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A study of the formation of magnesium stearate film on sodium chloride using energy-dispersive X-ray analysis

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Summary

Scanning electron microscopy (SEM) and energy-dispersive X-ray (EDX) analysis techniques have been successfully applied to make direct measurements of the lubricant distribution on selected excipient particles. Sodium chloride was chosen as a model to represent a tableting excipient and the formation of a magnesium stearate film on its surface was studied. Percentage surface coverage by the lubricant has been estimated from the EDX data for 0.1%, 0.5% and 2% w/w lubricant for several magnesium stearate samples. Film formation by lubricants from different manufacturers was examined and results suggested similarity in mechanism but different degree of host surface coverage for equivalent mixing conditions. Data also indicated that a molecular film is formed initially which, on further blending, was followed by the build-up of a particulate layer that may have been initiated at gross defect points on the host particle surface. Lubricant film formation on sodium chloride has been confirmed as being of the Langmuir type. The influence of the specific surface area of the lubricant on excipient surface coverage has also been discussed.

Introduction

In solid dosage formulations the primary function of magnesium stearate, the most frequently used powder lubricant, is to reduce frictional forces during tablet formation. However, including magnesium stearate in formulations may also cause deleterious changes in tablet crushing strength, disintegration time and drug dissolution. Because of its almost ideal lubrication properties and the notable disadvantages, magnesium stearate has been widely studied as a lubricant material as well as for the effects on pharmaceutical products (Butcher and Jones, 1972; Hölzer, 1983; Miller and York, 1985a; De Boer et al., 1978; Levy and Gumtow, 1963; Billany and Richards, 1982).

Traditionally, study of lubricants has involved examining their effects on the final product. Dissolution, disintegration time and tablet strength are the properties usually measured. Powder lubricants such as magnesium stearate are stated to reduce frictional forces by film formation at the interface. In an attempt to assess film formation and understand the causes of deleterious effects of magnesium stearate, a number of investigations have concentrated on studying the lubricant distribution on host powder particles, and conflicting

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statements are reported regarding the nature of the lubricant film. Most of these investigations have relied on indirect techniques such as host dissolution and contact angle measurements of powders and compacts (Nicklasson and Broden, 1982; Colombo and Carli, 1984). However, recently scanning electron microscopy (SEM) combined with energy dispersive X-ray (EDX) analysis has been used to generate qualitative data and examine visually the role of magnesium stearate as a lubricant on micronised drug particles (Pintye-Hodi et al., 1981). Qualitative and semiquantitatvie data presented by Anno and Rees (1986) for ordered drug–lubricant mixing has further highlighted this useful technique.

In this study the EDX analysis technique was applied to make direct measurements of the lubricant distribution as percentage coverage of the surface on selected excipient particles and to consider the role of lubricant surface area in film formation. Sodium chloride was selected as a model host to represent a tableting excipient and the formation of magnesium stearate film on the surface of host particles was monitored by SEM and EDX.

Materials and Methods

Materials

The following materials were used: sodium chloride, Analar (BDH Chemicals Ltd., Poole, U.K.); magnesium stearate (MS) BP grades from various manufacturers, namely MS.D (Durham Chemicals Ltd., Durham, U.K.), MS.H (Hopkin and Williams, Chadwell Heath, U.K.), MS.H (Hopkin and Williams, Chadwell Heath, U.K.), MS.J (James M. Brown Ltd., Fenton, U.K.), MS.M (Megret Ltd., Liverpool, U.K.) and MS.W (Witco Chemicals Ltd., Dronfield, U.K.).

Sieving and mixing

Sodium chloride as received was graded using an Endicott Test Sieve Shaker Model A (Endicotts Ltd., London). The sieved fraction (250–425 μm) was collected and stored in sealed containers at room temperature until required for mixing. Magnesium stearate samples were passed through a coarse sieve to break up any agglomerates prior to use.

A cube mixer of ca. 1850 ml volume was designed and constructed from perspex. Mixing of sodium chloride with appropriate quantities of lubricant in the range 0.1–2% w/w was carried out at 25 rpm. Each batch of 200 g of excipient and lubricant was mixed for a predetermined time interval and stored until required for further study.

Particle size and specific surface area

The particle size distribution was measured on a Laser Diffraction Particle Size Analyser, Series 2600 (Malvern Instruments Ltd., Malvern U.K.) and volume mean diameter was recorded. The BET (Brunauer, Emmett, Teller) surface area has been determined with an Orr Surface Area, Pore Volume Analyser Model 2100 (Micromeritics Instrument Corp., U.S.A.) using liquid nitrogen ($-196\,^{\circ}C$) as the adsorbed gas. Each determination was carried out at least in duplicate.

Differential scanning calorimetry

Differential scanning calorimetry (DSC) analyses were carried out on a Du Pont Model 910 differential scanning calorimeter linked to a Model 1090 thermal analyser (Du Pont, Stevenage, U.K.). For each sample, ca. 5 mg of material was analyzed in an open aluminium pan at a heating rate of $2\,^{\circ}C$/min. The instrument was calibrated using indium metal (99.9% pure) as a standard.

SEM and EDX studies

The SEM and EDX analysis techniques are based on the methods detailed by Goldstein et al. (1981).

The powder samples were prepared by fixing particles to a metal stub with a double-sided adhesive tape, vacuum coated with carbon and then placed in the instrument. For scanning electron micrographs either a Stereoscan 600 (Cambridge Instruments Ltd., Cambridge) or ISI Super IIIA (International Scientific Instruments, U.S.A.) was used.

In S.E.M. an electron beam bombards the sample surface through the carbon film. Upon impact electrons from the surface atoms and also from the bulk of the solid are liberated and these elec-

trons are detected to form an image of the solid. The beam electrons also form X-rays by deceleration of the beam and interaction with the atoms of the solid. The X-ray signals were detected by passing through a thin beryllium window into a cooled lithium-drifted silicon PGT X-ray Detector (Princeton Gamma-Tech, Princeton, NJ, U.S.A.) and analysed with a Link Systems Model 860 Series 2 (Link Systems Ltd., High Wycombe, U.K.). For EDX analysis 10 particles selected at random from each mix were counted for X-ray photons. An incident electron beam of 10 kV was considered most suitable since generation of secondary electrons is more efficient at low electron energies.

For counting, a flat particle surface of equivalent area was counted in each case. The analysis system was programmed to count 2000 background X-ray photons, and the characteristic elemental radiation. The characteristic photon energy count for magnesium was obtained from a window set at 1.254 keV.

For a control to provide 100% surface coverage data, an approximately 1-mm-thick compressed disc of magnesium stearate powder samples was used to determine the magnesium counts. From the magnesium photon counts for the powder samples, the percentage coverage of the excipient by the lubricant was then estimated.

Results and Discussion

Lubricant film formation

The surface coverage profiles for sodium chloride by magnesium stearate MS.D are shown in Fig. 1. The maximum rate of coverage occurred during the first 2 min of mixing for all experimental concentrations. With increasing mixing time the rate of lubricant uptake was reduced until after 10 min the surface coverage reached a limiting value. These results also showed the highest surface coverage for 2% w/w mix at 17.70% whilst for 0.1% w/w concentration the coverage was 2.60% after 60 mins. Thus, increased host particle surface coverage is clearly indicated for higher lubricant concentrations. Although mixing was carried out for 1 h the results indicated no further

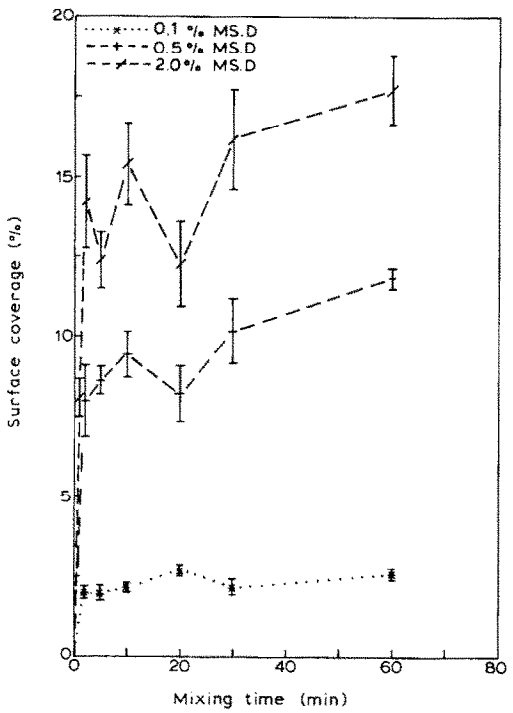

Fig. 1. Sodium chloride surface coverage by magnesium stearate (MS.D). Values depicted represent the mean $\pm$S.E.M. ($n = 10$).

increase in coverage. Subsequently, all mixing experiments were stopped after 30 min.

Fig. 2 shows the rate of film formation under equivalent mixing conditions for 0.5% w/w concentration of the lubricants obtained from different manufacturers. The rate of film formation for the first min is rapid and similar for the 5 samples studied. On further mixing the rate is reduced but is different for each sample. A plateau region is reached after 10 min and the surface coverage at 30 min reflects the film formation capacity of each lubricant at 0.5% w/w concentration for the defined mixing conditions.

The gradual build-up of the lubricant on sodium chloride was also observed using SEM, but to characterise the nature of the lubricant film the EDX data in Fig. 2 were treated in accordance with the Langmuir type adsorption equation (Langmuir, 1918). A typical Langmuir type plot is given in Fig. 3, where equilibrium pressure and the quantity of gas adsorbed per unit surface, or unit mass of solid, has been replaced by the mixing

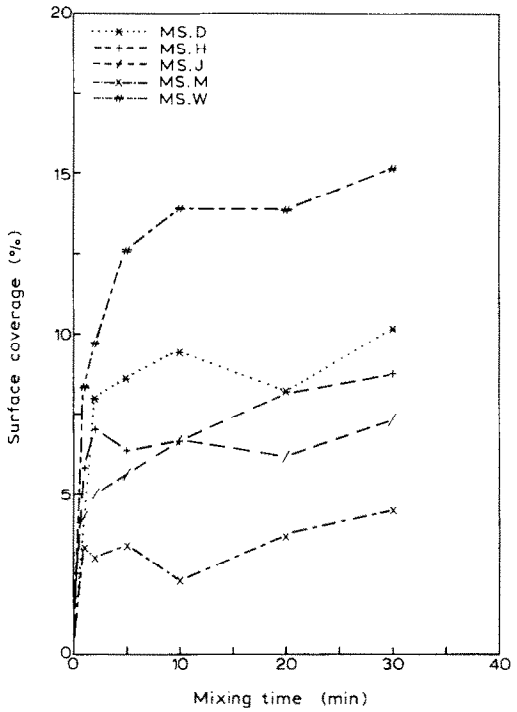

Fig. 2. Surface coverage profiles for 0.5% magnesium stearate concentration. Values depicted represent the mean ($n = 10$).

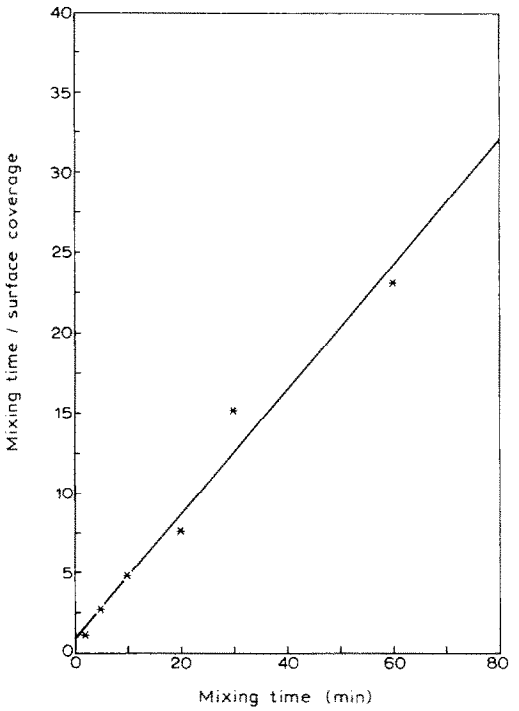

Fig. 3. Langmuir type plot for magnesium stearate 0.1% MS.D ($r = 0.9872$).

time and percentage surface coverage respectively in the classical equation. From the reciprocal of the slope, the infinite surface coverage was estimated.

The estimated infinite surface coverage and the experimental values after 30 min are given in Table 1 and are extremely close. The Langmuir type plot for each magnesium stearate sample shows good approximation to a straight line, thus confirming the overall film formation to be of the Langmuir type as reported by Johansson and Nicklasson (1986). The fact that EDX data fit the Langmuir type adsorption isotherm suggests that a molecular film is formed initially on the sodium chloride, followed by a gradual buildup of the particulate film. The SEM photomicrographs of unlubricated and lubricated samples are given in Figs. 4 and 5. Samples mixed for longer periods show the presence of magnesium stearate particles on the sodium chloride forming randomly located clusters constituting the particulate coverage. Particulate attachment may be initiated at gross defect points on the host particle surface and then increase to a maximum. Shah and Mlodozeniec (1977) proposed a similar type of mechanism for magnesium stearate film formation on spray dried lactose granules employing different experimental techniques.

It is interesting to note that the estimated values of percentage surface coverage by the lubricants in this work are lower than figures recently

TABLE 1

Comparison of EDX data for commercial magnesium stearates

Magnesium stearate	Infinite surface coverage (%)		Correlation coefficient
	Estimated	Experimental (30 min)	
MS.D	11.85	10.16	0.9897
MS.H	8.58	8.76	0.9950
MS.J	6.94	7.31	0.9946
MAS.M	4.02	4.52	0.9458
MS.W	15.21	15.14	0.9980

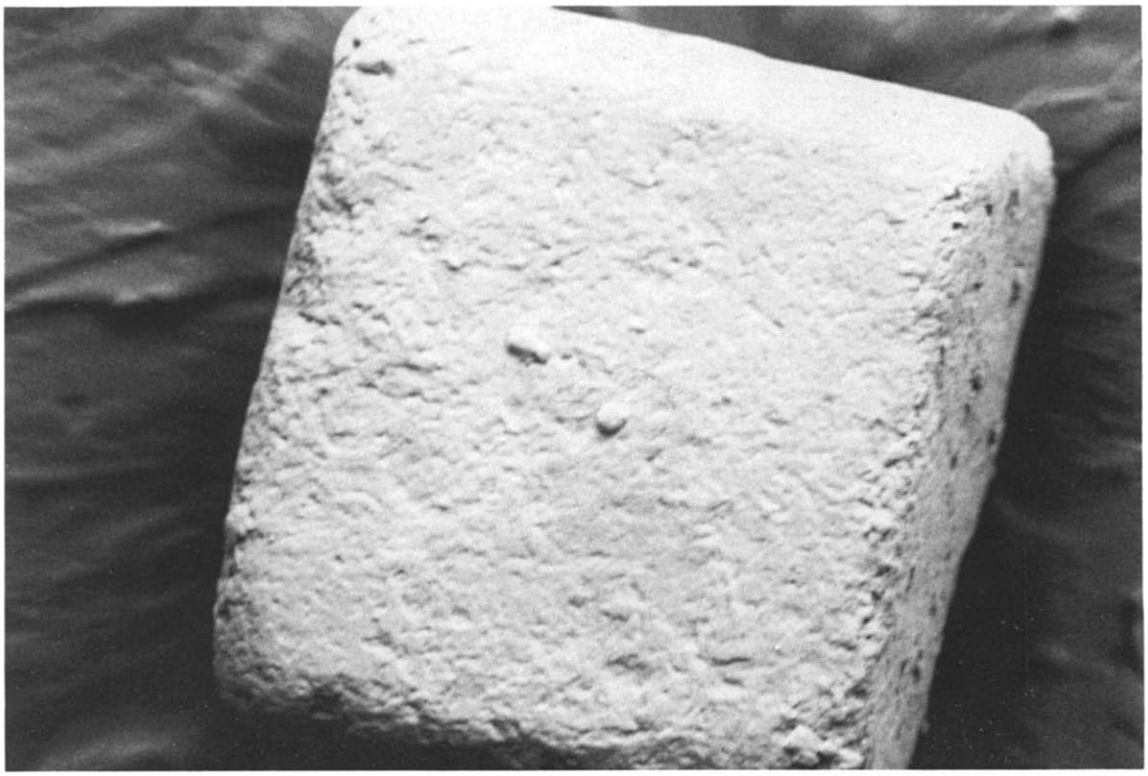

Fig. 4. SEM photomicrograph of a typical particle of sodium chloride ×200.

reported (Nicklasson and Broden, 1982; Johansson and Nicklasson, 1986). These workers measured changes in dissolution rates of powders and compacts to calculate the surface coverage. The discrepancy can be explained by the fact that this work monitors the lubricant film directly. In the dissolution technique the free fraction and loose agglomerates of the lubricant may also contribute to the estimate of percentage surface coverage of the host.

Specific surface area effects

It is often considered that the surface area of the lubricant is the most critical parameter of the material. Hölzer and Sjögren (1979) found a quantitative relationship between the ejection force, tensile strength and disintegration time of sodium chloride or lactose tablets and surface area of the lubricant sodium stearyl fumarate. A correlation between the lubricant surface area and coverage on the base material after a mixing period of 1 min has also been reported (Johansson and Nicklasson, 1986).

The surface coverage profiles seen in Fig. 2 and physical parameters listed in Table 2 indicate that a direct relationship between the surface area and the surface coverage at 0.5% w/w lubricant concentration does not exist for systems examined in this study. MS.H with a specific surface area of 8.92 m^2/g provided host surface coverage of 8.76%

TABLE 2

Physical characteristics of magnesium stearates

Magnesium stearate	Mean SSA (m^2/g) *	Volume mean diameter (μm)
MS.D	7.30	7.0
MS.H	8.92	10.0
MS.J	7.31	19.6
MS.M	2.83	18.9
MS.W	6.63	7.5

* SSA, specific surface area.

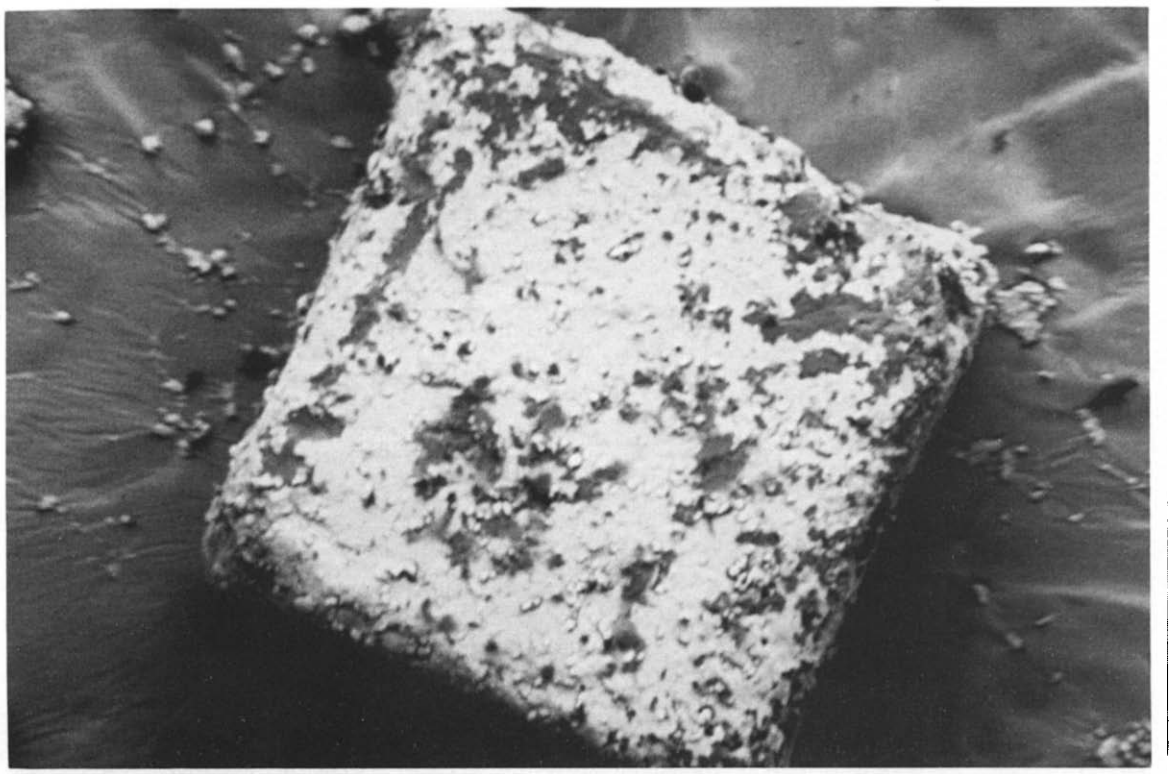

Fig. 5. Surface coverage of sodium chloride by magnesium stearate 2.0% MS.D after 10 min mixing ×200.

whilst MS.W had a surface area of 6.63 m^2/g but showed a surface coverage of 15.14%. These results, therefore, do not indicate that the specific surface area of a lubricant is the most critical parameter of the material. Surface area may play a role during the initial mixing stages. On further mixing, the delamination, propensity for film formation and the inherent material properties of the magnesium stearate as well as host powder surface properties will influence the total percentage surface coverage and eventual lubrication effects. Structural and crystalline characteristics discussed by Muller (1977) and Miller and York (1985a and b) are likely to be the important criteria in determining the rate and extent of surface coverage. Moreover, Miller and York (1985a) showed that the crystalline nature of the high-purity magnesium stearate and palmitate could be evaluated by DSC. Fig. 6 shows DSC profiles for the magnesium stearates studied. Endotherms observed at temperatures less than 85 °C are due to the presence of impurities originating from the starting raw materials used in the lubricant manufacture. The large endotherms at 100–110 °C correspond to the loss of structured water from the lubricant crystal structure. The bound moisture affects the degree of crystallinity as reflected by the endotherm peak temperatures of the materials and is thought to influence their lubrication properties. Further endotherms, beyond 110 °C, are associated with melting of magnesium stearate and its pseudopolymorphs. The DSC endotherms obtained therefore present a diverse description for each commercial magnesium stearate which may help to explain the differences in percentage surface coverage of sodium chloride.

Conclusions

EDX and SEM techniques were successfully used to study the process of lubricant film formation on a substrate.

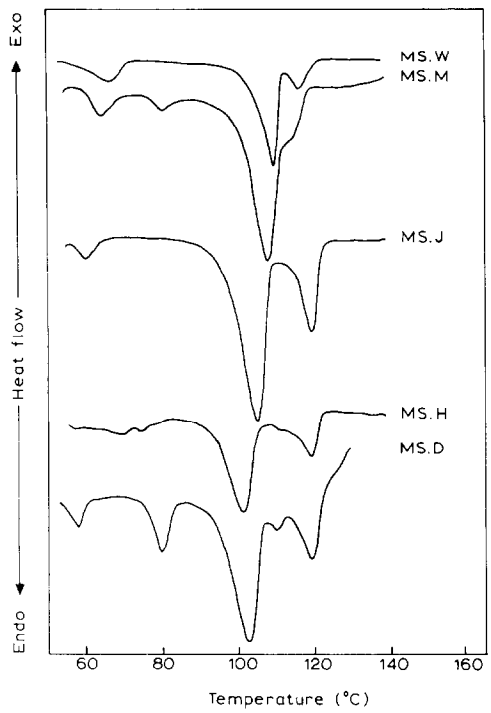

Fig. 6. DSC thermograms of commercial magnesium stearate samples.

Lubricant film formation on sodium chloride host particles by the magnesium stearate examined followed Langmuir-type adsorption. A similar film-forming mechanism was observed for all magnesium stearates studied but different degrees of host surface coverage for equivalent mixing conditions were obtained.

A simple and direct correlation between lubricant surface area and surface coverage of the host particles was not found.

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