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Measurement of the surface energy of lubricated pharmaceutical powders by inverse gas chromatography

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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

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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-