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Improvement of lubrication capacity of sodium benzoate: effects of milling and spray drying

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Summary

The lubrication properties of sodium benzoate were studied and were found highly dependent on its particle size. Milling and spray drying techniques were studied in order to improve the lubrication properties of sodium benzoate. A simple method was applied for the optimisation of particle size of spray-dried sodium benzoate. Both milled and spray-dried sodium benzoate showed far better lubrication properties than 250 μm sodium benzoate particles.

Introduction

During tablet compression process, lubricants decrease friction between particles or granules themselves and between them and the die walls, and prevent sticking or picking to the punch faces, thus facilitating tablet ejection. The type, concentration, method of incorporation, time and conditions of mixing, and efficiency of lubricant affect many properties of the produced tablets such as tablet weight, hardness, disintegration time and even stability (Juslin, 1972).

The magnesium, calcium and zinc salts of stearic acid are the most efficient substances commonly used as lubricants. Unfortunately, those lubricants are water-insoluble; a fact that excludes their incorporation into hypodermic tablets, solution tablets or effervescent tablets where a clear final solution is desired. There are, however, relatively few lubricants, antiadherents and glidants which are non-toxic, tasteless and water-soluble.

Sodium benzoate has a modest lubrication capacity, thus it must be used in a high concentration. On the other hand, siliconized sodium benzoate in combination with polyethyleneglycol was reported to be an efficient lubrication system for effervescent tablets (Cordoba-Espinosa, 1983). Furthermore, sodium benzoate was found to possess the worst lubrication capacity, although it has best water solubility, among some water soluble lubricants (Saleh et al., 1984).

A micronized lubricant is more efficient than a coarse fraction and it is better to take into consideration the surface area of the added lubricant

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than its actual amount (Hölzer and Sjögren, 1979). The objectives of this work were to try out the improvement of lubrication properties of sodium benzoate, a water-soluble lubricant with a modest lubrication capacity, through two manners of treatment: firstly, milling in order to increase surface area, hence improve lubrication efficiency, and secondly, spray-drying to obtain in addition to the large surface area, free-flowing individual spherical particles of sodium benzoate and studying its resultant lubrication properties. The application of the direct simplex method of optimisation to adjust the conditions of the spray drying process was also one of the purposes of this study.

Materials and Methods

Materials

- Sodium benzoate (Prolabo, France).
- Polyethyleneglycol (PEG) 6000 (Merck, Darmstadt, F.R.G.).
- Rhodorsil (silicon oil) fluid 47 V 5000 C (Rhone Poulenc, France).
- Tween 80: polyoxyethylenated sorbitan monooleate (Merck, Darmstadt, F.R.G.).
- Emdex: spray-crystallized maltose dextrose (Edward Menell Co., Inc., New York, U.S.A.).
- Tablettose: direct compressible lactose (Seppic, France).

Equipment

- Forplex F00 hammer mill (Boulogne Billancourt, Paris, France).
- Niro Atomizer (Niro Atomizer Ltd., Copenhagen, Denmark) spray dryer fitted to an air compressor (Maco Meudon type FP-507) (Maco Meudon, France) and a peristaltic pump (Masterflex) (Cole-Parmer, Chicago, U.S.A.).
- JSM-840 scanning electron microscope (Jeol, Tokyo, Japan).
- Locally made apparatus for the determination of the angle of repose.
- Locally made flow balance equipped with strain gauges and fitted to a UV recorder to measure the flow rate.
- Measuring cylinder, 100 ml capacity, for the determination of bulk density.
- Turbula T2A mixer (Bachofen Maschinenfabrik, Basel, Switzerland).
- Instrumented tablet machine (single punch Korsch EK/O) (Korsch, Berlin, F.R.G.) fitted with 12 mm flat punches and attached to a system of measurement and registration.
- Erweka TBT hardness tester (Erweka Apparatbau F.R.G.).
- Primax mixer (Kl. Kupper, Labor- und Elektronische Geräte, Swisttal F.R.G.).
- Set of sieves (Prolabo, France), and an electric shaker (EML, F.R.G.).

Methods

Size separation of sodium benzoate. Sodium benzoate was milled in a simple Primax unit and the resultant powder was put on the top sieve of a set of sieves having the following decreasing order of sieve opening: 250 μm, 125 μm, 80 μm, 40 μm, receiver. The sieves were shaken for 10 min and the sodium benzoate fractions retained on the 125 μm, 80 μm, 40 μm and receiver were collected and considered to have 250 μm, 125 μm, 80 μm and 40 μm particle sizes, respectively. It is worth mentioning that in reality, the mean particle diameter of each fraction will be less than the given values but these values were given for easiness of comparison.

Milling of sodium benzoate. Sodium benzoate was milled in a hammer mill working at a speed of 15000 rpm.

Spray drying of sodium benzoate. Solutions of sodium benzoate were prepared by dissolving sodium benzoate in distilled water in the needed concentration levels. Sodium benzoate solutions were fed to the spray dryer working under the conditions that will be mentioned later. In case of including PEG, it was dissolved in a part of distilled water and added to the dissolved sodium benzoate, then completed to the required volume, whereas in the case of silicon oil, it was mixed firstly with Tween 80 and then gradually diluted with solution of sodium benzoate to ensure complete miscibility and distribution of silicon oil in the solution.

Particle shape and size. Particle shape was inspected by scanning electron microscopy and microphotographs were taken to enable the compari-

TABLE 1

Effect of particle size on the lubrication properties of sodium benzoate (5%) tested on Tablettose

Part. size	Angle of repose	Bulk density (g/cm)		Flow rate (g/s)	E.F.%	R.F. %	R	Compression difficulties
		Before tapping	After tapping					
250 μm	47°	0.56	0.68	4.62	9.12	3.61	0.72	impossible to compress
125 μm	44°	0.56	0.69	4.64	7.03	2.89	0.77	difficult
80 μm	46°	0.58	0.70	4.61	5.59	2.62	0.78	difficult
40 μm	48°	0.58	0.69	4.59	5.31	2.30	0.81	difficult

E.F., ejection force; R.F., residual force; R, force transmission index.

son between the different products and measure the particle size by a photographic counting method.

Flow rate. The flow rate acquired by Tablettose upon mixing with 5% w/w of the different lubricants in a Turbula mixer for 5 min at 25 rpm was measured using a locally made recording powder flowmeter consisting of a hopper, a strain gauges balance and a UV recorder. The apparatus is similar to that described previously (Gold et al, 1966). 100 g of each mixture was put into the funnel of the apparatus; then let to pass through the orifice into the receiver of the balance. From the obtained records, the flow rate in g/s was calculated.

Angle of repose. The angle of repose of Tablettose mixed with 5% w/w of the different lubricants in a Turbula mixer for 5 min at 25 rpm was investigated as described elsewhere (Saleh and Stamm, 1988).

Bulk density. The acquired bulk density of Tablettose mixed with 5% w/w of the different lubricants in a Turbula mixer under the conditions mentioned before was determined as described previously (Saleh and Stamm, 1988) and the Hausner factor was calculated.

Preparation and evaluation of tablets. Tablets of either Tablettose or Emdex were compressed after being mixed as mentioned before with the appropriate amount of lubricant in an instrumented tablet machine which permits to study the *R* value (force transmission index), the ejection force and the residual force. The procedure for the compression of tablets and their evaluation with regard to uniformity of weight and hardness was the same as described elsewhere (Saleh and Stamm, 1988).

Results and Discussion

Effect of particle size on the lubrication properties of sodium benzoate

The separated size fractions of sodium benzoate were studied as lubricants for Tablettose tablets. The effect of particle size on the lubrication properties as measured through the effect of lubricant on the angle of repose, bulk density, flow rate, ejection force, residual force and *R* value (force transmission index calculated by dividing the force at the level of the lower punch by the force at the level of the upper punch) of Tablettose. The above mentioned parameters were used by many authors to judge the efficiency of lubricants such as (Lewis and Shotton, 1965; Manna and Shotton, 1970; Juslin, 1972; Linderberg, 1972; Graf et al., 1981). Table 1 summarises the effect of particle size on these lubrication parameters.

From Table 1, it could be seen that the differences in angle of repose, bulk density and flow rate were not significant but it was noticed that when the particle size was decreased, the percentage ejection force and the percentage residual force were lower and the force transmission index (*R*) was higher. This can also be seen from Figs. 1–3 which demonstrate the effect of particle size

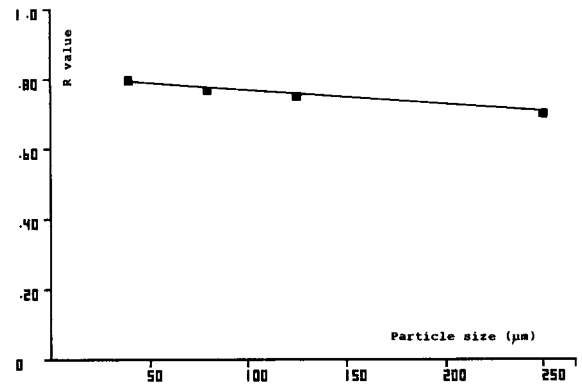

Fig. 1. Effect of particle size of sodium benzoate on the force transmission index (R).

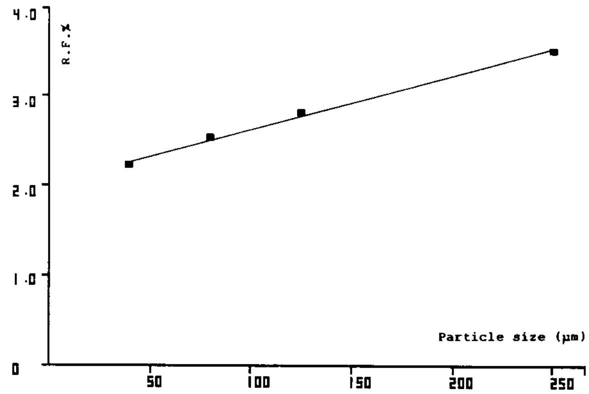

Fig. 3. Effect of particle size of sodium benzoate on the residual force percent (R.F.%).

on force transmission index (R), percentage ejection force and percentage residual force, respectively. These results indicate the correlation between particle size and lubrication properties and show that the smaller the particle size the better the distribution and utilization of compression force. Similar results were previously reported (Hölzer and Sjögren, 1979). With regard to the difficulties encountered upon compression, it is worth mentioning that it was impossible to continue compression of Tablettose tablets lubricated with 5% w/w of 250 µm sodium benzoate while the difficulties decreased upon decreasing the lubricant particle size. These results pointed out the importance of particle size on the lubrication properties and led to the consideration of the minute particle size as a researched objective in the optimisation of spray-drying conditions.

Optimisation of particle size of spray-dried sodium benzoate.

Many factors may affect the particle size of the spray-dried products. The most important factors that we have considered to affect particle size of spray-dryed sodium benzoate were: air pressure which affects the rotation speed of the spraying disc, inlet temperature, liquid feed rate controlled

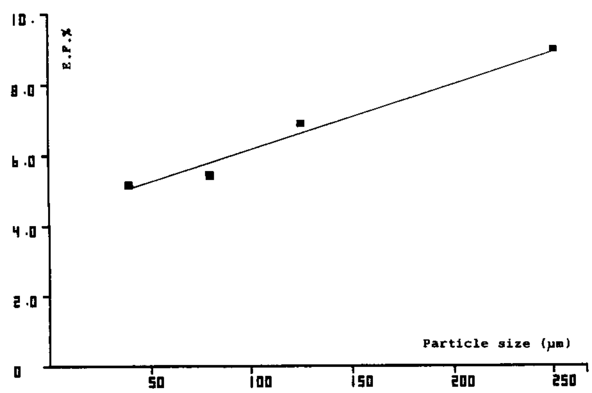

Fig. 2. Effect of particle size of sodium benzoate on the ejection force percent (E.F.%).

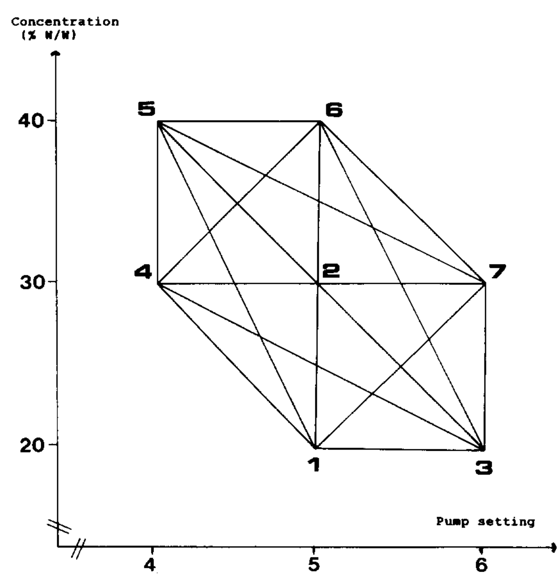

Fig. 4. Simplex optimisation of the concentration and the feeding rate of sodium benzoate solution.

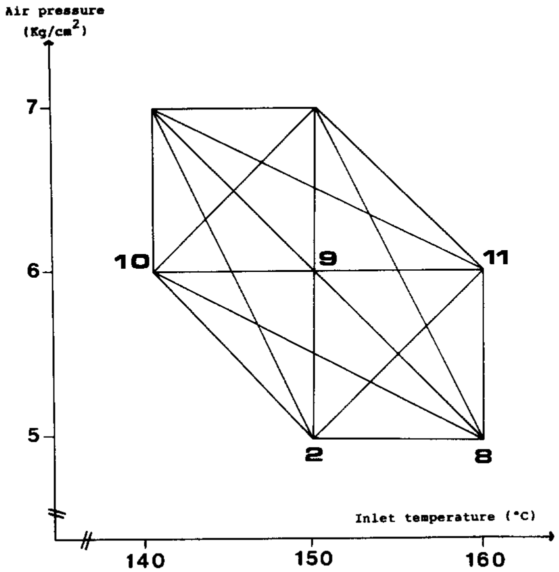

Fig. 5. Simplex optimisation of the air pressure and inlet temperature of spray-dried sodium benzoate.

by pump setting and concentration of sodium benzoate solution. We have applied an optimisation technique in order to obtain the smallest particle size of spray-dried sodium benzoate with the least number of experiments. The early published (Spendley et al., 1962), recently reviewed (Porte et al., 1984) simplex method of optimisation was studied. The application of methods of optimisation in the field of pharmaceutical research has increased especially with the introduction of computers in this domain (Nelder and Mead, 1965; Bindschaedler and Gurny, 1982; Chariot and Ser, 1983; Briquet et al., 1986).

Figs. 4 and 5 represent the constituted simplex which we have divided into two steps. In the first step (Fig. 4), we fixed the inlet temperature at 150 °C and air pressure at 5 kg/cm^2 while the concentration of sodium benzoate solution and its feeding rate were interchanged. From point no. 2 in Fig. 4 and Table 2, the optimum concentration of sodium benzoate solution that gave rise to the smallest particle size was found to be 30% w/w fed at a rate of 31 ml/min (pump setting 5). In the second step demonstrated by Fig. 5, the concentration of sodium benzoate solution was fixed at 30% w/w and the feeding rate at 31 ml/min, while air pressure and inlet temperature were changed.

From Fig. 5 and Table 2, the point corresponding to the smallest particle size was point 9 and the working conditions at this point were considered the optimum conditions that led to an optimum particle size of the spray-dried sodium benzoate. These conditions were:

- concentration of sodium benzoate: 30% w/w;
- feeding rate: 31 ml/min (pump setting 5);
- inlet temperature: 150 °C;
- air pressure: 6 kg/cm^2.

These conditions were kept constant during the combined spray-drying of sodium benzoate with

TABLE 2

Optimisation of the particle size of spray-dried sodium benzoate

Number of experiment	Air pressure (kg/cm)	Inlet temperature (°C)	Pump setting	Liquid feed (ml/min)	Concentration (%)	Mean part. (μm)
1	5	150	5	31	20	10.84
2	5	150	5	31	30	10.38
3	5	150	6	38	20	21.10
4	5	150	4	25	30	11.06
5	5	150	4	25	40	14.32
6	5	150	5	31	40	18.12
7	5	150	6	38	30	11.58
8	5	160	5	31	30	13.66
9	6	150	5	31	30	8.62
10	6	140	5	31	30	10.16
11	6	160	5	31	30	8.90

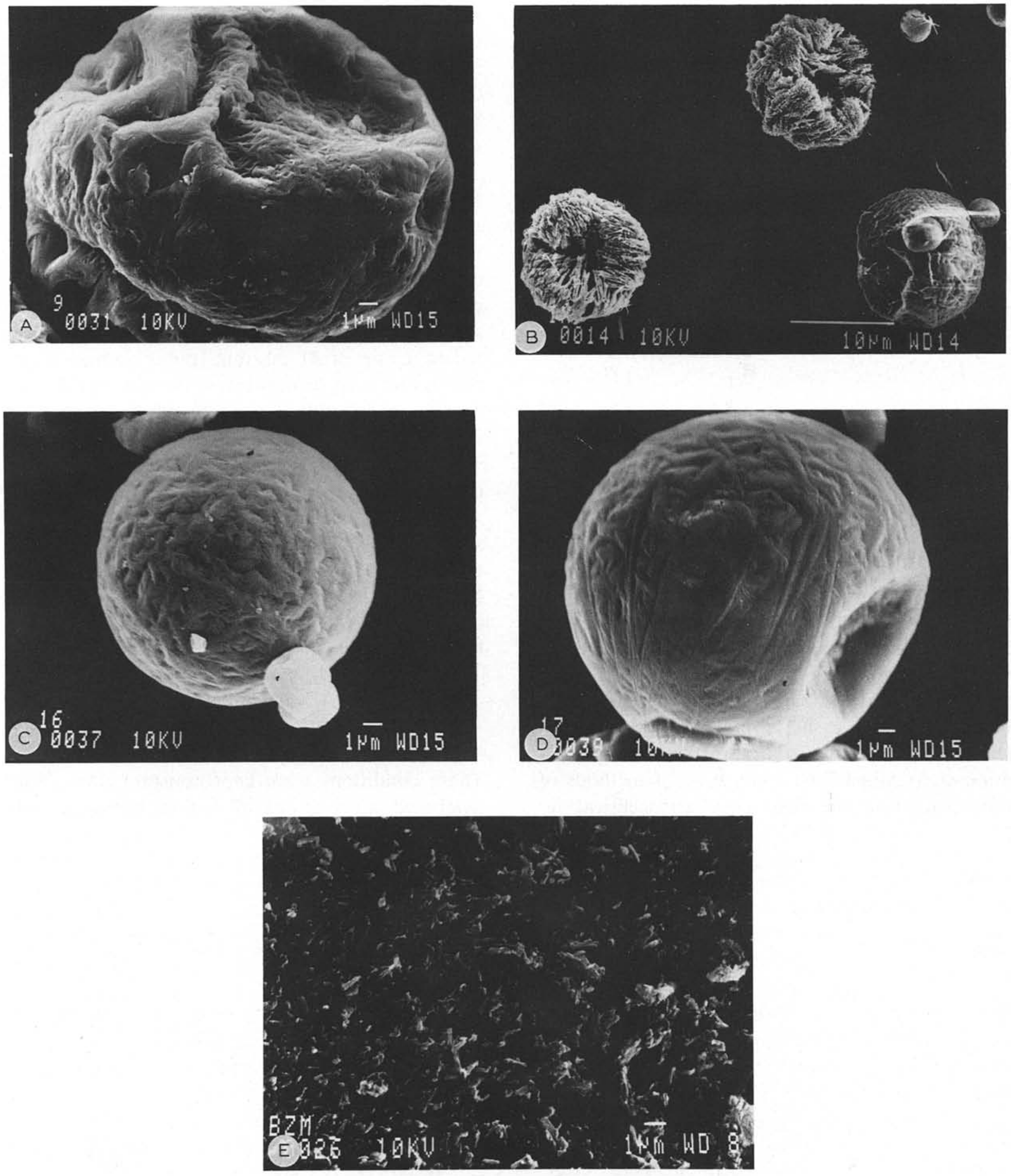

Fig. 6. Microphotographs of spray-dried and milled sodium benzoate. A: sodium benzoate spray-dried alone; "S.D.1". B: sodium benzoate spray-dried with 20% PEG 6000; "S.D.2". C: sodium benzoate spray-dried with 1% silicon oil; "S.D.3". D: sodium benzoate spray-dried with 20% PEG 6000 and 1% silicon oil; "S.D.4". E: sodium benzoate milled.

TABLE 3

Effect of spray-drying and milling techniques on the lubrification properties of sodium benzoate

Sodium benzoate	Angle of repose	Bulk density (g/cm)		H.F.	Flow rate g/s	E.F.%	R.F.%	R
		Before tapping	After tapping					
250 μm	47°	0.56	0.68	1.23	4.62	9.12	3.61	0.72
S.D.1	50°	0.56	0.70	1.26	3.78	5.20	2.60	0.82
S.D.2	50°	0.57	0.72	1.28	3.94	4.95	2.97	0.82
S.D.3	50°	0.57	0.73	1.29	3.94	5.05	3.03	0.80
S.D.4	49°	0.58	0.73	1.27	3.93	5.11	3.28	0.80
Milled	48°	0.54	0.66	1.23	3.90	4.69	2.20	0.84

S.D.1, Sodium benzoate spray dried alone; S.D.2, Sodium benzoate spray dried with 20% PEG 6000; S.D.3, Sodium benzoate spray dried with 1% silicon oil; S.D. 4, Sodium benzoate spray dried with 20% PEG 6000 and 1% silicon oil; H.F., Hausner factor.

PEG 6000 (3 proportions were tested, 5, 10 and 20% but 20% w/w was the best), dimethylpolysiloxan (1% w/w in addition to 0.5% w/w of Tween 80 to aid the miscibility) and combined PEG and silicon oil (the same proportions as the individuals).

Evaluation of milled and spray-dried sodium benzoate

The particle shape as seen from the microphotographs of scanning electron microscope were found to be uniform spherical in case of spray dried sodium benzoate with the smoothest surface and most spherical form in case of combined spray drying of sodium benzoate and silicon oil. Milled sodium benzoate was found to have the shape of very thin platelets (mean particle size 5 μm calculated by particle counting method) as seen in Fig. 6.

Table 3 summarises the lubrication properties of milled and spray-dried sodium benzoate compared to 250 μm sodium benzoate. There was no great difference in the measured values of angle of repose of Tablettose using the different lubricants. On the other hand, spray-dried sodium benzoate showed higher bulk density than milled or 250 μm varieties. Hausner factor (H.F.) as a parameter of compressibility (Sucker, 1982) was found to be higher in the case of spray-dried sodium benzoate than in the case of milled or 250 μm benzoate which indicates that spray-dried sodium benzoate improves the compressibility of Tablettose.

With regard to the flow rate of Tablettose mixed with 5% of the different lubricants, Table 3 shows no great difference between milled and combined spray-dried sodium benzoate with additives while the latter showed better flow properties than sodium benzoate spray-dried alone.

Table 3 shows also the ejection and residual forces in percent. Milled sodium benzoate showed somewhat smaller ejection and residual forces than spray-dried, while the two showed great diminution especially in ejection force compared to 250 μm sodium benzoate. The two techniques led also to a highly improved force transmission as indicated by the *R* values in Table 3.

Induced filling capacity (I.F.C.)

In addition to the parameters, compared above, of lubrication, die-filling during compression was noticed through fixing die capacity (position of the lower punch) during the compression of Emdex lubricated using the different types of benzoate as well as 0.5% magnesium stearate. We have calculated the percentage increase in tablet weight upon changing the lubricant and considering the weight of Emdex tablets lubricated using magnesium stearate as corresponding to 100% filling capacity. The induced filling capacity % and its effect on hardness of tablets was were investigated in case of the different lubricants as shown in Table 4.

Spray-dried sodium benzoate showed higher I.F.C. than milled sodium benzoate. 6% w/w spray-dried sodium benzoate showed higher I.F.C.% even than magnesium stearate. The hardness of the produced Emdex tablets correlated well with the I.F.C.%, i.e. the higher the I.F.C.% the harder the tablets obtained. The higher values

TABLE 4

Induced filling capacity (I.F.C.%) of milled and spray-dried sodium benzoate compared to magnesium stearate and its effect on hardness of EMDEX tablets

	Magnesium stearate 0.5%	milled sodium benzoate 5%	S.D.1		S.D.2		S.D.3		S.D.4	
			5%	6%	5%	6%	5%	6%	5%	6%
Mean weight g	0.562	0.482	0.545	0.573	0.561	0.566	0.570	0.574	0.566	0.574
I.F.C.%	100	85.7	97	102	99.7	100.7	101.3	102.1	100.7	102.1
Hardness (kg) *	6.38	3	5.70	8.6	5.63	5.83	6.55	7.25	4.53	5.83

* Hardness measured directly after compression

of I.F.C.% in case of spray-dried sodium benzoate can be explained on the basis of its smooth spherical shape of particles as shown in Fig. 6. Spray-dried sodium benzoate combined with silicon oil had the smoothest surface and led to the highest I.F.C.% when used in 5% w/w (Table 4). The smooth surfaces of spray-dried lubricant facilitate the sliding of particles and enhance the flowability and die filling. This may be also the principal cause of the increased values of H.F. (Table 3) in case of spray-dried sodium benzoate especially in case of that spray-dried combined with silicon oil. Moreover, the smooth spherical shape of these products facilitate the arrangement of particles leading to high after-tapping bulk density.

Furthermore, Table 5 summarizes the difficulties encountered during the compression of Tablettose or Emdex tablets lubricated using different sodium benzoate or magnesium stearate. The Table indicates the impossibility of compressing tablets using 5% of 250 μm sodium benzoate as lubricant due to difficulties including sticking, picking, striation and expansion (all manifestations of insufficient lubrication). 5% w/w of milled sodium benzoate was a good lubricant for both Tablettose and Emdex tablets. On the other hand, 5% w/w of some spray-dried sodium benzoate ensured enough lubrication in case of Emdex tablets whereas 6 or 7% w/w were necessary in case of Tablettose tablets. The combined spray-dried sodium benzoate (containing additives) showed less compression difficulties than sodium benzoate sprayed alone.

TABLE 5

Tableting properties of milled and spray-dried sodium benzoate

Observations	Mg. St. 0.5%	250 u 5%	Micro		S.D. 1					S.D. 2					S.D. 3					S.D. 4				
			E	T	E		T			E		T			E		T			E		T		
			5	5	5	6	5	6	7	5	6	5	6	7	5	6	5	6	7	5	6	6	6	7
Very difficult to compress		*																						
Striation		*																						
Sticking		*			*		*			*														
Picking		*			*					*		*	*				*	*				*		
Little picking								*			*			*										
Expansion		*																						
Good tablets			*	*				*	*		*			*					*	*	*		*	*
No problem	*					*									*	*								

E, Emdex; T, Tablettose; 5, 6, 7 mean 5%, 6%, 7%.

Conclusions

Lubrication properties of sodium benzoate depend greatly on its particle size and the smaller the particle size the better the lubrication properties.

Either milling or spray-drying represent a good enhancement of the modest lubrication properties of sodium benzoate. The two techniques highly improved the lubrication capacity of sodium benzoate through increasing flowability, decreasing friction and overcoming compression difficulties.

Milled sodium benzoate showed better antiadherent properties than spray-dried sodium benzoate while the latter imparted better flowability and die filling of Tablettose or Emdex.

Combined spray-dried sodium benzoate (containing other additives showed better lubrication properties than sodium benzoate spray-dried alone.

Application of the simplex optimisation technique for the optimisation of particle size of spray-dried sodium benzoate was concluded to be a rapid method that avoids the trial and error technique and decreased the amount of experimental work required.

References

Binschaedler, C. and Gurny, R., Optimisation de formulations pharmaceutiques par la méthode du simplex au moyen d'une calculatrice TI59, *Pharm. Acta Helv.*, 57 (1982) 251–255.

Briquet, F., Brossard, C., Ser. J. and Duchêne, D., Optimisation de la formulation par extrusion-sphéronisation de microgranules matricielles à libèration prolongée. *S.T.P. Pharma* 2 (1986) 986–994.

Chariot, M. and Ser, J., Optimisation de la granulation en lit fluidisé, *Labo-Pharma Prob. Tech.*, 31 (1983) 456–460.

Cordoba-Espinosa, J. *Nouvelle Technologie des Formes Effervescentes.* Ph.D. thesis, University of Montpellier, 1983, France.

Gold, G., Duvall, R.N. and Palermo, B.T., Powder flow studies. I Instrumentation and applications. *J. Pharm. Sci.*, 55 (1966) 1333–1336.

Graf, E., Sakr, A. and Nada A., Studies on the direct compression of Pharmaceuticas, 5-Pancreatin, c) evaluation of some lubricants and their effect on amylase and lipase activities., *Pharm. Ind.*, 43 (1981) 282–286.

Hölzer, A.W. and Sjögren, J., Evaluation of sodium stearyl fumarate as a tablet lubricant. *Int. J. Pharm.*, 2 (1979) 145–153.

Juslin, M., *Studies on Tablet Compression with Special Reference to the Use of Lubricants.*, Pharmaceutical thesis, University of Helsinki, 1972, Helsinki, Finland.

La Manna, A. and Shotton, E., The effect of polytetrafluorethylene (FLUON) on the characteristics of compressed tablets. *Farmaco*, 25 (1970) 689–699.

Lewis, C.T. and Shotton, E., Some studies of friction and lubrication using an instrumented tablet machine. *J. Pharm. Pharmacol.*, 17 Suppl., (1965), 71S-81S.

Lindberg, N.O., Evaluation of some tablet lubricants, *Acta Pharm. Suec.*, 9 (1972) 689–699.

Nelder, J.A. and Mead, R., A simplex method for function minimisation, *Comput. J.*, (1965) 308–313.

Porte, C., Debreuille, W. and Delacroix, A., La methode simplex et ses dérivées: application à l'optimisation dans le laboratoire de developpement en chimie. *Acta. Chim.*, (1984) 45–54.

Saleh, S.I., Aboutaleb, A., Kassem, A.A. and Stamm, A., Evaluation of some water soluble lubricants for direct compression. *Labo-Pharma*, 32 (1984) 588–591.

Saleh, S.I. and Stamm, A., Evaluation of some directly compressible L-ascorbic acid forms. *S.T.P. Pharma,* (1988) 10–14.

Spendley, W., Hext, G.R. and Himsworth, F.R., Sequential application of simplex designs in optimisation and evolutionary operations. *Technometrics*, 4 (1962) 441–461.

Sucker, H., Test methods for granulates. *Pharm. Ind.*, 44 (1982) 312–316.