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LUBRICANTS AS A FORMULATION FACTOR AFFECTING IN-VITRO PROPERTIES OF DOUBLE COMPRESSED TABLETS

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ABSTRACT

The effect of some lubricants and their concentrations on the in-vitro properties of aspirin tablets as a model of tablets prepared by double compression was studied. The formulated tablets were evaluated using the U.S.P XX official tests and some other selected non-official tests. These tests include: uniformity of weight, uniformity of content, disintegration, dissolution, hardness, friability and thickness. The obtained results showed that all the prepared formulae fulfilled the requirements of such tests. Talc at a concentration of 3% w/w was found to be the most suitable lubricant for the formulation of aspirin tablets. On the other hand, magnesium stearate was found to be the worst lubricant in this study.

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INTRODUCTION

The formulation of a solid dosage form often requires precise processing control of the powder mixture to ensure a volumetric delivery of a homogenous aliquot. Thus, various adjuvants are gravimetrically added to form the bulk mixture to achieve uniform mixing and flow of the powder as in capsule or tablet die filling.

In tablet formulation, a lubricant usually permits resolution of several production problems related to compression. As an essential unit operation in the production of a compressed tablet, lubrication facilitates glidancy of the powders during material flow, eliminates binding of the compact to the die, and minimizes sticking and picking by the punch face surfaces in contact with compressed tablet.

Many studies evaluated different types of lubricants (1-8). Among the various types of lubricants, hydrophobic substances are the most commonly used. In this paper, the effect of some hydrophobic lubricants on the in-vitro properties of tablets prepared by double compression was studied using aspirin as a model.

EXPERIMENTAL

Materials

Aspirin powder (Veb Dutcher, through Al Goumhouria Co. for Trading Medicines, Chemicals & Medical Appliances); Lactose (El-Nasr Pharmaceutical Chemicals Co.,

Abu Zaabal); Maize starch (Alexandria Co. for Pharmaceutical and Chemical Industries); Stearic acid (El-Nasr Pharm. Chem. Co., Abu Zaabal); Talc (Al Goumhouria Co. for Trading Medicines, Chemicals & Medical Appliances); Magnesium stearate (E. Merck, Darmstadt, W. Germany) and Hydrochloric acid 32% (E. Merck, Darmstadt, W. Germany) were used in this study.

Apparatus

Korsch Single Punch Tablet Machine, Type EKo,Erweka, G.m.b.H., W. Germany, with 12 mm flat punch for the slugs and 9 mm slightly concave punch for tablets; Dry Granulator, Type TG 2, Erweka, G.m.b.H., W. Germany; Erweka Disintegration Apparatus, Type ZT4, W. Germany; Erweka Hardness Apparatus, Type TB24, W. Germany; Roche Friabilator, England; Unicam SP 1800 U.V. Spectrophotometer and The Basket Rack Assembly Dissolution Apparatus (9) were employed.

Methods

Preparation of tablets

The different formulae of tablets each containing 300 mg of aspirin are presented in Table 1. All tablet ingredients were passed through a 0.5 mm sieve opening before use. The active ingredient was then mixed thoroughly with half the amounts of both disintegrant and lubricant in an ascending technique using a porcelin morter. The mixture was compressed into flat surface

Table 1. Formulations of Aspirin Tablets

Ingredients	Amount (mg) per each tablet									
Formula No.	1	2	3	4	5	6	7	8	9	10
Aspirin	300	300	300	300	300	300	300	300	300	300
Lactose	16	16	16	16	20	18	12	8	4	-
Maize starch	80	80	80	80	80	80	80	80	80	80
Stearic acid	4	-	-	-	-	-	-	-	-	-
Magnesium stearate	-	4	-	-	-	-	-	-	-	-
Talc	-	-	4	-	-	2	8	12	16	20
Magnesium stearate-talc mixture*	-	-	-	4	-	-	-	-	-	-

* 1 % mixture magnesium stearate-talc , consists of one part of magnesium stearate and nine parts of talc.

tablets (slugs). The prepared slugs were passed through 0.8 mm sieve opening and retained on 0.63 mm sieve opening. The rest of disintegrant and lubricant were added on the retained granules, thoroughly mixed and compressed into tablets.

Evaluation of tablets

Tablets were evaluated using the U.S.P. XX official tests (9) and some other selected non-official tests. These tests include: uniformity of weight, uniformity of content, disintegration time, dissolution rate, hardness, friability and thickness.

Dissolution procedure

All dissolution studies were carried out using the basket rack assembly at 37°C ± 0.5°C in 900 ml 0.1N HCl. At zero time, one tablet was placed in the basket and the apparatus was operated. At various time intervals, 10 ml samples were withdrawn using a glass pipette fitted with an adaptor containing cotton wool. Fresh volume of the dissolution medium at 37±0.5°C was immediately added to componsate the sample withdrawn. At least three determinations of each formula were performed and the average result was recorded.

Method of analysis

Samples were assayed spectrophotometrically at 278 nm after suitable dilution with 0.1N HCl. Measurements taken at 302 nm showed negligible contribution for the presence of salicylic acid.

Determination drug content

The amount of active ingredient in a single tablet was assayed spectrophotometrically at 278 nm and the average of five determinations was calculated.

RESULTS AND DISCUSSION

In this study, the effect of some commonly used hydrophobic lubricants on the in-vitro properties of aspirin tablets as an example of drugs prepared by double compression was studied. Lubricants used in this study were stearic acid, magnesium stearate, talc and a mixture of magnesium stearate and talc. These lubricants are commonly used in concentrations up to 1% of tablet weight except for talc where we can use concentrations up to 5%, so some formulae (formulae 1-4) of aspirin tablets were prepared containing 1% w/w of these lubricants to study their effects on the in-vitro properties of aspirin tablets. The results of this study showed that tablets which contained 1% talc showed the best results. Further study was made to investigate the effect of different concentrations of this lubricant on the in-vitro properties of aspirin tablets, so other formulae (formulae 6-10) were prepared containing different concentrations of talc.

The results of tests of the uniformity of weight of the prepared formulae of aspirin tablets are shown in Fig. 1. The weight of tablet was represented by a bar indicating at its ends the lower and upper values of the

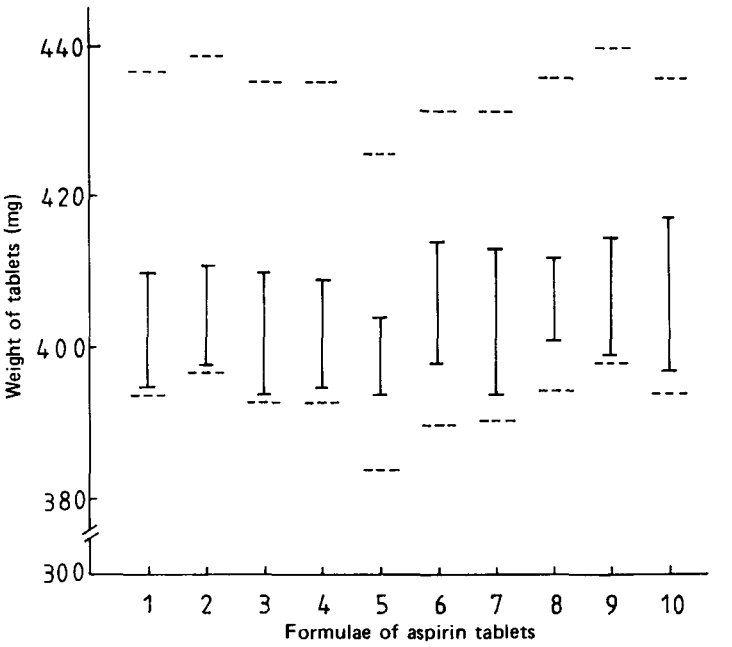

FIGURE 1. Uniformity of weight of different formulae of aspirin tablets.
--- Upper and lower limits for each formula of tablets
I Weight variation for each formula of tablets.

tablets weights. Also, the dotted lines expressed the calculated upper and lower limits of variation for each formula of tablets according to the U.S.P. XX (9). Examination of the data indicated that all the prepared formulae passed the U.S.P. XX test for weight uniformity. All the prepared formulae showed minimum variations in the weights of their tablets. These results were reflected by the minimum values of their standard deviations of weight uniformity (Table 2).

The percent variations in thickness of the different formulae of aspirin tablets are shown in Table 3.

Table 2. Evaluation of Formulated Aspirin Tablets

Formula	S.D. of weight (mg)****	Thickness range (mm)*	Hardness range (Kg)***	Friability (%)***	Disintegration time (sec)**
1	± 0.53	4.77-4.80	6.25-7.00	0.92	18.00
2	± 0.39	4.80-4.85	5.25-6.25	2.85	23.00
3	± 0.55	4.76-4.80	7.25-8.75	1.48	13.00
4	± 0.38	4.75-4.82	6.00-7.25	2.08	20.00
5	± 0.31	4.69-4.75	9.75-12.75	0.84	52.00
6	± 0.50	4.78-4.80	7.75-8.75	1.77	16.00
7	± 0.52	4.73-4.77	6.00-9.75	1.46	12.00
8	± 0.31	4.73-4.77	7.50-9.75	1.35	13.00
9	± 0.55	4.79-4.82	8.50-9.75	1.66	12.00
10	± 0.62	4.75-4.80	8.00-9.75	1.64	12.40

* Each is an average of 5 determinations.

** Each is an average of 6 determinations.

*** Each is an average of 10 determinations.

**** Each is an average of 20 determinations.

Table 3. % Variation in Thickness of Formulated Aspirin Tablets.

Formula	% Variation	S.D.
1	0.63	± 0.02
2	1.04	± 0.02
3	0.84	± 0.02
4	1.46	± 0.03
5	1.27	± 0.03
6	0.42	± 0.01
7	0.84	± 0.02
8	0.84	± 0.02
9	0.63	± 0.01
10	1.05	± 0.02

The results showed that all the prepared formulae met the requirement for thickness set by King (10). Such results proved that changing the type or the concentration of lubricant did not significantly affect tablet thickness.

Hardness is an important parameter used to describe the resistance of tablets to chipping or breaking during handling. The hardness values of the different formulae of aspirin tablets are shown in Table 2. All the prepared formulae met the limit for minimum hardness value of

tablets set by King (10). Neither the type nor the concentration of the used lubricants had an effect on the hardness of the formulated tablets.

Friability, on the other hand was related to the strength of tablets. The results of friability of the formulated tablets are shown in Table 2. Gunsel and Kaning (11), specified a value of 0.8% as an upper permitted value for tablet friability. Although the prepared formulae failed to meet this requirement, they could be considered acceptable as their friability values were higher by a relatively small values.

Hardness has been associated with other properties such as density and porosity, all of which affect the disintegration time of tablets. The disintegration test as specified in the U.S.P. XX (9), was performed on all the formulated tablets. All the prepared formulae met the U.S.P. requirement for disintegration.
Non of the used lubricants had a significant effect on the disintegration time of tablets. Formula 2 which contained 1% w/w magnesium stearate showed slightly prolonged disintegration time than the other formulae,while formula 3 which contained 1% w/w talc showed the shortest disintegration time. These results were in good agreement with some reported studies (12,13). However, some other studies showed little effect for lubricants on the disintegration time (14,15).

Increasing the concentration of talc in formulae 3, 6, 7, 8, 9, & 10 had a little effect on the disintegration time of tablets. This result agreed with that reported by Maly and Jaros (16).

Since several publications have appeared in the literature which have shown that the bioavailability of many drugs is markedly influence by the inert igredients and this effectis also reflected in the in-vitro tests like the "dissolution rate" testing. Therefore the effect of the used lubricants on the dissolution rate of aspirin tablets was studied.

The official monograph of aspirin in the U.S.P. XX (9), stated that, not less than 80% of the labeled amount of acetyl salicylic acid in tablets dissolves in 30 minutes. Table 4 shows that all the prepared formulae fulfilled this requirement.

The effects of 1% w/w different concentrations of different lubricants (formulae 1-4) on the dissolution rate of aspirin from tablets are shown in Fig. 2. The figure also included the dissolution profile of another formula (formula 5) which contained no lubricant for comparison. The dissolution rate was found to be decreased in the following order : formula 3 > formula 1 > formula 5 > formula 4 > formula 2. This result showed that talc and stearic acid enhanced the dissolution rate of aspirin tablets while magnesium

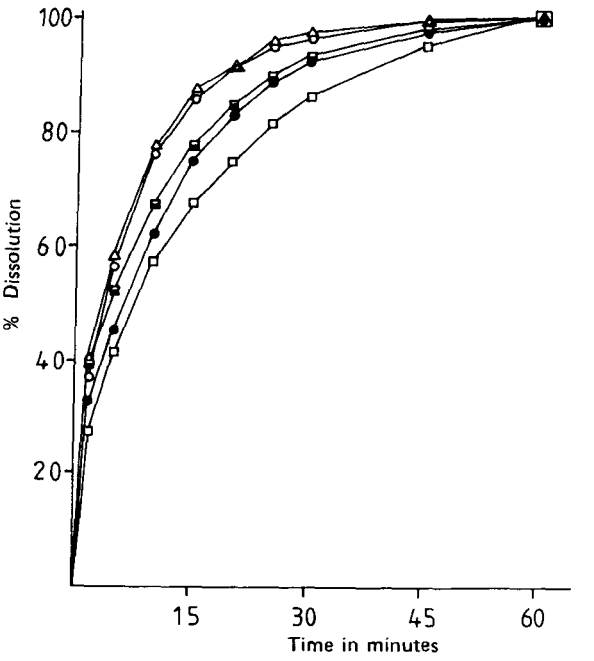

FIGURE 2. Effect of 1% of different lubricants on the dissolution rate of aspirin tablets in 0.1N HCl at 37°C.

○—○ , stearic acid: △—△ , talc:
□—□ , magnesium stearate:
●—● , magnesium stearate-talc mixture:
▣—▣ , no lubricant:

stearate and the mixture of magnesium stearate and talc retarded aspirin dissolution, that was in comparison to the dissolution of tablets contained no lubricant. This result was in a good accordance with several studies (6, 7, 17, 18), in which magnesium stearate showed a retarding effect on the dissolution of drugs from their tablets.

All the studied formulae (1-5) showed regular dissolution behaviour which was reflected by the values of

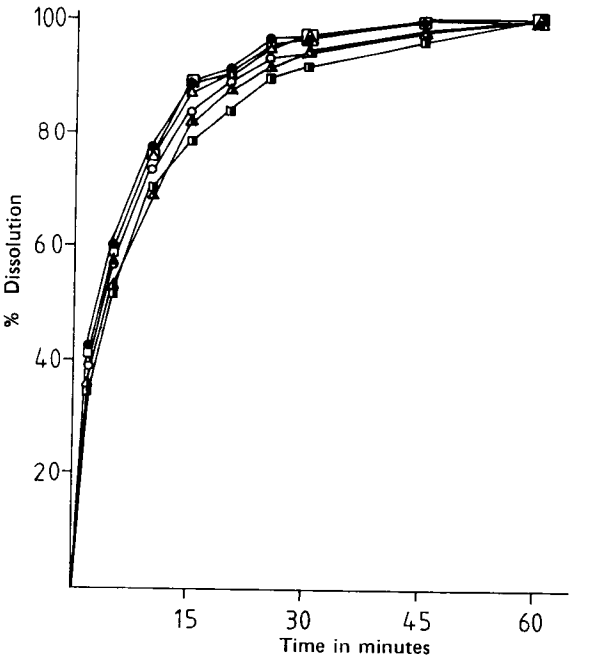

FIGURE 3. Effect of different concentrations of talc on the dissolution rate of aspirin tablets in 0.1N HCl at 37°C.
○—○, 0.5%: △—△, 1%: □—□, 2%:
●—●, 3%: ▲—▲, 4%: ■—■, 5%:

their standard deviations at t_{10}, i.e., the amount dissoluted within 10 minutes (Table 4).

The use of 1% w/w talc as lubricant in the formulation of aspirin tablets was found to decrease the disintegration time and enhance the dissolution rate. Therefore, the effect of different concentrations of talc on the dissolution rate of aspirin was further studied and the results are shown in Fig. 3. It was found that changing the concentration of talc did not significantly affect the dissolution rate of aspirin. Increasing the

Table 4. Percent Drug Dissolved* From Various Formulae of Aspirin Tablets in 0.1 N HCl at 37°C.

Formula	% Dissolved within 10 min. ± S.D.	% Dissolved within 30 min. ± S.D.
1	76.75 (± 4.24)	96.50 (± 1.75)
2	57.27 (± 3.86)	85.93 (± 3.98)
3	76.60 (± 7.46)	96.80 (± 2.84)
4	62.12 (±10.06)	91.83 (± 6.12)
5	66.91 (± 6.90)	93.01 (± 2.64)
6	73.42 (± 1.79)	94.31 (± 2.68)
7	76.00 (± 2.31)	97.14 (± 1.03)
8	76.70 (± 2.30)	97.22 (± 1.00)
9	69.47 (± 6.43)	91.56 (± 2.76)
10	69.08 (± 2.78)	96.71 (± 0.93)

* Each value is the average of three tablets.

concentration of talc from 0.5 up to 3% w/w showed a very slight increase in the dissolution rate of aspirin from tablets. Further increase in talc concentration showed a very slight decrease in the dissolution rate of aspirin. On the other hand, Iranloye and Parrott (19), in their study on the effect of some formulation factors including lubricant concentrations on the dissolution rates of compressed disks of salicylic acid, aspirin and

Table 5. Drug Contents of Formulated Aspirin Tablets.

Formula	% Drug Content*	S.D.
1	100.00	± 1.40
2	97.00	± 0.00
3	98.20	± 0.00
4	96.00	± 1.06
5	96.00	± 1.90
6	99.50	± 1.70
7	97.00	± 0.00
8	96.00	± 0.00
9	96.00	± 0.00
10	96.00	± 0.00

* Each is an average of five determinations.

an equimolar mixture of aspirin and salicylic acid,reported that, the dissolution rates were essentially independent on concentrations of talc as great as 5%. The dissolution rates of the different formulae (6-10) showed regular dissolution behaviour. The values of the standard deviations of these formulae at t_{10} were shown in Table 4.

Finally, the aspirin content in each formula of tablets was evaluated. Table 5 shows that all the

studied formulae complied with the requirement for content uniformity (95-105%) as specified in the official monograph of aspirin in the U.S.P. XX (9).

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