variability at low air velocities, as presented in Fig. 6.

Flowability energy of AR D-mannitol was observed here reducing from 333.0 to 50.0mJ, before fully aerates and stabilises at 32.4mJ. Silanised D-mannitol however has a much lower flowability energy and aerated energy, implying a less cohesive (more free-flowing) powder property.

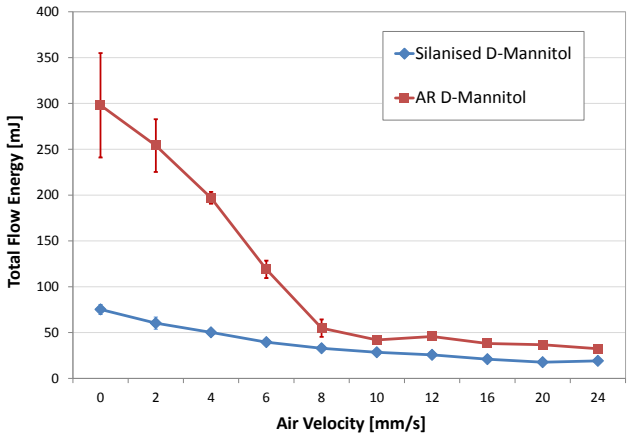

Fig. 6 Flowability energy as a function of aeration.

Surface energy is directly related to the thermodynamic work of adhesion[2] between two materials. When irreversible chemical interactions are neglected and only physical interactions are present, the total work of cohesion can be determined according to geometric mean method, as follows:

$$W_{Coh}^{total} = 2[(\gamma_s^D * \gamma_s^D)^{½} + (\gamma_s^+ * \gamma_s^-)^{½} + (\gamma_s^- * \gamma_s^+)^{½}]$$

…… eqn. (1)

Similar trend can be observed in Fig. 7, of which AR D-mannitol, due to its more active surface sites and heterogeneous surface property, has variable and higher cohesive strength.

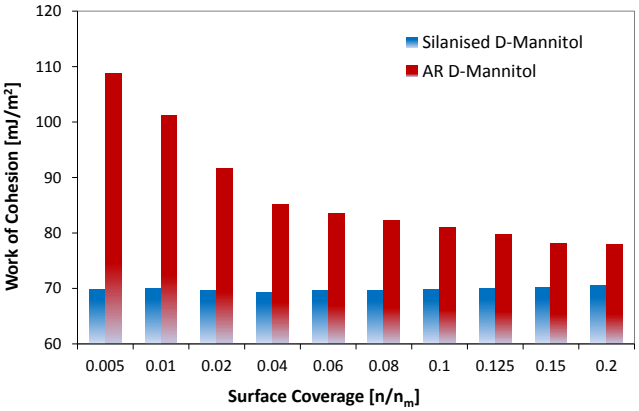

Fig. 7 Thermodynamic work of cohesion as a function of surface coverage.

[1] Ability of a powder to be influenced by air is a very good indicator of the cohesive strength of powder, relating to the capacity of air required to separate individual particles.

[2] Thermodynamic work of adhesion is the work required to reversibly separate an interface between two bulk phases.

Variability of AR D-mannitol is also evident in the consolidation test. Consolidation Index (CI) refers to the ratio of energy needed to displace the consolidated powder (after 50 taps) to the basic flowability energy. This further confirms that silanised D-mannitol is the more free-flowing of the two.

Silanised D-mannitol generates a slightly lower wall friction angle (24.9°), indicating that it is likely to flow more easily over typical metal surfaces, such as those found in storage vessels or in processing equipment.

Table 1: Key flow characteristics of D-mannitol

Flow Measurement	AR D-Mannitol	Silanised D-Mannitol
Flowability Energy [mJ]	333 ±4.6%	87.7 ±1.7%
Aerated Energy [mJ]	32.4 ±5.7%	19.1 ±2.4%
Stability Index [-]	1.05 ±1.1%	1.06 ±0.1%
Consolidation Index [-]	2.14 ±14.5%	1.46 ±3.6%
Wall Friction Angle [°]	26.2 ±0.4%	24.9 ±0.6%

It can be certain that both samples were stable during the powder flow tests. There is neither significant particle attrition nor segregation, as indicated by the Stability Indices (SI values close to unity for both samples).

Conclusions

In summary, methylation process has clearly improved the flow properties of D-mannitol in a low-stress environment. Change in surface chemistry; from a heterogeneous surface property to a homogeneous and low wettability surface property has reduced the variability in all powder flow properties, hence a more repeatable processing performance can be achieved.

Powder behaviours of D-mannitol samples are in excellent agreement with the detailed surface energy distributions determined by iGC SEA. It is evident that energetic heterogeneity and homogeneity of bulk powders, reflecting the surface chemical environment, can be easily distinguished using this technique.

References:

[1] Yoshinari, T. et al. (2002) Moisture induced polymorphic transition of mannitol and its morphological transformation. *Int. J. Pharm.*, 247, p69-77.

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Appendices:

Table A: Surface energy values for Silanised D-Mannitol

S.E.	Min.	Max.	γ_{10}	γ_{50}	γ_{90}
γ^D	33.29	34.68	34.62	34.10	33.51
γ^{AB}	1.54	1.62	1.62	1.60	1.56
γ^T	34.83	36.16	36.10	35.62	35.05
γ^{AB}/γ^T	0.0441	0.0449	0.0448	0.0448	0.0445

Table B: Surface energy values for AR D-Mannitol

S.E.	Min.	Max.	γ_{10}	γ_{50}	γ_{90}
γ^D	37.51	52.63	37.82	40.34	46.42
γ^{AB}	2.67	4.93	2.72	3.09	4.01
γ^T	40.21	57.42	40.56	43.43	50.34
γ^{AB}/γ^T	0.0665	0.0858	0.0670	0.0713	0.0796

Definitions

(Basic) Flowability Energy [mJ]

BFE is the energy needed to displace a conditioned and stabilised powder at a given flow pattern and flow rate. BEF is calculated from the work done in moving the blade through the powder in a downward anti-clockwise motion.

In this study, BFE was based on a sample volume of 160ml, using -5° helix blade and 100 mm/s of blade tip speed.

Aerated Energy [mJ]

The flow energy measured when air is being passed through the powder at a velocity (mm/s). The capacity of a gas to separate the individual particles of a powder can be evidenced by the changes in flow energy measured under the influence of increased air content. When aerated, less energy is normally required to move the powder.

Stability Index

Stability Index is the factor by which the flow energy requirement changes during repeat testing. Particle attrition, segregation, (de)agglomeration and (de)aeration could result in instability.

Consolidation Index

Consolidation Index refers to the factor by which the flow energy is increased as a result of consolidation of the powder before testing (by direct pressure, tapping or storage, to specific conditions).

CI = energy of consolidated sample / BFE

Wall Friction Angle [°]

Similar to Shear Cell test however instead of the powder being forced to shear against itself, a disc of a known surface roughness (Ra) is forced to shear against the surface of the powder bed whilst subjected to varying normal stresses.

Wall friction angle is the shear angle required to initiate steady-state flow for a powder sample relative to a given material of Ra (µm), for an applied normal consolidating stress (kPa).

**Further explanation of FT4 methodologies can be found at www.freemantech.co.uk

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