International Journal of Pharmaceutics, 43 (1988) 249–255
Elsevier

IJP 01473

Structure–lubricity evaluation of magnesium stearate

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(Received 22 May 1987)
(Modified version received 9 November 1987)
(Accepted 22 November 1987)

Key words: Magnesium stearate; Lubricant; Lubricity; Magnesium palmitate; Tablet lubricant; Lubricant surface area

Summary

Six batches of magnesium stearate containing 0% : 100%, 10% : 90%, 15% : 85%, 25% : 75%, 30% : 70% and 100% : 0% magnesium stearate : magnesium palmitate have been synthesised. The specific surface area and differential thermal analysis of each lubricant was measured together with X-ray diffraction studies on the 15% : 85% sample. 1% w/w of each lubricant was mixed with lactose and the mixture was compressed at various compaction pressures and speeds. It was found that there was no correlation between the surface area of the lubricants, their chemical composition and lubricant efficiency. The X-ray crystallographic data indicated that the unit cell was a primitive tricyclic subcell of the P′2 arrangement. An evaluation of the compaction characteristics of the lubricants indicated that minimal energy is required to compress satisfactorily the 25% : 75% sample and this lubricant also required the least amount of energy to eject tablets from the die. It was concluded that the best lubricant was a 25% : 75% ratio of magnesium stearate to palmitate, which was found to be far superior to the technical grade of magnesium stearate also investigated.

Introduction

Magnesium stearate is an effective tablet lubricant, but marked differences in lubricity can exist from batch to batch and indeed within an individual batch (Moody, 1981). This is not surprising since magnesium stearate used in tableting is not a pure chemical entity, but primarily consists of a mixture of magnesium stearate and magnesium palmitate in various proportions together with very small amounts of magnesium laurate and myristate. Studies by Hölzer (1983) have shown that the percentage of fatty acid esters present in commercial grades of magnesium stearate can vary significantly. Using X-ray crystallography, infrared and differential thermal analysis Müller (1977) showed that there were three crystal forms of magnesium stearate dependent on the state of hydration. He observed that the trihydrate existed as needle-like crystals, whereas the dihydrate and the monohydrate were plate-like. Müller suggested that the dihydrate with plate-like crystals conferred optimum lubricating properties.

In order to measure the effect of the fatty acid composition of magnesium stearate on resultant lubricity, various synthetic samples of magnesium stearate have been prepared containing varying and known ratios of magnesium stearate to magnesium palmitate. Previous studies by Moody (1981) concluded that a ratio of 25% stearate and

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75% palmitate exhibited marked improvements in tablet lubrication. In this study magnesium stearate samples have been synthesised containing percentage ratios (stearate to palmitate) of 10 : 90, 15 : 85, 25 : 75 and 30 : 70, as well as pure magnesium stearate and magnesium palmitate. The composition, lubricant and tableting properties of these substances have been evaluated.

Materials and Methods

The small-scale laboratory manufacture of 6 lubricant batches was undertaken and the following lubricant batches were synthesised: 100% magnesium palmitate (100%P), 100% magnesium stearate (100%S), 25% magnesium stearate and 75% magnesium palmitate (25 : 75), 30% magnesium stearate and 70% magnesium palmitate (30 : 70), 15% magnesium stearate and 85% magnesium palmitate (15 : 85) and 10% magnesium stearate and 90% magnesium palmitate (10 : 90).

Calculated weights of stearic acid or palmitic acid (reagents of especially pure quality, B.D.H. Chemicals Ltd., Poole, U.K.) and 1% w/w ammonia solution (Analar grade, B.D.H. Chemicals Ltd., Poole, U.K.) were mixed in a flask containing 1.2 litres of water. The flask was heated to 90 ° C before a fixed volume of hydrated magnesium chloride (B.D.H. Chemicals Ltd., Poole, U.K.) was added. The hot solution was allowed to cool to room temperature overnight and the crystals were collected by filtration. The crystals were washed with water and hot acetone and then refluxed at 60 ° C with further acetone overnight. This latter refluxing was continued until a small dried sample of the crystals showed the absence of the 170-cm stretching group of the carboxylic radical, as determined by infra-red spectroscopy. The remainder of the crystals were then dried in a vacuum oven at 56 ° C and 45 mm Hg and allowed to cool.

Purity determinations of each of the samples synthesised were performed by gas-liquid chromatography using linoleic acid as the internal standard and boron trifluoride/methanol as a methylating agent. Table 1 depicts the results obtained.

The specific surface area of each of the synthetic lubricants was measured by a continuous gas adsorption method. The apparatus employed was the Quantasorb (Quantachrome Co., U.S.A.). Both the adsorption and desorption isotherms were recorded with nitrogen and helium gases and the results were calculated by the B.E.T. single-point method.

Differential thermal analysis of the lubricant samples was carried out using a Stanton-Redcroft Thermal Analyser, model 671, coupled with a supply of liquid nitrogen. Approximately 10 mg of the lubricant was transferred to the open aluminium pans of the instrument. Samples were initially cooled to approximately −50 ° C and the heating system activated. When the samples had reached a temperature of 130 ° C the heating system was inactivated and the pans were allowed to cool to room temperature before the next analysis was performed. At least 3 thermograms for each sample were obtained.

X-ray powder diffraction studies were performed utilising the 15 : 85 sample only. A small quantity of powder was used sufficient to fill the micro-sample holder of a Hewlett Packard computerised X-ray diffractometer set at 40-kV, 30 mA step size and count of 0.04 s and a wavelength examination at 1.54056 and 1.54435 Å.

1% w/w of each synthetic lubricant was mixed with spray-dried lactose (178–125 μm) in a tumbler mixer for 10 min. The batch size was 50 g; 200-mg samples were then taken and compressed between 8.7-mm flat-faced punches on a Universal Testing Machine (Instron Ltd., Model 1102, High Wycombe, U.K.). Various compaction pressures (up to 112 MPa) and speeds (0.2–1000 mm/min) were selected. Compaction energy was evaluated from integrator readings on the Instron machine and the amount of work required to eject the tablet from the die was also measured from integrator readings taken when each tablet was ejected.

Results and Discussion

From gas–liquid chromatographic determinations the ratio of magnesium palmitate to mag-

TABLE 1

Purity of the synthetic samples of magnesium stearate measured by gas-liquid chromatography

Lubricant	Percentage composition		
100% magnesium palmitate	98.0	98.6	98.3
100% magnesium stearate	98.5	97.6	99.2
25%S:75%P	23.4/76.6	22.4/77.6	23.3/76.8
30%S:70%P	29.1/68.6	29.5/72.4	28.8/68.9
10%S:90%P	9.4/90.6	10.6/89.5	11.7/88.3
15%S:85%P	17.2/94.6	14.6/84.2	15.5/85.9

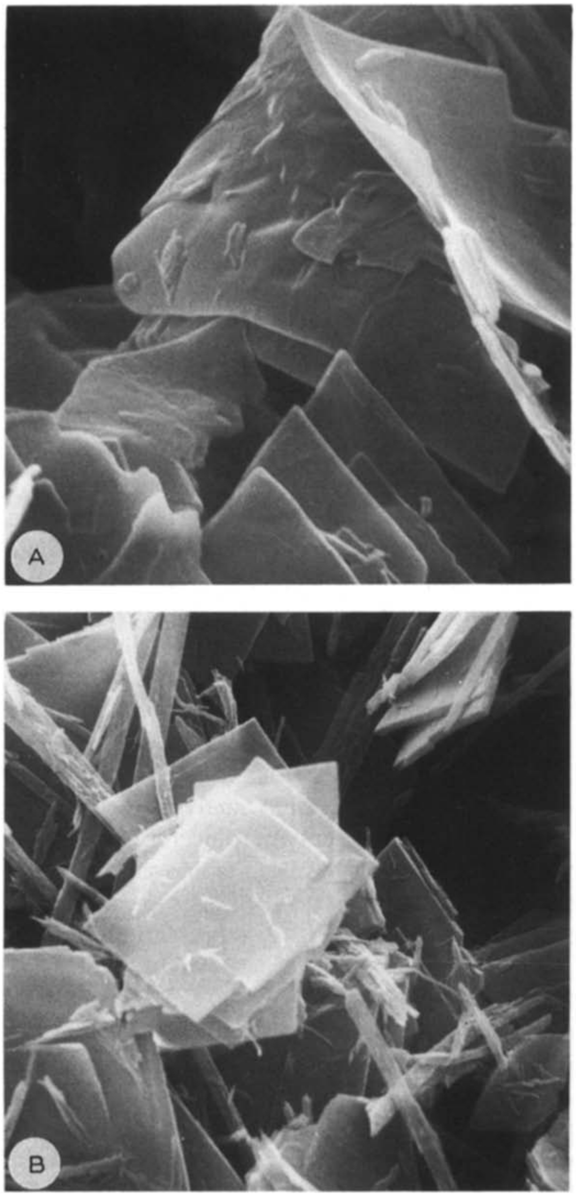

Fig. 1. Photomicrographs of the synthetic lubricants. A: 25%S:75%P. B: 100%P.

nesium stearate is shown in Table 1. From these results it can be seen that there is a good correlation between the expected and the measured G.L.C. composition. This verifies the validity and efficiency of the synthesis of the salts from their free fatty acids. Photomicrographs of two of the synthetic lubricant samples are shown–Fig. 1. These photographs show crystals with large laminates and there is some evidence of needle-like material interposing the plates. It is thought that these needle-like shapes are artifacts of electron microscope preparation, since Müller (1977) stated that the addition of excess magnesium chloride solution rendered the crystallising solution to be distinctly acidic, thus promoting the growth of plate-like crystals. Visual examination showed that the synthetic lubricant samples, 10 : 90, 15 : 85 and 30 : 70 were below 5 μm and that the 25 : 75 sample was 4–10 μm, whilst 100%P and 100%S were in the ranges 55–65 μm and 80–120 μm respectively.

The results obtained from the surface area determinations are shown in Table 2, together with the corresponding ejection energies of the lubricants after mixture with spray-dried lactose. It can be seen that there is no definite correlation between surface area of the lubricants, their chemical composition and ejection energies (which is a measure of lubricant efficiency (Rubinstein et al., 1979)). However, the less efficient lubricants, for example 100%P and 100%S, appear to possess relatively low surface areas, whereas the more effective lubricants appear to possess surface areas in excess of 9 m^2/g. This is in agreement with the work of Hölzer (1983). The most efficient lubricant, the 25 : 75 sample, ironically has the lowest surface area of the magnesium stearate/palmitate mixtures. It is suggested that lubricants with a high surface area increase the charge production within a compact. Thus the 25% : 75% lubricant does not generate as much electrostatic charge as the other lubricants during the compression of

TABLE 2

Surface areas and ejection energies of the synthetic lubricants

Lubricant	Ejection energy J/m	Specific surface area of the lubricant m^2/g
100% MgS	666	1.54
100% MgP	419	2.52
10%S:90%P	181	18.75
15%S:85%P	108	19.35
25%S:75%P	84	9.94
30%S:70%P	119	25.65
Technical grade magnesium stearate	126	24.63

powder blends, due to its lower surface area. As a result, migration of magnesium stearate/palmitate to the periphery of the tablet can take place more easily (Rubinstein and Moody, 1985). Too low a surface area results in lubricant particles that are too large to migrate effectively and thus there would appear to be an optimum surface area range for maximum lubricant efficiency. Hölzer (1983) has suggested that this range is 3–10 m^2/g.

The differential thermal analysis method for the identification of polymorphic forms of pharmaceutical materials has been employed by several workers (Lee and Hersey, 1977). A typical thermogram is illustrated – Fig. 2, representing the synthetic lubricant sample 25% : 75%. In most cases pre-cooling the sample to −50 °C and the use of open pans has led to the production of thermograms exhibiting little or no base line distortions (Daniels, 1973). Liquid nitrogen was employed so as to freeze the water molecules in the lubricant and so prevent interference with the rest of the thermogram. Thermograms of lubricant samples heated from room temperature showed melting-point ranges slightly higher than those samples that had been cooled. This validates the earlier suggestions that the incorporated water does in fact interfere with the true melting point range. The results of the melting point ranges are shown in Table 3. It can be seen that both the 100P% and 100%S possess two well defined peaks/transitions. Thus it seems that these samples exist in two states; one state possessing a higher kinetic energy than the other transition state. Since the monocomponent lubricants produce two transitions, it is logical to assume that the bicomponent lubricants would exhibit four transitions. This is in-

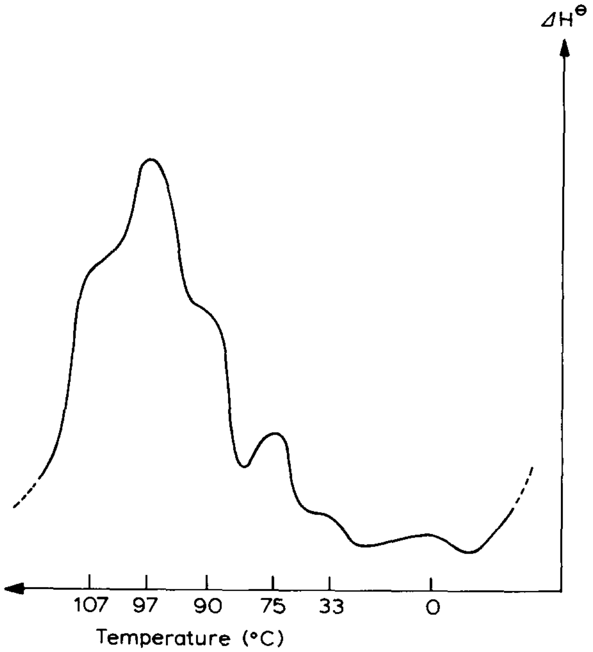

Fig. 2. A thermograph of the 25%S: 75%P synthetic lubricant.

TABLE 3

Observed melting point ranges of the synthetic lubricants

Samples	Temperature ranges °C
100%P	Shows an initial melting point at 67–71 °C and also a peak is observed at 103–107 °C.
100%S	Exhibits peaks 103 °C and at 112–114 °C
25%S:75%P	Shows an initial melting point at 22–30 °C and two inflexions, i.e. slight changes in the thermogram curve, at 90 °C and 107 °C. Two distinct peaks occur at 75 °C and 108 °C.
15%S:84%P	As above 1st peak at 18–32 °C and two peaks at 76 °C and 108 °C. Two possible peaks at 89 °C and 95 °C.
10%S:90%P	A broad initial peak at 16–32 °C and three peaks at 78, 97 and 103 °C
30%S:70%P	1st peak at 21–29 °C and two inflexions at 89 °C and 106 °C. Two distinct peaks at 77 °C and 107 °C.

deed observed. However, the bicomponent lubricants produce transitions 15–35 °C, which is not observed with the monocomponent lubricants. This transition manifests itself as a shallow endotherm and is only visible when the samples have been precooled to −50 °C and reheated. This unique endotherm has interesting implications during tablet compression. It has been reported (Travers and Merriman, 1970) that a temperature rise of up to 30 °C can occur during power compaction. If these temperature rises do occur in compacts containing magnesium stearate/palmitate, then the lubricant would very easily attain its softening point and become fluid-like. In this liquid state, lubricant mobility would be enhanced. Of the two mono-component lubricant samples, the 100% MgP exhibits the lower temperature endotherm. The addition of a component of a higher endotherm, that is stearate to palmitate, increases the melting-point range of the 100% MgP from 65–70 °C to 75–80 °C (Dansereau, 1984). It is noticeable that both the monocomponent lubricants exhibit similar transitions at 100–105 °C and that the highest transition range of the palmitate corresponds to the lower transition range of the stearate. The synthetic samples of 25% : 75% and 30% : 70% are the only two samples to exhibit inflexions, that is, well defined peaks are not present and the transitions run continously from one state to another. It is thought that this may be a prerequisite for good lubricating properties, as shown by the 25%S : 75%P lubricant. However this type of thermogram is also observed for the 30%S : 70%P, which ironically is not as successful a lubricant.

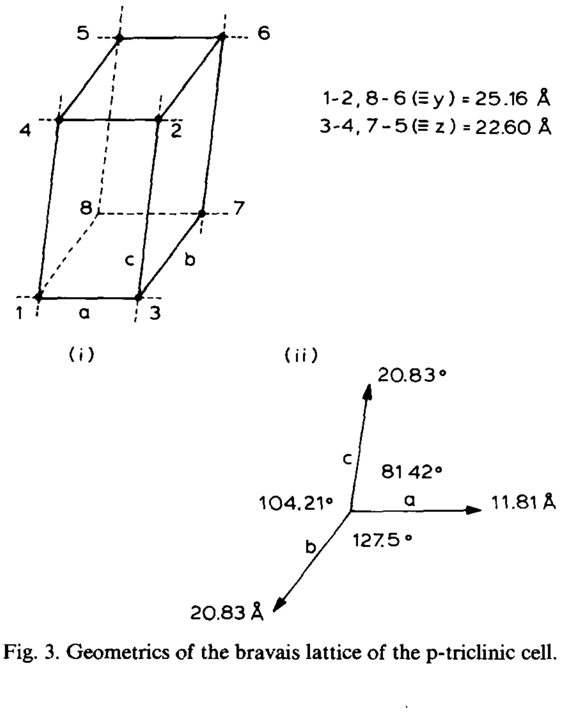

Fig. 3. Geometrics of the bravais lattice of the p-triclinic cell.

Using the 15% : 85% lubricant sample, extensive X-ray crystallographic data was obtained such that the parameters of the unit cell could be evaluated by the methods of Azaroff and Buerger (1958). The unit cell was found to be a primitive tricyclic subcell probably of the P′2 arrangement, similar to other divalent fatty-acid esters. The cell had a co-ordination number of 2 and the cell parameters were:

$a = 11.81$ Å $\quad \alpha = 127.44$ Å
$b = 12.19$ Å $\quad \beta = 104.21$ Å
$c = 20.83$ Å $\quad \gamma = 81.42$ Å

A geometrical representation of the unit cell is shown – Fig. 3. Knowing that two molecules of magnesium stearate exist per unit cell, this implies that 4 chains of hydrocarbon are present. In the case of the 25% : 75% lubricant, one unit cell possesses one chain of stearate and 3 chains of palmitate by simple proportion. The alignment of the chains is simply governed by the chain length accommodation within the cell. It is thus possible to build up a sequence of unit cells in which there exists a displacement between unit cells due to the overlap of hydrocarbon chains from one unit cell to the other. The displacement factor is dependent upon the chemical composition of the lubricant. The 15% : 85% lubricant exhibits a continuous array of displacements so as to form dislocations in the crystal structure. 100% magnesium stearate and 100% magnesium palmitate have no displacements between the unit cells, since their molecules are contained within each unit cell. Thus, these latter lubricants shear only between lattice planes. The other lubricants, because they are bicomponent, and have internal dislocations, shear both

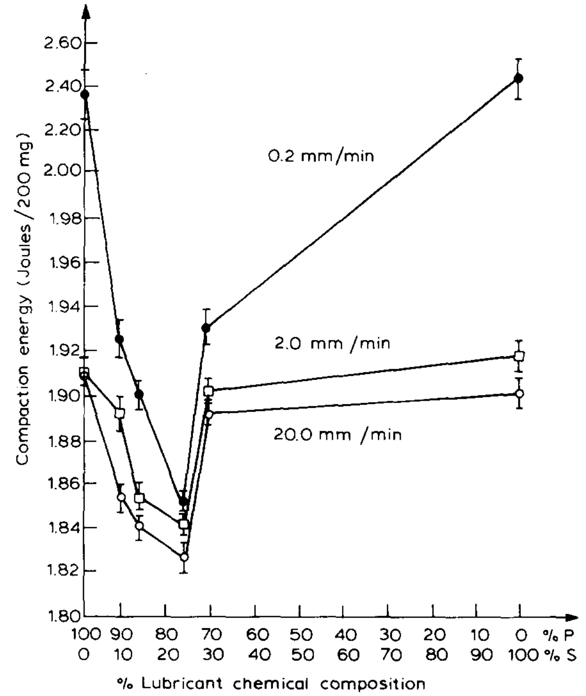

Fig. 4. The relationship between the compaction energy and the lubricant composition of a powder blend consisting of 1% w/w of lubricant in spray dried lactose compressed at 112 MPa and at speeds of 0.2, 2, and 20 mm/min.

between the lattice planes and across the internal dislocations. As a result it would be expected that mixtures of magnesium stearate and magnesium palmitate would have superior lubricant properties.

An evaluation of the compaction characteristics of each of the lubricants (1% w/w) in spray dried lactose is shown – Figs. 4 and 5. Fig. 4 depicts the compaction energies (Joules) for tablets compressed at speeds of 0.2, 2 and 20 mm/min at a constant compaction load of 112 MPa. Fig. 5 shows the compaction energies of the tablets produced at varying compaction pressure of 4.5, 11.2 and 45 MPa at a constant compression speed of 2 mm/min. On increasing the speed of compression, the compaction energy of the powder bed exhibits a marginal decrease. However, the compaction energy significantly increases as the compaction load increases, with speed kept constant. In all instances the relationship between the energy of compression and the chemical composition of the lubricant remains the same. The compressibility of powder samples is thought to be a function of the load-dependent dislocations in the structure of the crystal lattice. It has been postulated from X-Ray powder diffraction studies that both the 100% magnesium palmitate and stearate lubricants possess fewer dislocations compared to the other lubricants. This in effect implies that a lower load is required to propagate the dislocations present in the bicomponent lubricants and thus as shown in Fig. 4, these lubricants exhibit lower compression energies. A minimum compression energy was found with the 25% : 75% sample. It is suggested that the stearate chain possesses dislocations of higher resistance. Addition of more stearate chains in excess of 25% increases the uniformity of the unit cell of the lattice plane and consequently the inter-lattice plane movement is impeded. Thus the sample

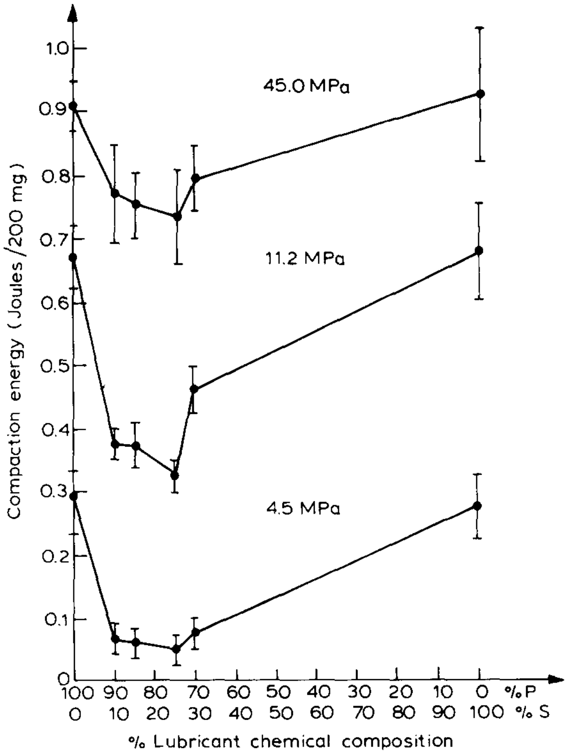

Fig. 5. The relationship between the compaction energy and the lubricant composition of a powder blend consisting of 1% w/w of lubricant in spray dried lactose compressed at 4.5, 11.2 and 45 MPa at a constant speed of 2 mm/min.

becomes less compressible and the energy required to produce dislocations is increased.

Table 2 shows the ejection energy results. Tablets of 1% w/w lubricant in spray-dried lactose were ejected from the die at a speed of 2 mm/min and a pressure of 4.48 MPa. For this study, all the tablets were initially compacted at a pressure of 93 MPa and at a speed of 2 mm/min. Again a definite relationship exists between the ejection energy and the lubricant composition. 100%P appears to exhibit a lower ejection energy than 100%S. However, a combination of the two produces a much reduced ejection energy, especially the 25% : 75% lubricant which was the best lubricant of all. Ejection energies can be thought of as the resistance to shearing at the tablet surface–die wall interface. The quality of a lubricant is then expressed as the ability to shear readily under an applied load. The 25% : 75% sample, having a large number of internal dislocations, can shear very readily and thus this lubricant required the least amount of energy to eject tablets from the die.

It is thus concluded that the best lubricant was a 25% : 75% ratio of magnesium stearate to palmitate, which was found to be far superior to the technical grade of magnesium stearate also investigated.

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