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International Journal of Pharmaceutics 312 (2006) 158–165
INTERNATIONAL JOURNAL OF PHARMACEUTICS
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Measurement of the surface energy of lubricated pharmaceutical powders by inverse gas chromatography

Vidya Swaminathan *, Jaclyn Cobb, Ilie Saracovan

Pfizer Global R&D, Groton Laboratories, Groton, CT 06340, USA

Received 29 August 2005; received in revised form 9 January 2006; accepted 10 January 2006
Available online 15 February 2006

Abstract

The objective of the study was to determine whether lubrication of pharmaceutical powders with magnesium stearate (MgSt) results in a change in the surface energy of the powder, and to assess whether surface energy changes, if any, are correlated to lubricant concentration and blend time. The surface energies of microcrystalline cellulose (MCC), lactose, and blends of each material with MgSt, prepared at a range of concentrations and blending times were measured using inverse gas chromatography. The physical distribution of MgSt in the blend was mapped by energy dispersive spectrometry. Overall, there was a reduction in the dispersive surface energy of MCC–MgSt blends with increase in MgSt concentration, that was attributed to increasing coverage of the high-energy sites on microcrystalline cellulose by magnesium stearate. MgSt concentration had a larger effect on dispersive energy than the blending time of the powder with lubricant. X-ray maps of blend samples indicated a heterogeneous distribution of the lubricant in the blend and on the excipient particles. Measurement of the specific component of surface energy indicated that MgSt interacts with excipient powders through non-specific forces rather than acid–base interactions. No distinction among lactose–MgSt blends could be made on the basis of dispersive energy because of similar surface energies of the native materials.

Keywords: Inverse gas chromatography (IGC); Surface energy; Lubrication; Magnesium stearate

1. Introduction

The interaction of a solid with another solid, liquid or gas is governed by its surface properties. The latter are determined by the physicochemical properties of the solid and its processing history. The behavior of pharmaceutical powders can be affected by the surface properties of the constituent particles (Buckton, 1995); the effects may be evident during processing and in the characteristics of the finished product.

Surface properties are widely described in terms of the surface free energy, commonly referred to as simply 'surface energy'. Generally higher surface energy is associated with increased propensity for interaction. For example, drug powders having high surface energies were found to adhere more strongly to inert carrier particles than those with lower surface energy (Feeley, 2002). It is likely that similar considerations hold in the interaction of powders with surfaces or with other powders—such as during the blending of powder formulations with a lubricant. The latter is a critical unit operation in the manufacture of oral solid dosage forms. In the manufacture of tablets, for example, mixtures of active ingredient(s) and excipients are blended with a lubricant to aid in relieving die-wall stress during compaction, and to prevent sticking of powder to punch surfaces. The most widely used lubricant is magnesium stearate (MgSt). The concentration of magnesium stearate in the formulation and the time of blending of the powder with magnesium stearate can affect the extent of lubrication (Bolhuis and Holzer, 1996). The consequences of inadequate and excessive lubrication are well known and extensively documented in the pharmaceutical literature (Jarosz and Parrott, 1984; Sheskey et al., 1995). A measurable change in the surface energy, if any, resulting from lubrication, would be useful to the formulation scientist in targeting a specific surface energy for a given formulation by selecting the optimal lubricant concentration and blending time.

Several methods exist for measuring the surface energy of powders; many of these, however, are subject to limitations of experimental technique that compromise measurements or

* Corresponding author. Tel.: +1 860 686 1890; fax: +1 860 686 5198.
E-mail address: vidya.swaminathan@pfizer.com (V. Swaminathan).

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doi:10.1016/j.ijpharm.2006.01.014

are otherwise difficult to implement reproducibly (Schrader and Loeb, 1992; Dove et al., 1996). Inverse gas chromatography (IGC) offers certain advantages over conventional methods such as contact angle measurement—notably, its applicability to fibrous materials and powders, relative lack of sensitivity to surface rugosity, simple experimental setup and rapid data collection (Lloyd et al., 1989; Guillet, 1973). Surface energy measurements in IGC are made at infinite probe dilution, where only a few probe molecules are made available for interaction with the solid. At this condition only the highest energy sites on the solid interact with the probe and are detected. The dispersive component of the surface energy (dispersive energy) of a solid is determined using *n*-alkane probes that interact with the solid by non-specific van der Waals forces, and the specific component, from its interactions with acidic, basic and amphoteric probes.

The feasibility of using IGC to measure potential surface energy changes resulting from the lubrication of powders with magnesium stearate was investigated in this study. The underlying hypothesis is that lubrication of a powder with MgSt results in a change in its surface energy. The specific goals of the study were to determine: (i) if there is a change in the surface energy of model pharmaceutical powders following lubrication with MgSt, (ii) whether surface energy changes, if any, are correlated with the concentration of MgSt and blending (lubrication) time. Two widely used excipients in tablet formulation—microcrystalline cellulose (MCC) and lactose—and blends of the each excipient with MgSt at 0.1, 1 and 5% (w/w) concentrations, prepared at a range of blending times were used as model powders in this study.

2. Materials and methods

MCC (Avicel PH102 from FMC BioPolymer, Philadelphia, PA) and lactose (α-lactose monohydrate, Grade 310 from Foremost Farms, WI) were used as received from the vendor. MgSt (Hyqual grade, Mallinckrodt, St. Louis, MO) was passed through 20-mesh (840 μm) screen before being mixed with each excipient. MCC and lactose were blended with MgSt in a tumbling V blender (2L Patterson Kelly, East Stroudsburg, PA); the concentrations of MgSt and blending times used in preparing blends are listed in Table 1.

2.1. Measurement of the size and surface area of powders

The size distribution of the powders was measured by laser diffraction (Sympatec HELOS/RODOS, Sympatec GmBH, Rosenheim, Germany). The 10th, 50th and 90th percentiles of the number distribution are listed in Table 2. Each value is the average of two measurements. The surface area of the powders was obtained from nitrogen adsorption by the BET method (Micromeretics, Norcross, Ga). MCC and lactose were dried at 40 °C, and MgSt at 30 °C, for 16 h prior to the measurement.

Table 1
Composition of blends used for surface energy measurements

Blend	MgSt concentration (%)	Lubrication time (min)
MCC–MgSt	0.1	3 and 9
	1	3 and 9
	5	10
Lactose–MgSt	0.1	5
	1	5

Table 2
Particle size and surface area of powders

Material	Surface area (m^2/g)	D10 (μm)	D50 (μm)	D90 (μm)
MCC	1.2	33.9	105.3	212.7
Lactose monohydrate	0.3	7.9	66.2	167.4
Magnesium stearate	5.2	1.2	4.3	9.6

2.2. Surface energy measurement by IGC

A sample of each powder was packed in a silanized glass column. Columns of 30 cm length and 3 mm inner diameter (i.d.) were used for packing MCC and lactose; MgSt was packed in wider columns of 4 mm i.d. to accommodate its small particle size (Table 2) and minimize column plugging. Uniform packing was achieved by loading the column with small portions of the powder at a time and tapping; column outlets were loosely stoppered with silanized glass wool. The packed columns were mounted on a fully automated IGC system (Surface Measurement Systems Ltd. (SMS), London, UK) equipped with flame ionization and thermal conductivity detectors, and conditioned at 30 °C and 0% RH under helium flow prior to the surface energy measurement. Solvents (probes) were held at a temperature of 30 °C throughout the experiments. All solvents were HPLC-grade.

Adsorption measurements were performed at 30 °C and 0% RH at infinite probe dilution (relative pressures of 0.10 of decane and 0.03 of all other solvents). The carrier gas was helium at a flow rate of 10 mL/min, at which a good balance was achieved between the speed of elution and the pressure drop across the column. The homologous series of *n*-alkanes (from hexane to decane) comprised the apolar probes; chloroform, methylene chloride and ethanol were the lewis acid probes, tetrahydrofuran, the base, and acetone and diethylacetate were the amphoteric probes used in the study. Methane was used as the non-interacting marker to measure the void space in the column. Two columns of each sample were prepared. A single measurement was made on one of the columns while duplicate measurements were made on the second. The results of the three measurements were averaged. The variability associated with samples and with the measurement were reflected in the results. Surface energy calculations were performed using SMS iGC Analysis software v1.3. Signals from the detectors were collected at intervals of 0.02 s during the course of each measurement. The retention time was obtained from the peak maximum. The net retention time was obtained by subtract-

ing the 'dead time' that corresponds to the void space in the column.

2.3. X-ray map of MgSt distribution in blends with MCC and lactose

An automated X-ray photon mapping technique—scanning electron microscopy in conjunction with energy dispersive spectrometry (SEM/EDS) (Goldstein, 2003) targeting the element Mg—was used to map the distribution of MgSt in the blends. The SEM/EDS instrument used in this study was the ASPEX VP (Application Specific Products based on Electron optics X-ray technologies manufactured by Aspex LLc, Delmont, PA) equipped with a Silicon-Lithium EDS detector and a digital X-ray pulse processor. Powder samples were immobilized on standard SEM stubs using carbon double-sided adhesive tapes and directly scanned without sputter-coating. Measurements were taken at a pressure of 0.1 Torr in the sample chamber using the following parameters: electron beam acceleration voltage of 20 kV; spot size of 40%; working distance of 16.6 mm; EDS detector settings of 2048 channels; 10 eV per channel and 25.6 μs pulse processing time. X-ray maps were acquired at 512 × 512 pixel resolution with a dwell time of 3 ms per pixel. Appropriate positive and negative controls were used to establish that the technique was indeed capable of mapping Mg (Fig. 1), and that it did not falsely detect Mg where the latter was not present, such as in samples of MCC and lactose.

Table 3
Effect of conditioning temperature and time on the dispersive energy of lactose

Conditioning temperature (°C)	Conditioning time (h)	Dispersive energy range (mJ/m^2)[a]
30	3	40.1–41.2
30	1	40.1–40.5
40	3	40.5–40.6
60	3	41.0

[a] Minimum and maximum values are listed.

3. Results and discussion

3.1. Effect of column conditioning time and temperature on surface energy

The selection of column conditioning time and temperature used in the IGC measurement was based on the results of preliminary experiments performed to evaluate these effects on surface energy. The dispersive energy of lactose samples conditioned for 1 and 3 h at 30, 40 and 60 °C temperatures is given in Table 3. There was no significant difference in the dispersive energy of samples conditioned at the temperatures and times examined. Columns were conditioned for an hour at 30 °C for the remainder of the study.

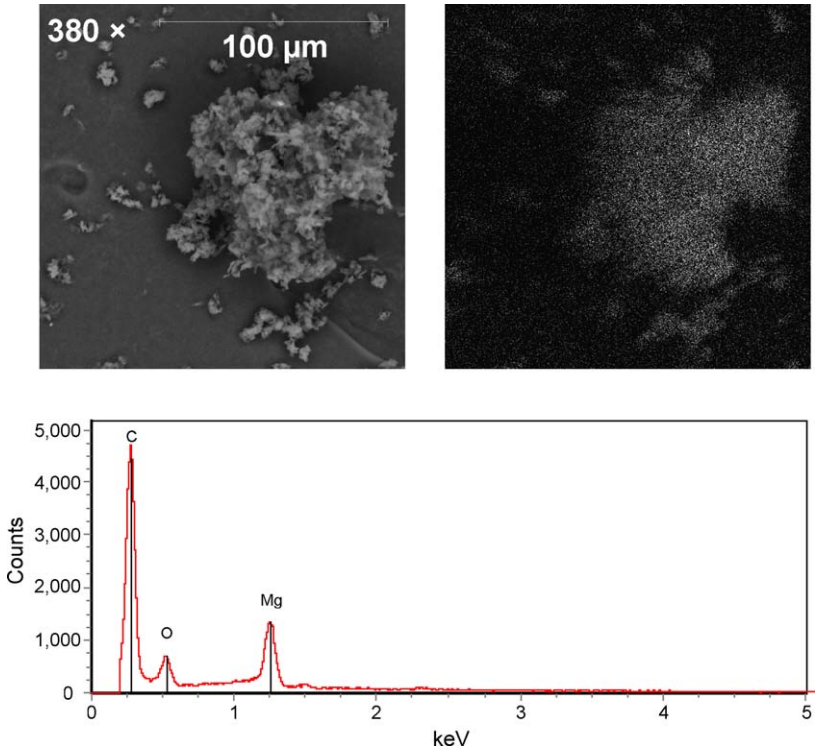

Fig. 1. SEM image of MgSt on carbon substrate (top-left) and the corresponding X-ray photon energy-dispersive map of Mg element (top-right). EDS spectrum showing the presence of Mg element in the sample (bottom).

Table 4
Dispersive surface energy of powders

Material	Average dispersive energy (mJ/m^2)	Standard deviation of dispersive energy (mJ/m^2)
MCC	66.8	1.14
MgSt	41.1	0.2
Lactose	40.6	0.5

3.2. Peak reproducibility

Peak reproducibility was confirmed from multiple injections of probes into the columns. There was no significant change in either the residence time or the shape of the curve at the measurement conditions. The chromatographic peaks of alkanes, polar probes and the non-interacting marker, methane were reproducible; permanent sorption of the probes into the powder could therefore be neglected. The exception to this was chloroform, which exhibited significant tailing—indicative of diffusion of the probe into the bulk of the material and/or mechanical retention of the probe in the sample. Interactions among adsorbate molecules that complement adsorbate–adsorbent interactions can also contribute to the dissymmetry of the peak. No inferences could therefore be drawn from the retention times of chloroform.

3.3. Dispersive surface energy of model powders

The dispersive energies of MCC and MgSt calculated from IGC measurements in this study are listed in Table 4. The mean dispersive energy of MCC is 67 mJ/m^2. This value is in the proximity of 70 mJ/m^2 reported for amorphous cellulose beads in the literature (Garnier and Glasser, 1996), and is significantly larger than the reported surface energy of 50 mJ/m^2 of crystalline cellulose (Dorris and Gray, 1980).

The dispersive energy of MCC can be attributed to its microstructure. MCC is partially depolymerized cellulose consisting primarily of aggregates of cellulose microcrystals; it is produced by controlled acid hydrolysis of α-cellulose, followed by spray drying of the resultant aqueous slurry to form porous particles (Battista, 1958; FMC Corporation, 1986). The higher dispersive energy of MCC relative to crystalline cellulose may arise from the amorphous sites in the material that are remnants from acid hydrolysis of cellulose. At infinite probe dilution, the highest energy sites on MCC interact with the probe and are detected. Although the composition of MCC is largely crystalline, the small amorphous content of the material apparently dominates the measured surface energy. The higher surface energy of the amorphous material is consistent with its being thermodynamically less stable than the crystalline material (Buckton and Darcy, 1996). The cleaner material resulting from acid extraction used in the manufacture of pharmaceutical grade MCC, and the porosity of the sample, specifically, the microporosity, can potentially contribute to the larger surface energy of MCC compared to crystalline cellulose.

The dispersive energy of lactose was 41 mJ/m^2 and is in good agreement with values reported in the literature (Newell et al., 2001). The dispersive energy of MgSt was 41 mJ/m^2; there are no reported values in the literature for comparison with those obtained in this study. The dispersive energy of MCC is significantly different from that of MgSt, while lactose and MgSt have similar dispersive energies.

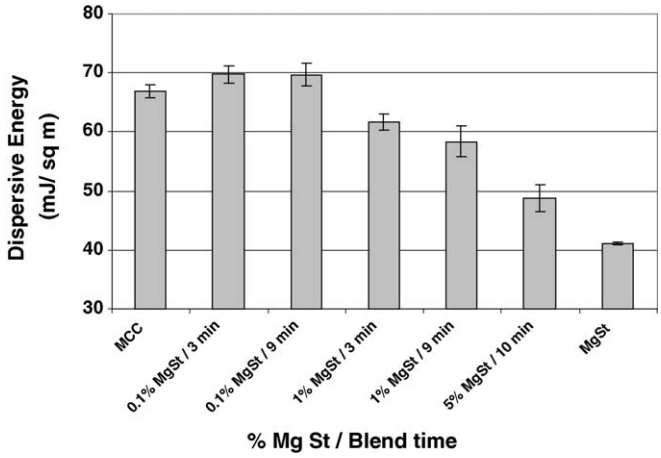

Fig. 2. Dispersive surface energy of MCC–MgSt blends.

3.4. Dispersive energy of MCC–MgSt blends

The dispersive energies of MCC–MgSt blends are plotted in Fig. 2. The dispersive energy of blends containing 1% MgSt was 62 mJ/m^2 (3 min blend time) and 58 mJ/m^2 (9 min blend time). The dispersive energy of the blend containing 5% MgSt was 49 mJ/m^2. The difference in dispersive energy between the blends and the individual components was statistically significant.

The effect of the mixing process on the dispersive energy was evaluated using a control, i.e., *mixing* MCC under the same conditions used in the preparation of blends and measuring the dispersive energy of the material. There was no significant difference in the dispersive energy of MCC before and after mixing. It was established that the mixing procedure per se did not result in a change in the dispersive energy of the powder. The measured difference in dispersive energy between the blend and the native materials was therefore attributed to the lubrication process. The results support our hypothesis positing a change in the surface energy with lubrication. Sufficient discrimination in the dispersive energies among blends could be made on the basis of MgSt concentration and to a much smaller extent on blend time. The effect was pronounced at higher concentrations of MgSt in the blend.

With the addition of 0.1% MgSt to MCC, there was a small increase in the dispersive energy of the mixture relative to pure MCC. Increasing the concentration of MgSt to 1% and 5% resulted in a reduction in the dispersive energy of the mixture (Fig. 2). The small increase in dispersive energy measured following the addition of 0.1% MgSt to MCC can be attributed to an increase in the overall specific surface area of the powder mixture because of the addition of a fine component. Since only the highest energy sites are detected in IGC at infinite probe dilution, the concentration of MgSt at 0.1% concentration may be too small, or its distribution in the mixture insufficient for a

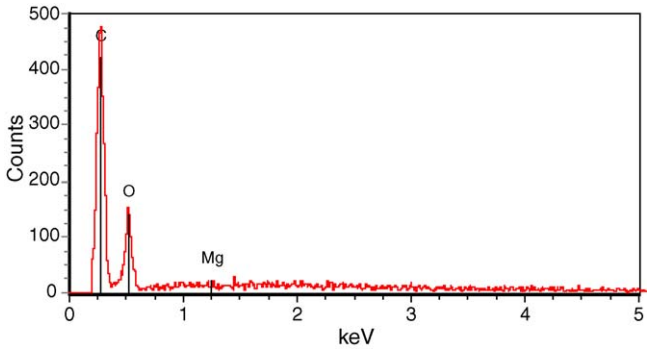

Fig. 3. ED spectrum of Mg in 0.1% MgSt–MCC blend.

measurable effect on the high energy sites on the excipient. The X-ray map of Mg from samples of the powder mixture showed very little MgSt on the carrier particles as indicated by the small abundance (count) of Mg relative to the 1% and 5% mixtures (Figs. 3–5). At higher concentrations, MgSt is distributed on the surface of relatively coarse MCC particles, as indicated by the larger abundance of Mg in the ED spectra.

The reduction in the dispersive energy of MCC as a result of blending with MgSt can be attributed to coverage of some of the high-energy sites on MCC by MgSt. With increase in the concentration of MgSt, a larger number of these sites are occupied, rendering them inaccessible to the probes, and resulting in the measured reduction in the dispersive energy. The distribution of MgSt on the carrier particles is not uniform but "patchy" with some domains having a higher concentration of Mg (MgSt) than others, even at concentrations as large as 5%.

There was no correlation of the dispersive energy of the blend to the mass or surface area fraction of MgSt in the mixture or to the calculated surface coverage of MCC by MgSt. The latter is not unexpected because of the heterogeneous or patchy distribution of MgSt on the surface of MCC particles as evident from the x-ray maps, and the presence of a variable fraction of the MgSt in the blend on the surface of the excipient particles, including the highest-energy sites. The propensity of MgSt to undergo delamination under shear, such as during the mixing process, that has been reported in the literature can contribute to the lack of the aforementioned correlation (Shah and Mlodozeniec, 1977); no direct inference on delamination could however, be drawn from the current study. The square root linear relationship of the effective surface area of the mixture to the surface area fractions of the components proposed by Sun and Berg (2003) was not found to apply in this instance because of the interaction among the components (non-random nature of the mixture) and the difficulty in computing the fraction of the surface areas of the two powders accessible to the probe gases due to the morphology, surface roughness and porosity factors.

Overall, the concentration of MgSt had a larger effect on the dispersive energy than the blending time in the range used in the study (Fig. 2) as evident from the small difference in the dispersive energy of mixtures blended with the lubricant for 3 and 9 min. In other words, MgSt is sufficiently well distributed in the mixture in 3 min and its effect on the highest-energy sites of the carrier is not greatly changed by an increase in lubrication time.

A point worth mention here is that this inference specifically pertains to the high-energy sites that are detected by IGC at infinite probe dilution. These sites may constitute only a small

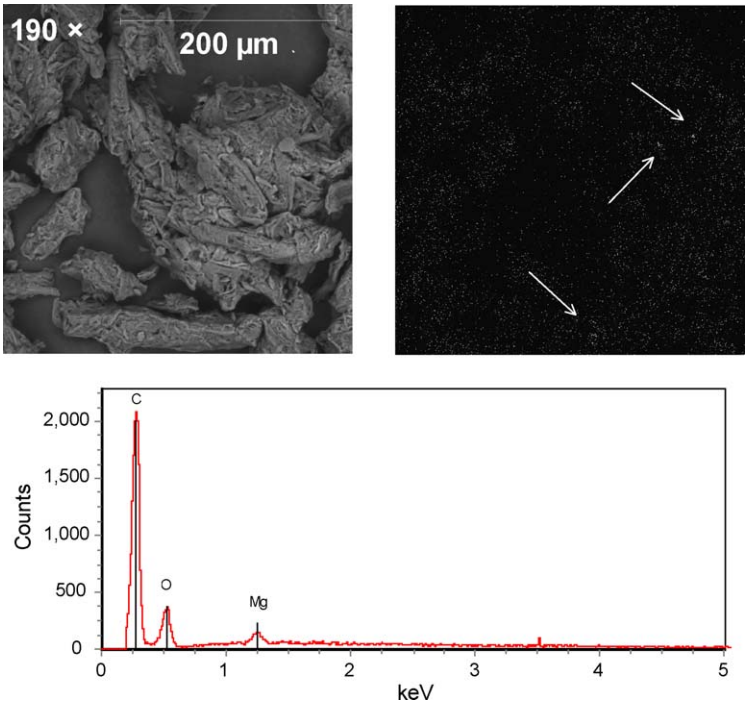

Fig. 4. SEM image (top left), X-ray map (top right) and EDS spectrum of Mg in 1% MgSt–MCC blend. *Note*: the arrows point to the regions of high concentration of Mg.

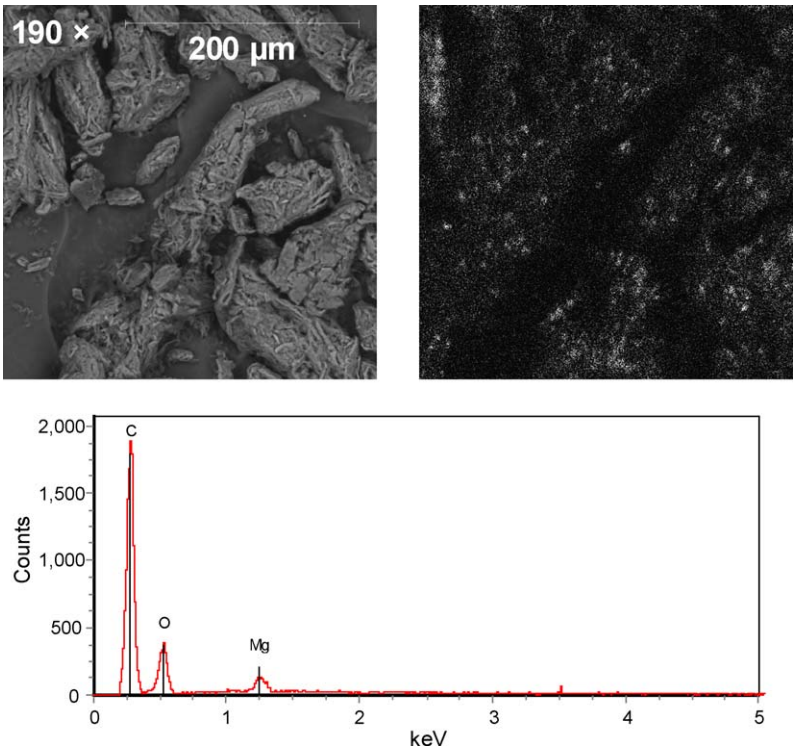

Fig. 5. SEM image (top left), X-ray map (top right) and ED spectrum of Mg in 5% MgSt–MCC blend.

fraction of the energetic surface(s) of the powder (most solid surfaces are energetically heterogeneous and have a distribution of high, medium and low energy sites). While there may only be a small change in the interaction of MgSt with the high energy sites on MCC at 3 and 9 min blending times, there may be an overall greater coverage of the excipient surface at larger blending times, with potentially adverse impact on tablet characteristics such as tablet strength, disintegration and dissolution.

3.5. Lactose–MgSt blends

The dispersive energies of lactose, MgSt and blends of the two components are listed in Table 5. The dispersive energies of lactose and MgSt are similar (41 mJ/m^2); no distinction between the native components and blends of the two components could be made on the basis of dispersive energy. However, the X-ray map of Mg of blend samples showed nonuniform distribution of magnesium stearate similar to that seen in MCC–MgSt blends (Fig. 6).

Table 5
Dispersive surface energies of lactose–MgSt mixtures

Material	MgSt concentration (%)	Average dispersive energy (mJ/m^2)
MgSt	100	41.1
Lactose–MgSt blend	1	40.7
Lactose–MgSt blend	0.1	40.0
Lactose	0	40.6

3.6. Specific interactions of powders

The relative acidity or basicity of the individual powders was estimated by a direct comparison of the free energy of adsorption (technically desorption) of acidic, basic and amphoteric probes. It must be pointed out that the determined surface characteristics are not material constants because they depend upon the polar probes selected (Nardin and Papirer, 1990), at best, these are semi quantitative estimates of the specific interactions of the solid surface. They can however, be used for making relative qualitative comparisons of surface polarities in reference to specific pairs or sets of probes. No attempt was made at estimating the specific components of the surface energies of powder blends because of the obvious difficulties in eliciting meaningful information from physical mixtures of chemically heterogeneous solids from these measurements.

The interaction of MCC with tetrahydrofuran and amphoteric probes was stronger than with acidic probes, indicating that the surface is neutral to mildly acidic (Table 6). MgSt has an acidic surface, based on its greater interaction with tetrahydrofuran, than with acidic and amphoteric probes. Lactose inter-

Table 6
Specific interactions of powders with polar probes

Material	Specific energy of interaction, ΔG (kJ/mol)			
	Tetrahydrofuran	Acetone	Ethylacetate	Ethanol
MCC	13.8	13.1	15.3	7.3
Lactose	9.0	8.0	9.7	11.5
MgSt	10.0	7.0	8.0	5.2

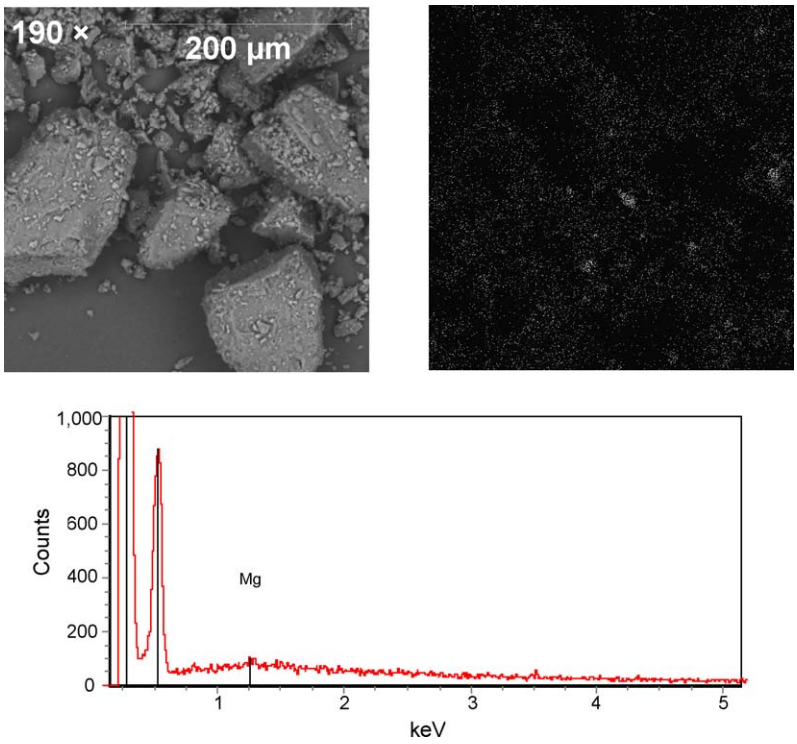

Fig. 6. SEM image (top left), X-ray map (top right) and EDS spectrum of Mg in 1% MgSt–lactose blend.

acted strongly with ethanol, presumably by hydrogen bonding. Overall, given the neutral to mildly acidic nature of the components of the mixture, it is likely that non-specific dispersive forces are primarily involved in the interaction of MgSt with the excipients.

4. Conclusion

The surface energy of MCC, lactose and blends of each powder with MgSt was measured using IGC. Overall, there was a measurable reduction in the dispersive energy of MCC–MgSt blends with increase in lubricant concentration (>0.1%). The results support our hypothesis that postulated a change in dispersive energy with lubrication. The reduction in the dispersive energy of MCC with lubrication was attributed to coverage of some of the high-energy sites on the MCC by MgSt. X-ray map of blend samples indicated non-uniform distribution of MgSt in the blend and on the excipient particles.

The pharmaceutical applications of IGC have typically involved measurements on single component powders. The present study indicates that changes in surface energy of blends can be measured using IGC, provided that the components have different surface energies. Sufficient discrimination among blends having a range of lubricant concentrations could be made on the basis of surface energy measurements using IGC. The study also indicated that MgSt interacts with powders through non-specific forces rather than acid–base interactions. The non-specific nature of the interaction suggests a plausible reason for the efficacy of MgSt in reducing the propensity of a range of active compounds (acidic, basic and neutral) to stick to process surfaces. Further studies are needed to relate the surface energy of a blend to its tableting performance or to adhesion-related phenomenon such as sticking to punch surfaces.

There are limitations in using IGC for measuring the surface energies of heterogeneous systems such as mixtures of solids that individually have similar surface energies. Thus, while X-ray mapping indicated a similar distribution of MgSt in lactose–MgSt blends as in the MCC–MgSt blends, no distinction among lactose–MgSt blends containing a range of lubricant concentrations could be made on the basis of dispersive energy measurements by IGC because of the similar dispersive energies of the individual components of the blend.

Acknowledgement

The authors thank Dr. Cynthia Oksanen and Dr. Thomas Garcia for their support of this work and Dr. Martyn Ticehurst and Dr. Kenneth Waterman for useful comments.

References

Battista, O.A., 1958. Fundamentals of High Polymers. Reinhold Publishing Corporation, New York.

Bolhuis, G.K., Holzer, A.W., 1996. In: Alderborn, G., Nystrom, C. (Eds.), Pharmaceutical Powder Compaction Technology, Drugs and the Pharmaceutical Sciences, vol. 71, Marcel Dekker, NY, pp. 517–560.

Buckton, G., 1995. Surface characterisation: understanding sources of variability in the production and use of pharmaceuticals. J. Pharm. Pharmacol. 47, 265–275.

Buckton, G., Darcy, P., 1996. Water mobility in amorphous lactose below and close to the glass transition. Temp. Int. J. Pharm., 136–141.

Dorris, G.M., Gray, D.G., 1980. Adsorption of *n*-alkanes at zero surface coverage on cellulose paper and wood fibers. J Colloid Interf. Sci. 77, 353.

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

Feeley, J.C., 2002. Prediction of surface properties by inverse gas chromatography. In: Proceedings of the Respiratory Drug Delivery VIII Conference, AZ, pp. 295–301.

FMC Corporation, Technical Literature Avicel PH microcrystalline cellulose, 1986.

Garnier, G., Glasser, W.G., 1996. Measuring the surface energies of spherical cellulose beads by inverse gas chromatography. Polym. Eng. Sci. 36, 885.

Goldstein, J.I., 2003. Scanning Electron Microscopy and X-Ray Microanalysis, 3rd ed. Kluwer Academic/Plenum Publishers, New York, pp. 485–499.

Guillet, J.E., 1973. In: Purnell, J.H. (Ed.), New Developments in Gas Chromatography. Wiley-Interscience, New York, p. 187.

Jarosz, P.J., Parrott, E.L., 1984. Effect of lubricants on tensile strengths of tablets. Drug Develop. Industr. Pharm. 10, 259–273.

Lloyd, D.R., Ward, T.C., Schreiber, H.P., Pizana, C.C., 1989. Inverse gas chromatography characterization of polymers and other materials. In: Proceedings of the ACS Symposium Series, No. 391, American Chemical Society, Washington DC.

Nardin, M., Papirer, E., 1990. Relationship between vapor pressure and surface energy of liquids: application of inverse gas chromatography. J. Colloid Interf. Sci. 137, 534–545.

Newell, H.E., Buckton, G., Butler, D.A., Thielmann, F., Williams, D.R., 2001. The use of inverse gas chromatography to measure the surface energy of crystalline, amorphous, and recently milled lactose. Pharm. Res. 18, 662–666.

Schrader, M.E., Loeb, G.I., 1992. Modern Approaches to Wettability: Theory and Applications. Plenum Press, London.

Shah, A.C., Mlodozeniec, A.R., 1977. Mechanism of surface lubrication: influence of duration of lubricant excipient mixing on processing characteristics of powders and properties of compressed tablets. J. Pharm. Sci. 66, 1377–1382.

Sheskey, P.J., Robb, R.T., Moore, R.D., Boyce, B.M., 1995. Effects of lubricant level, method of mixing, and duration of mixing on a controlled-release matrix tablet containing hydroxypropyl methylcellulose. Drug Develop. Industr. Pharm. 21, 2151–2165.

Sun, C., Berg, J.C., 2003. The effective surface energy of heterogeneous solids measured by inverse gas chromatography at infinite dilution. J. Colloid Interf. Sci. 260, 443–448.