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# Influence of the granulation technique and starting material properties on the lubricating effect of granular magnesium stearate

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Magnesium stearate has been granulated in four ways to produce lubricant granulations with different properties. The lubricating properties, as well as the tablet properties with the granulated lubricant, were evaluated on tablets prepared from a mixture of dicalcium phosphate, corn starch and microcrystalline cellulose. The lubricating effect of the magnesium stearate granulations showed a similar pattern regardless of the granulation technique used except for a granulation with providone. Increasing the particle size of the magnesium stearate granulation increased the amount of lubricant required to obtain lubrication similar to powdered magnesium stearate. Variations in the specific surface area of the starting materials could be masked by using them in granular form.

Magnesium stearate is a boundary lubricant which exhibits its lubricating properties by forming a boundary film between the die surface and the tablet granulation (Lachman et al 1976). During the mixing stage magnesium stearate forms a hydrophobic film around the granules which can affect tablet properties such as tensile strength, disintegration time, friability and dissolution rate (Bolhuis et al 1975; Strickland et al 1960; Hölzer & Sjögren 1979; Ragnarsson et al 1979).

A wide batch to batch variation in magnesium stearate has been reported. Billany & Richards (1982) showed differences in dissolution behaviour owing to the presence of water soluble components. Difference in film formation properties between batches prepared by different techniques was shown by Miller et al (1983). The effect of lubricant particle size on the lubricating effect and tablet properties has also been investigated. Steffens (1978) showed only small effects of magnesium stearate particle size on the lubricating properties on a lactose granulation. However, lubricant particle size has been demonstrated to have a great influence on lubricating effect and tablet properties both for commercial batches of magnesium stearate (Hölzer 1984) and for sodium stearyl fumarate (Hölzer & Sjögren 1979). Shotton & Lewis (1964) found that crushing strength was not affected by the particle size of magnesium stearate as a chloroform granulation at 2% concentration for a range of materials. Frattini & Simioni (1984) found a direct relation between lubricating effect and specific surface area as well as tablet properties at a magnesium stearate concentration of 0·5% in a direct compressible pyrazinamide mass.

Schrank-Junghäni et al (1984) proposed that it would be advantageous to add the lubricant directly to the tool surface. Thus the formation of a hydrophobic film around the granules is avoided and the detrimental effects on tablet properties eliminated or reduced. This is difficult to obtain in practice. If, however, the lubricant is added in granular form, it can be delivered at the tool surface without having formed a hydrophobic film around the tablet granules.

It has previously been shown for a range of materials, that by using granular magnesium stearate in high concentrations, lubricating properties equal to powdered lubricant were obtained without destroying the tablet properties (Johansson 1984). In the present paper variations in lubricant granulation properties and starting material properties on lubrication and tablet properties have been investigated.

## MATERIALS AND METHODS

### *Materials*

Magnesium stearate (Ph Eur, from three different sources), dicalcium phosphate (EMCOMPRESS, Edward Mendell), microcrystalline cellulose (AVICEL PH 101, FMC corp), corn Starch (Sta-Rx 1500, Staley Mfg. comp, USA), povidone (Kollidon K-25, BASF, West Germany), gelatin and chloroform were of commercial grades.

### *Preparation of magnesium stearate granulations*

Magnesium stearate was granulated in four different ways: (1) by the compaction technique described earlier (Johansson 1984), (2) as a gelatin granulation with 10% gelatin by weight as an aqueous solution,

(3) as a povidone granulation with 10% of povidone by weight in ethanol, (4) as a chloroform granulation without a binder (Shotton & Lewis 1964). For each granulation the fraction between 71 and 500 μm was used unless otherwise stated. The particle size of each granulation is given in Table 1. As reference, untreated magnesium stearate of the same batch was used throughout (source A, specific surface area by permeametry 3·2 $m^2 g^{-1}$, porosity = 0·5, loss on drying (LOD) 105 °C 5·0%).

Table 1. Properties of the magnesium stearate granulations.

| Magnesium stearate source | Method of preparation | Median particle size by sieve (μm) (Geom s.d.) | Friability index (%) |
|---|---|---|---|
| A | Compaction | 240 (1·7) | 71 |
| A | Povidone | 280 (2·0) | 89 |
| A | Gelatin | 260 (1·7) | 77 |
| A | Chloroform | 290 (2·4) | 38 |
| B | Compaction | 240 (1·9) | 67 |
| C | Compaction | 240 (1·6) | 75 |

To test the influence of the starting materials, magnesium stearate from two other sources was used (Source B, specific surface area by permeametry 6·1 $m^2 g^{-1}$, porosity = 0·5, LOD 105 °C 4·7%. Source C, specific surface area by permeametry 1·2 $m^2 g^{-1}$, porosity = 0·5, LOD 105 °C 5·7%).

*Measurement of granule strength*

The granule strength was measured by milling 10 g of the granulation for 10 min at 75 rev $min^{-1}$ in a ball mill of 70 mm inner diameter, the drum was filled with thirty 1·5 cm ceramic balls. A friability index was calculated in accordance with Rubinstein & Musikabhuma (1978). F = Df/Di × 100, where F is the friability index in %, Di is the initial median particle size by weight determined by sieving and Df is the final median particle size obtained after the milling operation. The coefficient of variation of 8 successive measurements of one granulation was 6·5%. The friability indices for all magnesium stearate granulations are given in Table 1.

*Preparation of tablet masses*

Throughout this study a direct compressible mixture consisting of dicalcium phosphate 80%, corn starch 4% and microcrystalline cellulose 16% was used. The components were mixed in a 3 litre glass double cone mixer for 10 min at 60 rev $min^{-1}$.

The lubricants were mixed with the tablet mass in the stated amounts for 2 min in the double cone mixer. In the cases with binder granulations the amount of binding agent was corrected to give the stated amount of lubricant in each tablet. The powdered magnesium stearate was passed through a 0·5 mm sieve prior to mixing.

*Compaction to tablets*

The lubricated tablet masses were compressed on an instrumented excenter press at 200 ± 10 MPa and a weight of 200 ± 5 mg. The ejection force was recorded after the machine had been running for at least 5 min at 30 rev $min^{-1}$ at the stipulated settings (Johansson 1984). The ejection force was compensated for variation in contact area between the tablet and the die wall (EJF/A) (Hölzer & Sjögren 1977). The results are given as the mean of 10 tablets. The tablet properties were evaluated 24 h after compaction. Crushing strength was measured on a motorized instrument (Heberlein) and recalculated to tensile strength (Fell & Newton 1968). The results are given as the mean of 10 tablets. Tablet friability was measured after 100 rev in the Roche apparatus. The disintegration time was measured in the BP 73 apparatus without discs using water as medium. The results are the median of 6 tablets.

## RESULTS AND DISCUSSION

The influence of different granulation techniques on the lubricating properties can be seen in Fig. 1. Powdered lubricant shows an immediate decrease in EJF/A to a plateau value of about 0·18 which is not further changed. The granulated lubricants show a somewhat slower decrease but at 2% all granulations except the povidone granulation gave values that were comparable with powdered lubricant. The high value for the povidone granulation can probably be explained by the high value of the friability index compared with the other granulations.

No differences were found between the lubricant granulations in tensile strength or friability measurements. However, powdered magnesium stearate gave compacts of lower tensile strength and higher friability over the whole concentration range studied, with the exception of tensile strength with the chloroform granulation at 0·5%.

Compacts prepared with powdered magnesium stearate showed a dramatic increase in disintegration time at high concentrations of the lubricant compared with tablets with granulated lubricants. At the 5% level of powdered magnesium stearate, compacts showed a disintegration time of more than 2 h while none of the granulations gave disintegration times

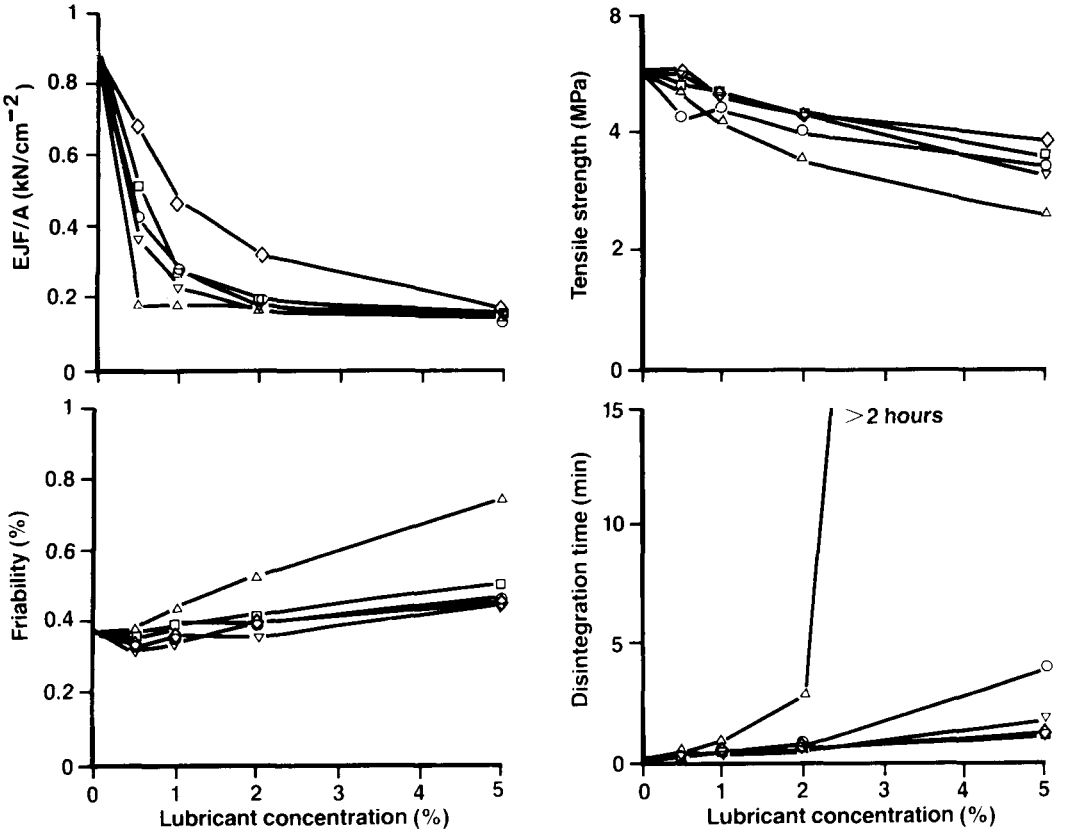


FIG. 1. EJF/A, tensile strength, friability and disintegration time vs lubricant concentration for tablets prepared with different lubricant granulations. △ Powdered lubricant, ▽ compacted granulation, □ gelatin granulation, ◇ povidone granulation, ○ chloroform granulation.

exceeding 5 min. This is in agreement with the finding of Bolhuis et al (1975, 1981) who showed that magnesium stearate interfered with various disintegrants, especially low swelling disintegrants such as starch, by forming a hydrophobic film and thus impeding wettability. With the granulations there was probably no film formation taking place to the same extent. Taking into consideration the variation of EJF/A with increasing amount of lubricant it seems likely that the film formation is not a prerequisite for good lubrication. This is in agreement with the findings of Schrank-Junghäni et al (1984) which have shown that the internal friction of a tablet mass within itself has no demonstrable influence on the compaction properties but it is the lubricating effect at the die wall that is of importance.

The influence of the lubricant granulation particle size on lubrication and tablet properties can be seen in Fig. 2 where different sized fractions of the compacted magnesium stearate were used as lubricant. The coarser fractions showed slower decrease in the EJF/A with increasing amount of lubricant than the finer fractions, as expected. There were no noticeable differences in friability or tensile strength of compacts prepared with the different size fractions of lubricant. This is in agreement with the results of Shotton & Lewis (1964) who used chloroform granulations of approximately the same size ranges as used herein.

The influence of the starting material properties on lubrication and tablet properties were studied at 0·2 and 2·0% of lubricant using the compaction technique for the manufacture of lubricant granulations. The results are summarized in Table 2. At the 0·2% level there is a more than two fold difference in EJF/A between the low surface area lubricant (c) and the high surface area lubricant (b) when using the lubricants in powdered form. At the same time there were only small differences in the tablet properties. At the 2% level the difference in lubrication properties between the powdered lubricants was negligible, probably due to over lubrica-

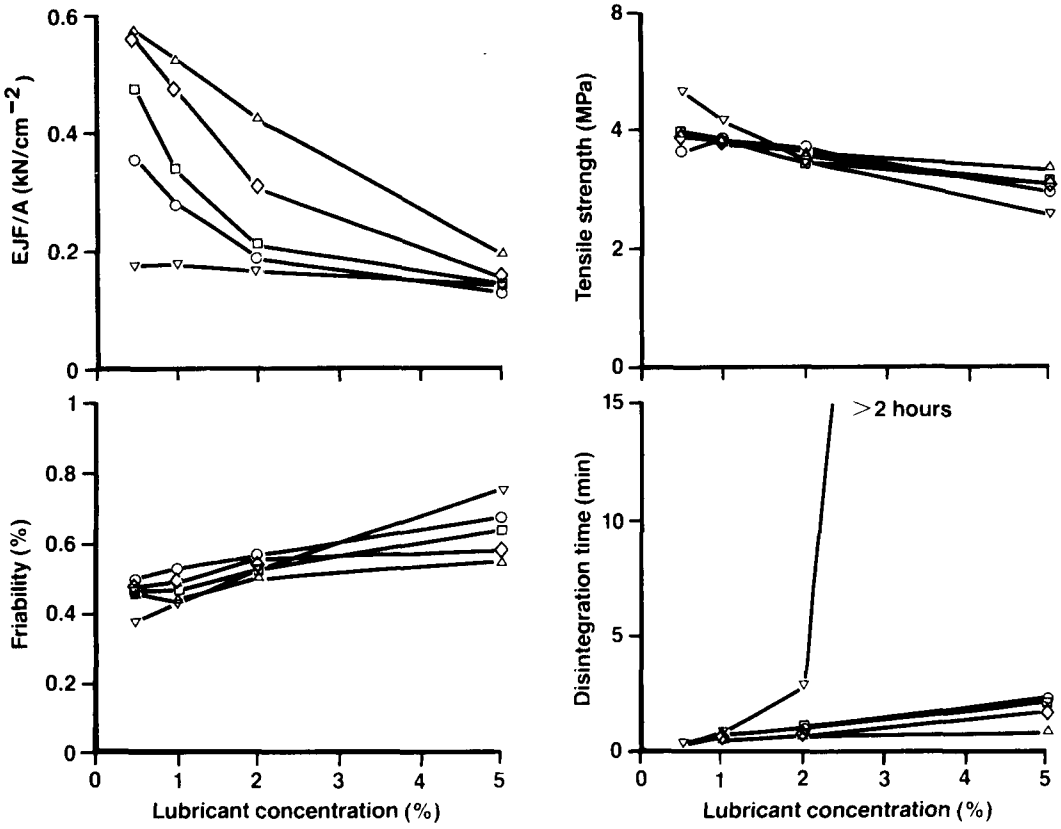


FIG. 2. EJF/A, tensile strength, friability and disintegration time vs lubricant concentration for tablets prepared with different size fractions of compacted lubricant granulation. △ > 355 μm, ◇ 250–355 μm, □ 180–250 μm, ○ 90–180 μm, ▽ powdered lubricant.

Table 2. Lubrication and tablet properties of tablets prepared with powdered and granular lubricants from different sources.

| | 0·2% Source | | | 0·2% Source | | |
|---|---|---|---|---|---|---|
| | A | B | C | A | B | C |
| Powdered lubricants | | | | | | |
| EJF/A (kN cm$^{-2}$) (s.d.) | 0·34 (0·0075) | 0·19 (0·0071) | 0·50 (0·0079) | 0·16 (0·0037) | 0·16 (0·0037) | 0·17 (0·0035) |
| Tensile strength (MPa) (s.d.) | 4·4 (0·25) | 4·0 (0·17) | 4·5(0·18) | 3·1 (0·12) | 2·8 (0·12) | 3·6 (0·14) |
| Friability (%) | 0·3 | 0·3 | 0·3 | 0·5 | 0·5 | 0·5 |
| Disintegration time(s) | 22 | 28 | 17 | 108 | 690 | 60 |
| Granular lubricants | | | | | | |
| EJF/A (kN cm$^{-2}$) (s.d.) | 0·59 (0·015) | 0·61 (0·023) | 0·64 (0·0098) | 0·20 (0·0058) | 0·22 (0·0082) | 0·25 (0·0052) |
| Tensile strength (MPa) (s.d) | 3·3 (0·14) | 3·8 (0·14) | 3·5 (0·15) | 3·8 (0·13) | 3·7 (0·14) | 3·5 (0·13) |
| Friability (%) | 0·5 | 0·5 | 0·6 | 0·6 | 0·6 | 0·6 |
| Disintegration time(s) | 21 | 16 | 22 | 50 | 50 | 61 |

tion of the die. Instead there was a 10 fold difference in disintegration time between the high and the low surface area lubricants. These results are in agreement with the results of Hölzer (1984).

In contrast to the findings of Frattini & Simioni (1984) the present results show the need to use both high and low concentrations of lubricant when studying the differences between batches of lubricant in order to elucidate differences both in lubricating effect and tablet properties.

Use of the granular lubricants prepared from the three batches revealed a different picture. At the

0·2% level there are fairly high but similar values of the EJF/A. Also the tablet properties show small differences for all the parameters studied. Increasing the amount of lubricant to 2% resulted in a reduction of the EJF/A to levels that were only slightly higher than the values obtained with the powdered lubricants and there were no differences between the three qualities. At the same time there were no differences in tablet properties that could be traced to differences in starting material surface area, in contrast to the findings with the powdered lubricants. Thus it seems to be possible to mask the differences in starting material surface area by using the lubricants in granular form. The slight decrease in lubricant efficiency could be overcome by using higher concentrations of lubricant without the risk of too high an increase in disintegration time especially with high surface area lubricants.

## REFERENCES


Billany, M. R., Richards, J. H. (1982) Drug Dev. Ind. Pharm. 8: 497–511

Bolhuis, G. K., Lerk, C. F., Zijlstra, H. T., De Boer, A. H. (1975) Pharm. Weekbl. 110: 317–325

Bolhuis, G. K., Smallenbroek, A. J., Lerk, C. F. (1981) J. Pharm. Sci. 12: 1328–1330

Fell, J. T., Newton, J. M. (1968) J. Pharm. Pharmacol. 20: 657–658

Frattini, C., Simioni, L. (1984) Drug. Dev. Ind. Pharm. 10: 1117–1130

Hölzer, A. W. (1984) Labo-Pharma Probl. Tech. 32: 28–36

Hölzer, A. W., Sjögren, J. (1977) Drug Dev. Ind. Pharm. 3: 23–37

Hölzer, A. W., Sjögren, J. (1979) Int. J. Pharm. 2: 145–153

Lachman, L., Lieberman, H. A., Kanig, J. L. (1976) The Theory and Practice of Industrial Pharmacy, 2nd Ed. Lea and Febiger, Philadelphia, p. 306

Johansson, M. E. (1984) Int. J. Pharm. 21: 307–315

Miller, T. A., York, P., Jones, T. M. (1983) J. Pharm. Pharmacol. 35: 43P

Ragnarsson, G., Hölzer, A. W., Sjögren, J. (1979) Int. J. Pharm. 3: 127–131

Rubinstein, M., Musikabhuma, P. (1978) Pharm. Acta Helv. 53: 125–128

Schrank-Junghäni, H., Bier, H. P., Sucker, H. (1984) Acta Pharm. Tech. 30(3): 224–234

Shotton, E., Lewis, J. (1964) J. Pharm. Pharmacol. 16: 111T–120T

Steffens, K. J. (1978) Inaugural Dissertation, University of Marburg

Strickland, W. A., Higuchi, T., Busse, L. W. (1960) J. Am. Pharm. Ass. Sci. edn. 49: 35–40