International Journal of Pharmaceutics, 2 (1979) 145–153

Research Papers

EVALUATION OF SODIUM STEARYL FUMARATE AS A TABLET LUBRICANT

ARNE W. HÖLZER and JOHN SJÖGREN

Department of Pharmaceutics, AB Hässle Fack, S-431 20 Mölndal (Sweden)

(Received January 4th, 1978)
(Revised version received June 7th, 1978)
(Accepted June 8th, 1978)

SUMMARY

The ability of sodium stearyl fumarate to reduce friction and adhesion to the punches was investigated as well as its influence on the tablet strength and the disintegration time. The effect of lubricant concentration, particle size and the mixing time was investigated using lactose and sodium chloride as tablet materials. A direct comparison with magnesium stearate in 6 tablet formulations was also made. The friction during compression and ejection of the tablets was measured in an instrumented tablet machine. Sodium stearyl fumarate reduced the friction and the adhesion to about the same degree as magnesium stearate and had also about the same influence on tablet strength and disintegration. The particle size of sodium stearyl fumarate was of great importance and all effects correlated better to the surface area than to the weight fraction. Prolonged mixing improved its lubricating effect and had no effect on the disintegration but reduced the strength of sodium chloride tablets. Sodium stearyl fumarate appears to be a good alternative to magnesium stearate.

INTRODUCTION

Lubricants are used in tableting to reduce the friction between the tablet and the die wall and to prevent adhesion of the material to punches or the die wall. Magnesium or calcium stearates are excellent lubricants but they are hydrophobic and may have a negative influence on the biopharmaceutical properties of the final product (Levy and Gumtow, 1963). This effect is more pronounced with prolonged mixing (Bolhuis et al., 1975; Ragnarsson et al., 1976).

Sodium stearyl fumarate (Pfizer Inf. sheet, 1964; Food Chemical Codex, 1972) has been suggested as a suitable lubricant in tableting (Pfizer Inf. sheet, 1967). It is claimed not to have the disadvantages of magnesium stearate in respect of tablet strength, disintegration and dissolution (Lindberg, 1972).

The purpose of this study was to evaluate the ability of sodium stearyl fumarate to reduce friction and adhesion as well as its effects on tablet strength and disintegration time. The influence of particle size and mixing time was also investigated.

MATERIALS

Sodium stearyl fumarate (Astra Pharmaceuticals, Södertälje, Sweden), m.p. 180–200°C (decomposition). Loss on drying 2.8% (105°C, 2 h). Density 1.14 gcm^{-3} (Beckman Air Comparison Pycnometer mod. 930). Four particle size fractions were obtained in a zig-zag air classifier (Alpine 100 MZR), see Table 1.

Magnesium stearate USP (Unilever Emery, Holland). Specific surface area by permeametry 6.3 m^2g^{-1} (Fisher Sub-Sieve Sizer, porosity 0.60). Loss on drying 3.6% (105°C, 2 h).

Cubic sodium chloride USP (KNZ Corp., Holland). Arithmetic mean sieve diameter 390 μm (Allen-Bradley Sonic Sifter). Specific surface area calculated 0.008 m^2g^{-1} (B.S. 4359: Part 3: 1970).

Anhydrous lactose USP (Sheffield Co., U.S.A.). Specific surface area by permeametry 0.17 m^2g^{-1} (Fisher Sub-Sieve Sizer, porosity 0.55).

Acetylsalicylic acid BP (ASA 7013, Monsanto Chem., U.K.).

Ascorbic acid USP (Hoffman-La Roche Inc., Switzerland).

Dibasic calcium phosphate dihydrate NF, granulated with polyvinylpyrrolidone (PVP K25, BASF, G.F.R.) in water. The granulate, containing 3% PVP, was passed through an 0.5 mm sieve and had a loss on drying of 2.2% (105°C, 15 min).

Microcrystalline cellulose NF (Avicel PH 101, FMC Corp., U.S.A.).

Granular starch (Sta-Rx 1500, A.E. Staley Mfg Comp., U.S.A.).

METHODS

The lubricants were sieved through a 0.2 mm sieve and mixed at 40 rpm in a small cubic-mixer (Erweka, G.F.R.) with the materials, see Tables 2 and 4. Ten tablets were

TABLE 1

CHARACTERIZATION OF SODIUM STEARYL FUMARATE SIZE FRACTIONS

Fraction No.	Size interval from 100 MZR μm	Specific surface area [a] m^2g^{-1}
1	<5	2.70
2	10–15	1.34
3	20–25	0.73
4	>25	0.27

[a] By air permeametry, Fisher Sub-Sieve Sizer, porosity 0.50.

TABLE 2

PER CENT OF SODIUM STEARYL FUMARATE USED IN THE EXPERIMENTS WITH DIFFERENT PARTICLE SIZE FRACTIONS

Lubricant fraction	Sodium chloride			Anhydrous lactose		
1	0.05	0.1 [a]	0.5	0.5 [a]	1.0	2.5 [a]
2	0.05	0.1	0.5	–	–	–
3	0.05	0.1	0.5	–	–	–
4	–	0.1 [a]	0.5	2.5 [a]	5.0	10.0

[a] Mixed at 20, 200 and 2000 revolutions. The others mixed at 200 revolutions only.

compressed at each load after conditioning the die wall with 50 tablets if not stated otherwise. An instrumented single-punch machine equipped with piezoelectric load washers (Hölzer and Sjögren, 1977) was used at a speed of 30 tablets per minute. The tablet weight was calculated from the density to provide a tablet of 0.4 cm height at zero porosity using flat 1.13 cm diameter punches. Due to practical reasons the tablets summarized in Table 4 were prepared without conditioning the die wall and the weight corresponded to 0.3 cm at zero porosity. The die and punches were cleaned with water and a mixture of acetone-carbon tetrachloride.

The friction during tableting and ejection of the tablets was characterized by the difference between the peak forces on the upper and lower punches (FD/A) and by the ejec-

TABLE 3

ADHESION OF LACTOSE–SODIUM STEARYL FUMARATE MIXTURES TO THE PUNCHES AT VARIOUS COMPRESSION LOADS

Surface ratio, %	Conc. %	Size fraction	Mixing rev.	Load, MPa		
				50	150	270
4.1	2.5	4	20	3 [a]	3	3
4.1	2.5	4	200	3	3	3
4.1	2.5	4	2000	3	3	2
8.0	0.5	1	20	3	2	2
8.0	0.5	1	200	3	2	2
8.0	0.5	1	2000	3	2	1
8.4	5.0	4	200	3	2	2
16.0	1.0	1	200	3	1	1
17.7	10.0	4	200	2	1	1
41.0	2.5	1	20	1	1	0
41.0	2.5	1	200	1	0	0
41.0	2.5	1	2000	1	0	0
38.0	1.0 Magnesium stearate		200	1	0	0

[a] 0, No adhesion; 1, thin coating on punch surfaces. Tableting is not disturbed; 2, few spots of material on punch surfaces; 3, marked adhesion. Tablet surfaces are damaged.

TABLE 4

EFFECTS OF SODIUM STEARYL FUMARATE AND MAGNESIUM STEARATE. TABLETS COMPRESSED AT 150 MPa

Materials	Lubricant conc. %	Sodium stearyl fumarate [a]					Magnesium stearate				
		FD/A [b] $kNcm^{-2}$	EJF/A [c] $kNcm^{-2}$	Adhesion [d] –	σ_t [e] MPa	Disintegr. min	FD/A $kNcm^{-2}$	EJF/A $kNcm^{-2}$	Adhesion –	σ_t MPa	Disintegr. min
Ascorbic acid + microcryst. cellulose, 1 + 1	0	4.1	1.29	0	>3.9	1.2	4.1	1.29	0	>3.9	1.2
	0.1	2.3	0.54	0	>3.9	0.8	1.2	0.21	0	>3.9	1.4
	1.0	0.6	0.08	0	2.8	1.2	0.5	0.05	0	2.3	1.5
Acetylsalicylic acid + gran. starch, 9 + 1	0	2.9	0.18	2	0.9	0.5	2.9	0.18	2	0.9	0.5
	0.1	1.5	0.10	1	0.6	0.5	1.6	0.10	1	0.3	0.2
	1.0	1.0	0.05	1	0.5	5.8	0.7	0.05	0	0.2	0.3
Gran. starch + lactose, 7 + 3	0	4.4	0.66	0	2.1	5.6	4.4	0.66	0	2.1	5.6
	0.1	2.5	0.25	0	2.0	5.7	1.1	0.04	0	2.3	6.2
	1.0	0.7	0.02	0	0.9	6.5	0.6	0.02	0	1.5	7.0
Calcium phosphate gran + gran. starch 9 + 1	0	4.2	1.56	1	1.0	1.3	4.2	1.56	1	1.0	1.3
	0.1	1.4	0.13	0	1.4	1.4	1.5	0.17	0	1.5	1.3
	1.0	0.8	0.07	0	1.3	0.9	0.8	0.06	0	1.3	0.8
Sodium chloride	0	2.9	1.00	0	1.1	3.1	2.9	1.00	0	1.1	3.1
	0.1	1.0	0.16	0	0.2	3.1	0.6	0.11	0	0.2	6.4
	1.0	0.7	0.10	0	0.2	12.4	0.5	0.07	0	0.2	17.6
Lactose	0	4.3	3.40	3	1.5	5.8	4.3	3.40	3	1.5	5.8
	0.1	3.9	3.06	3	1.7	6.7	3.4	2.43	3	1.8	6.8
	1.0	0.6	0.16	1	2.4	8.7	0.6	0.20	0	2.3	9.3

[a] Size fraction No. 1, see Table 1.
[b] Force difference.
[c] Ejection force
[d] Arbitrary units, see Table 3.
[e] Tensile strength.

tion force (EJF/A), both calculated per unit contact area between the tablet and the die wall, as previously described (Hölzer and Sjögren, 1978). The adhesion of the materials to the punch surfaces (picking) was observed by inspecting the surfaces after each series of ten tablets. The picking properties of the mixtures were classified in arbitrary units (see Table 3).

The tablets were kept 1 week in closed polyethylene bags before determination of the disintegration time according to USP XIX (37°C, water, without discs) and of the diametrical crushing strength (Schleuniger mod. 2E/205, Switzerland). The tensile strength of the tablets (σ_t) was calculated according to the method of Fell and Newton (1968). The results presented are the mean of 5 determinations.

RESULTS AND DISCUSSION

Friction

Increasing concentrations of sodium stearyl fumarate and magnesium stearate reduced both FD/A and EJF/A in the same way (Fig. 1 and Table 4). The particle size of sodium stearyl fumarate was as important as the concentration, as shown in Fig. 1. The lubricating effect was related to the total surface area of the added lubricant, see Fig. 2.

Prolonged mixing reduced the friction for sodium chloride (Fig. 2) especially when the coarse lubricant fraction of sodium stearyl fumarate was used. The effect of mixing may be due to milling or disaggregation of the lubricant by the heavier sodium chloride particles. A lubricant film may also be formed on the sodium chloride particles, as postulated for magnesium stearate (Bolhuis et al., 1975). The mixing time had very little influence on the friction of the lactose mixtures, Fig. 2, possibly due to the high degree of lubrication necessary to avoid the adhesion to the die wall.

At the 0.1% level magnesium stearate reduced the friction more than sodium stearyl fumarate for most of the tested materials (Table 4). The difference may be due to the

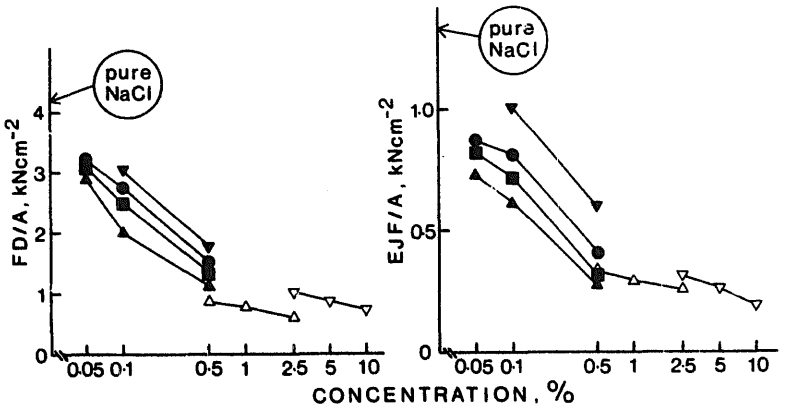

Fig. 1. Effect of sodium stearyl fumarate on friction of sodium chloride (closed symbols) and lactose (open symbols) during tableting measured as force difference (FD/A) and ejection force (EJF/A) at 200 MPa maximum upper punch pressure. Sodium stearyl fumarate added by mixing 200 revolutions as: ▲, fraction 1 (Table 1); ■, fraction 2 (Table 1); ●, fraction 3 (Table 1); ▼, fraction 4 (Table 1).

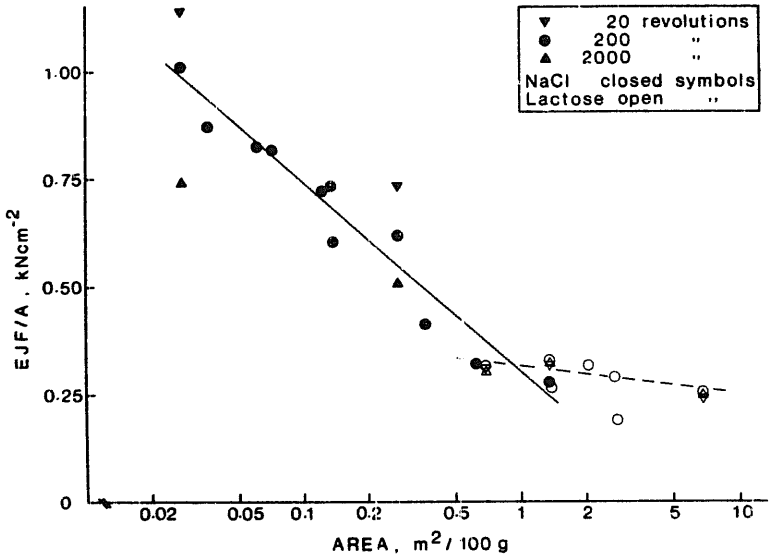

Fig. 2. Ejection force (EJF/A) vs surface area of sodium stearyl fumarate in 100 g tablet mixture. The tablets were compressed at 200 MPa maximum upper punch pressure after admixing the lubricant in various particle sizes and concentrations.

greater specific surface area of magnesium stearate as the lubricants were equally effective at the 1% level.

Adhesion to metal surfaces

Picking problems for lactose tablets were more pronounced at low pressures as expected (Table 3). The adhesion to the punches was reduced by increasing concentrations and surface areas of sodium stearyl fumarate. The greater the ratio between the lubricant surface area and the lactose surface area, the less marked was the picking problem. Increased mixing time reduced the adhesion to the punches further, see Table 3, although the friction measurements were not affected (Fig. 2). Sodium stearyl fumarate was almost as efficient as magnesium stearate as an antiadhesive (Table 4). There was generally a poor correlation between the friction estimates and the adhesion scores.

Tensile strength

All tablets showed normal tensile failure in the hardness tester. Both the concentration and the particle size of sodium stearyl fumarate influenced the tensile strength similarily to the friction. Fig. 3 shows the relationship between the tensile strength and the surface area of the lubricant. Sodium stearyl fumarate appears to differ from magnesium stearate, as the particle size of the latter lubricant had little influence on the tablet strength (Shotton and Lewis, 1964; Bolhuis et al., 1975).

Prolonged mixing with sodium stearyl fumarate reduced the strength of sodium chloride tablets but not of lactose tablets (Fig. 3), similar to the result reported for sodium stearate (Bolhuis and Lerk, 1977) and magnesium stearate (Ragnarsson et al., 1976: Lerk et al., 1977).

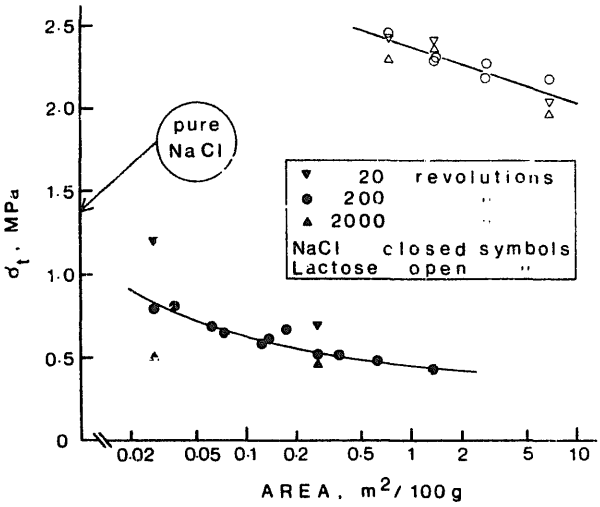

Fig. 3. Tensile strength (σ_t) vs surface area of sodium stearyl fumarate in 100 g tablet mixture. The sodium chloride and lactose tablets were compressed at 200 and 150 MPa maximum upper punch pressure, respectively, after admixing the lubricant in various particle sizes and concentrations.

Those materials which were affected by magnesium stearate were also similarily affected by sodium stearyl fumarate (Table 4), although to a lesser extent. The increase of tablet strength observed with calcium phosphate granulate and lactose when lubricants were added could be ascribed to the reduced friction, i.e. the severe adhesion of the unlubricated materials to the die wall caused great stresses during ejection which reduced the strength.

Disintegration

The tablets of sodium chloride and lactose without disintegrants did not disintegrate

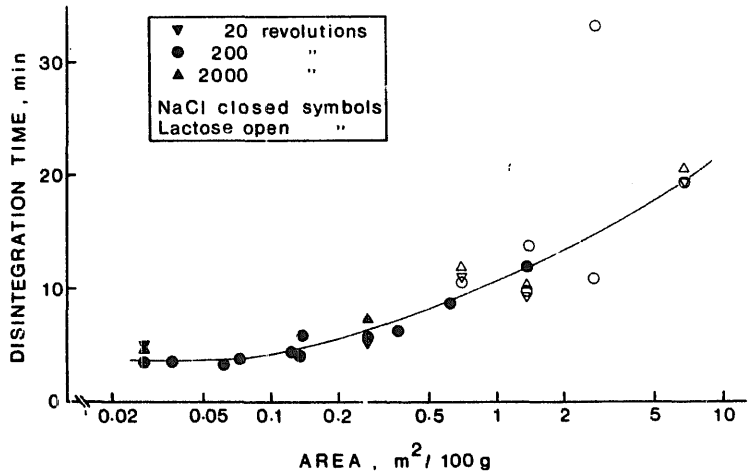

Fig. 4. Disintegration time vs surface area of sodium stearyl fumarate in 100 g tablet mixture. The tablets were compressed at 200 MPa maximum upper punch pressure after admixing the lubricant in various particle sizes and concentrations.

but dissolved from the surface. As with the friction and the tensile strength, the 'disintegration time' was related to the total surface area of the lubricant (Fig. 4). At very high lubricant concentrations, 10% of size fraction No. 4, the 'disintegration' was slower than expected and this may be due to the significant amount of the poorly soluble lubricant in the tablet.

The tablets containing a disintegrant (Table 4) disintegrated in the usual way and this process was generally slightly affected by the lubricants. The hydrophobizing effect was most pronounced in the tablets of plain sodium chloride or lactose. Both magnesium stearate and sodium stearyl fumarate gave such an effect.

The mixing time with sodium stearyl fumarate had no influence on the 'disintegration time' for either sodium chloride or lactose (Fig. 4). In this respect sodium stearyl fumarate differs from magnesium stearate, as mixtures of sodium chloride and magnesium stearate gave increasing disintegration (Ragnarsson et al., 1976) and dissolution times (Bolhuis et al., 1975) with increasing mixing time.

CONCLUSIONS

Sodium stearyl fumarate is an effective tablet lubricant and reduces the friction to about the same degree as magnesium stearate. It appears slightly less effective to counteract the adhesion to the punches. It affects the disintegration time and the tablet strength in a similar way as magnesium stearate.

The particle size of sodium stearyl fumarate is of great importance for all these effects and they correlate better to the surface area of added lubricant than to the actual amount. A micronized lubricant is more efficient than a coarse fraction and it is important that the surface area is standardized to obtain reproducible effects.

Prolonged mixing with sodium stearyl fumarate appears to improve the lubricating and the antiadhesive effect with less negative effects on the disintegration than magnesium stearate. The tablet strength may be reduced by prolonged mixing. In formulations where magnesium stearate causes problems sodium stearyl fumarate may be a good alternative.

ACKNOWLEDGEMENT

We are very grateful to Miss Karin Malmqvist, Uppsala, for preparing the lubricant size fractions.

REFERENCES

Bolhuis, G.K., Lerk, C.F., Zijlstra, H.T. and de Boer, A.K., Film formation by magnesium stearate during mixing and its effect on tableting. Pharm. Weekbl., 110 (1975) 317–325.

Bolhuis, G.K. and Lerk, C.F., Filmbildung von Tablettenschmiermitteln während des Mischvorganges von Feststoffen. Acta Pharm. Technol., 23 (1977) 13–20.

Fell, J.T. and Newton, J.M., The tensile strength of lactose tablets. J. Pharm. Pharmacol., 20 (1968) 657–659.

Food Chemical Codex, 2nd edn. National Academy of Sciences, Washington, D.C., U.S.A., 1972, pp. 773–775.

Hölzer, A.W. and Sjögren, J., Comparison of methods for evaluation of friction during tableting. Drug Dev. Ind. Pharm., 3 (1977) 23–37.

Hölzer, A.W. and Sjögren, J., The influence of the tablet thickness on measurements of friction during tableting. Acta Pharm. Suec., 15 (1978) 59–66.

Lerk, C.F., Bolhuis, G.K. and Smedema, S.S., Interaction of lubricants and colloidal silica during mixing with excipients. Pharm. Acta Helv. 52 (1977) 33–39.

Levy, G. and Gumtow, R.H., Effect of certain tablet formulation factors on dissolution rate of the active ingredient III. Tablet lubricants. J. Pharm. Sci., 52 (1963) 1139–1144.

Lindberg, N.-O., Evaluation of some tablet lubricants. Acta Pharm. Suec., 9 (1972) 207–214.

Pfizer, Information Sheet No. 2001, Pruv™ (Sodium Stearyl Fumarate), Pfizer Chemical Sales Division, July 1964, New York, N.Y., U.S.A.

Pfizer Information Sheet No. 2013, Pruv® for tablet lubrication, Pfizer Chemical Division, November 1967, New York, N.Y., U.S.A.

Ragnarsson, G., Sjögren, J. and Hölzer, A.W., The influence of concentration and mixing time for magnesium stearate on tablet friction, strength and disintegration. Paper presented at the Annual Swedish Pharmaceutical Congress, 1976, Swedish Academy of Pharmaceutical Sciences, Stockholm, Sweden.

Shotton, E. and Lewis, C.J., Some observations on the effect of lubrication on the crushing strength of tablets. J. Pharm. Pharmacol., 16 (1964) Suppl. 111 T-120 T.