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A COMPARATIVE EVALUATION OF SOME STARCHES AS DISINTEGRANTS FOR DOUBLE COMPRESSED TABLETS

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ABSTRACT

The effect of different types and concentrations of some starches as disintegrants on the properties of aspirin tablets as a model for double compressed tablets was studied. The formulated tablets were evaluated using the U.S.P. official tests and some other selected nonofficial tests. These tests include: uniformity of weight, uniformity of content, disintegration, dissolution, hardness, friability and thickness. Maize starch was found to be the most suitable disintegrant for the formulation of double compressed tablets while rice starch was the worst disintegrant, in this study, as it significantly increased the hardness of tablets and showed a prolonged disintegration time as well as a poor dissolution rate. Increasing

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the starch content of tablets resulted in a marked increase in their dissolution rate.

INTRODUCTION

In modern pharmaceutical manufacturing technology, ever greater stress is being placed on biological availability ... permitting, or even assisting, the medicament to become effectively available in the patient's system. Since it is known that if a swallowed tablet does not effectively disintegrate while in the gastrointestinal tract, dissolution is hindered, if not prevented alltogether, disintegration plays a parmount role in guaranteeing availability.

The full potential value of a compressed tablet is assured only when the tablet dissolves rapidly so that the active portion can effect the desired therapeutic action and in dissolution process, the primary action is disintegration.

Of all the commonly used disintegrating agents, ordinary starch is by far the most widely used material. It is readily available, inexpensive, white, inert, and it often increases capillary action within the tablet sufficiently to accomplish disassociation within required limits.

The physical and chemical properties of the substance have been studied by several workers (1-5). The unique

characteristics of starches derived from wheat, corn, rice and potato have led to their use in tabletting as diluents, binders, disintegrants and lubricants(6-8), although the most important role of starch is that of tablet disintegrant (9).

In this paper, the effect of different types and concentrations of starch on the in-vitro properties of aspirin tablets as a model for double compressed tablets was studied.

EXPERIMENTAL

Materials

Aspirin powder (Veb Dutcher, through Al Goumhouria Co. for Trading Medicines, Chemicals & Medical Appliances); Lactose (El Nasr Pharmaceutical Chemicals Co., Abu Zaabal, Cairo, Egypt); Potato, Wheat, Maize and Rice Starch (Alexandria Company for Pharmaceutical and Chemical Industries, Alexandria, Egypt); Stearic acid(El Nasr Pharmaceutical Chemicals Co.); and Hydrochloric acid (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 convave 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 (10) 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 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 tblets

Tablets were evaluated using the U.S.P. XX official tests (10) and some other selected non-official tests. These tests include: uniformity of weight, uniformity of content, disintegration time, dissolution rate, hardness, friability and thickness.

Table 1. Formulation of Aspirin Tablets.

Ingredients	Amount (mg) per each tablet						
Formula No.	1	2	3	4	5	6	7
Aspirin	300	300	300	300	300	300	300
Lactose	56	56	56	56	76	36	16
Potato starch	40	-	-	-	-	-	-
Maize starch	-	40	-	-	20	60	80
Wheat starch	-	-	40	-	-	-	-
Rice starch	-	-	-	40	-	-	-
Stearic acid	4	4	4	4	4	4	4

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 of 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 different types of starch on the in-vitro characteristics of aspirin as a model for double compressed tablets was studied.

An average concentration (10% w/w) for the concentration range of starch as tablet disintegrant was used. The results showed variable effects for the different types of starch. Therefore, the effect of different concentration of the best effective type of starch (maize starch) on the in-vitro properties of aspirin tablets was also studied.

The results of the uniformity of weight of the prepared formulae of aspirin tablets are shown in Fig. 1. The weight of tablets for each formula was represented by a bar indicating at its ends the lower and upper values of the 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 (10). Examination of the data indicated that all the prepared formulae passed the U.S.P. test for weight uniformity. All the prepared formulae showed a minimum variation in the weights of their tablets. These results were reflected by the minimum values of their standard deviations of weight uniformity (Table 2). These results indicated that neither the type nor the concentration of the used starch were markedly affect the uniformity of weight of the double compressed tablets.

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

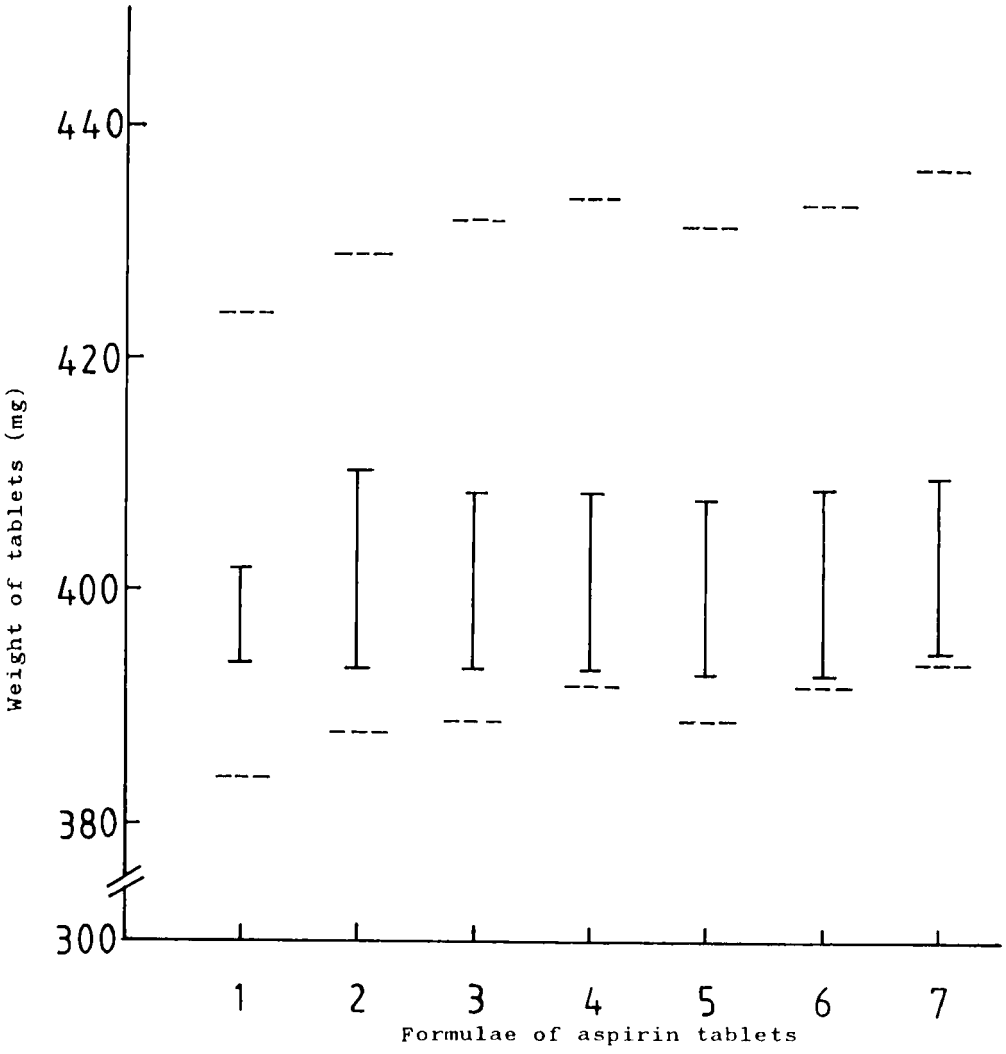

Fig. 1. Uniformity of weight of different formulae of aspirin tablets.

--- Upper and lower limit for each formula of tablets.

I Weight variation for each formula of tablets.

Table 2. Evaluation of Formulated Aspirin Tablets

Formula	S.D.**** of weight (mg)	Thickness* range (mm)	Hardness*** range (Kg)	Friability*** (%)	Disintegration** time (sec)
1	± 0.26	4.70-4.73	8.25-10.00	1.23	75.0
2	± 0.46	4.70-4.77	8.00-10.75	1.20	60.0
3	± 0.36	4.70-4.77	8.00-11.75	1.24	98.0
4	± 0.43	4.77-4.81	10.75-14.25	1.99	360.0
5	± 0.51	4.75-4.78	6.75- 8.25	1.17	192.0
6	± 0.35	4.78-4.81	6.75- 8.00	1.63	28.0
7	± 0.53	4.77-4.80	6.25- 7.00	0.92	18.0

* 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 hickness of Formulated Aspirin Tablets.

Formula	% Variation	S.D.
1	0.64	± 0.01
2	1.49	± 0.03
3	1.49	± 0.04
4	0.84	± 0.02
5	0.63	± 0.02
6	0.63	± 0.02
7	0.63	± 0.02

results showed that all the prepared formulae met the requirement for thickness set by King (11). Such results proved that changing the type or concentration of starch did not significantly affect the flow properties of granules, since, it was reported that the changes in tablet thickness manifested a problem in the flow properties of granules (8).

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 fulfilled the limit for minimum hardness value of tablets previously set by King (11). Formulae 1-4 were prepared using different types of starch at the same concentration. All tablets were compressed at the same pressure. Examination of the results showed that formula 4 which contains 10% rice starch had the highest hardness value in comparison to the other formulae. This indicated that rice starch had a pronounced increasing effect on the hardness of the double compressed tablets. On the other hand, changing the concentration of starch (formulae 2,5,6 & 7) did not affect the hardness of such 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 (8), specified a value of 0.8% as an upper permitted value for tablets friability. Although the prepared formulae failed to fulfill this test, 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 (10) was performed on all

the formulated tablets. All the prepared formulae met the U.S.P. requirement for disintegration except formula 4 for which the disintegration time was greater than 360 seconds (Table 2). The different starches used affected the disintegration time of tablets in the following descending order: rice-wheat-potato-maize, i.e., maize starch was the best disintegrant while rice starch was the least effective disintegrant in this study.

The rate of penetration of fluide into tablets is proportional to the mean pore diameter or porosity (12-14). As porosity or pore diameter increases, rapid fluid penetration and swelling of the disintegrant starch occurs and hence rapid tablet disintegration (12,15,16). This result for the rank order of the studied disintegrants was in a good accordance with the results obtained by different authors (17,18).

Increasing the concentration of disintegrant (Formulae 2, 5,6 & 7) was found to decrease the disintegration time of tablets. This result was in a good accordance with that reported by Higuchi et al. (19) and Levy et al. (20).

Several publications have appeared in the literature which have shown that the bioavailability of many drugs is markedly influenced by the inert ingredients and the manufacturing methods that are used for their preparation. Very often such in-vivo influence are also reflected in the in-vitro tests like the dissolution rate testing for

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	67.24 (± 0.28)	91.93 (± 3.38)
2	68.05 (± 2.67)	91.90 (± 0.83)
3	64.28 (± 8.62)	93.47 (± 4.24)
4	62.03 (±20.80)	91.51 (± 8.70)
5	54.67 (± 1.38)	89.40 (± 1.77)
6	69.78 (± 2.60)	96.34 (± 3.45)
7	76.75 (± 4.24)	96.50 (± 1.75)

* Each value is the average of three tablets.

the oral dosage forms. The dissolution rate test has come to be used as an important method to screen the effect of inert ingredients and the granulation and tableting variables during the preformulation stage, before a final formulation is selected for clinical testing or eventually marketed (21). Therefore, the effect of different types and concentrations of starches on the dissolution rate of aspirin as a model drug for double compressed tablets was studied.

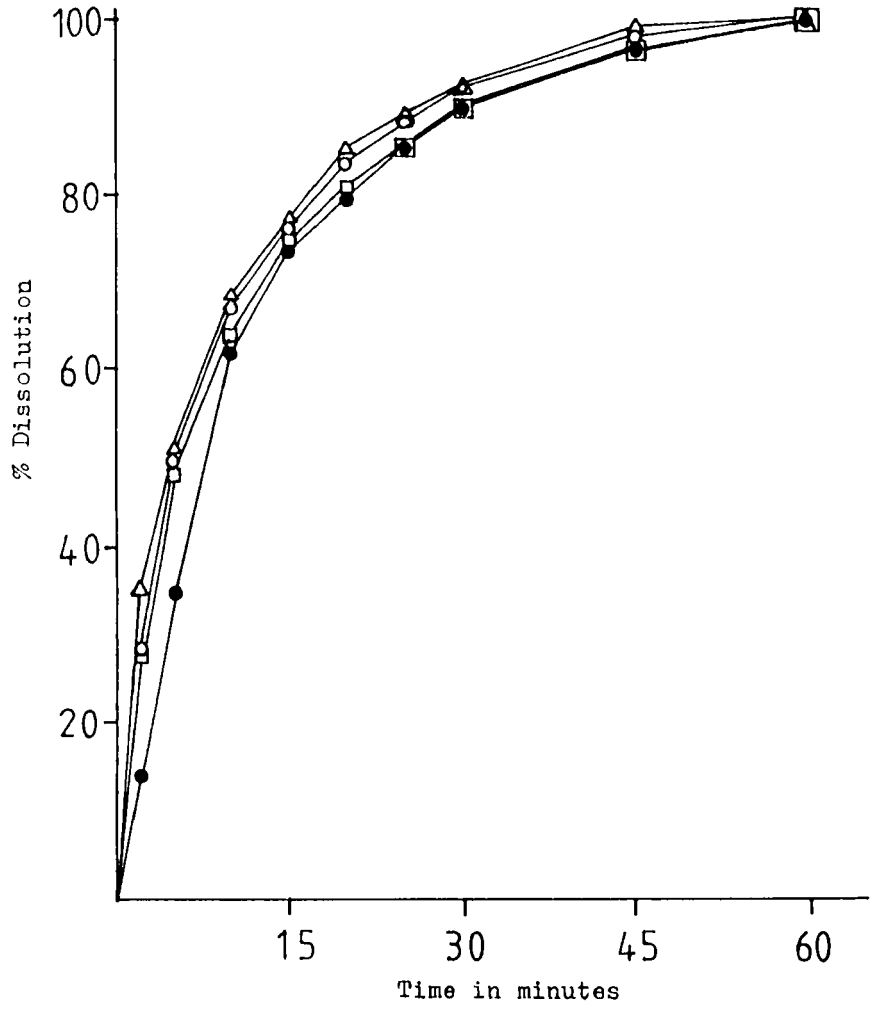

FIGURE 2. Effect of 10% of different disintegrants on the dissolution rate of aspirin tablets in 0.1N HCl at 37°C.

o—o, potato: △—△, maize:
□—□, wheat : ●—●, rice:

The official monograph of aspirin in the U.S.P. XX (10), stated that, not less than 80% of the labeled amount of acetylsalicylic acid in tablets dissolves in 30 minutes. Table 4 shows that all the prepared formulae fulfilled this requirement.

The effect of 10% concentration of different starches on the dissolution rate of aspirin from the prepared formulae (Formulae 1-4) is shown in Fig. 2. The results showed different dissolution rates in the following order: formula 2 > formula 1 > formula 3 > formula 4.
These results showed that the used disintegrant affected the dissolution rate of tablets in the following descending order: maize - potato - wheat - rice, i.e., maize starch was the best disintegrant while rice starch was the worst one in this study.
These dissolution results were in a good accordance with the disintegration time results showed by each disintegrant, where maize starch showed the shortest disintegration time and rice starch showed the longest one.
The dissolution rates of formulae 1 & 2 showed a regular dissolution behaviour, i.e., very small deviation of the three dissoluted tablets from their average dissolution rate. The standard deviations of these formulae at t_{10} (% dissolution after 10 minutes) were 0.28 and 2.67 respectively (Table 4). Formulae 3 & 4 showed greater dev-

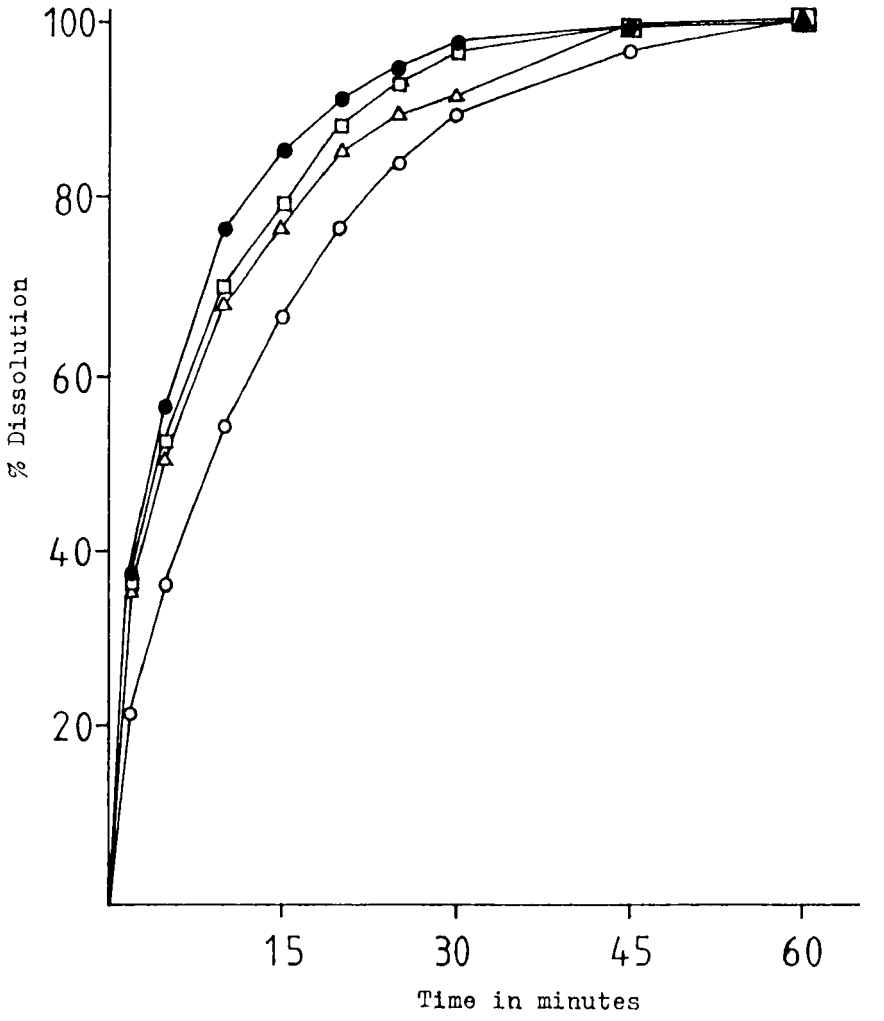

FIGURE 3. Effect of different concentrations of maize starch on the dissolution rate of aspirin tablets in 0.1N HCl at 37°C.

o—o , 5%: △—△ , 10%: □—□ , 15%: ●—● , 20%:

Table 5. Drug Contents of Formulated Aspirin Tablets.

Formula	% Drug Content*	S.D.
1	103.27	± 0.00
2	103.27	± 2.12
3	103.27	± 2.12
4	105.00	± 0.00
5	105.00	± 0.92
6	100.00	± 0.00
7	100.00	± 1.40

* Each is an average of Five determinations.

iations than formulae 1 & 2 where their standard deviations at t_{10} were 8.62 & 20.8 respectively.

From these results, maize starch was chosen as the best disintegrant used for the preparation of double compressed tablets as it had the highest dissolution rate out of all the used disintegrants in this study. This result was in a close agreement with that reported by Underwood and Cadwallader (9), in their study on the influence of various starches on the dissolution rate of salicylic acid from tablets. In addition, maize starch

showed a shorter disintegration time and better results for the non-official tests than the other starches (Table 2).

Fig. 3 shows the effect of different concentrations of maize starch on the dissolution rate of aspirin from tablets of formulae 2,5,6 & 7. Increasing the starch content of granules from 5 to 20% resulted in a marked increase in the dissolution rate of aspirin. This increase was probably because of more rapid and thorough disintegration of the granules. Formula 5 which contained 5% maize starch showed the lowest dissolution profile and the prolonged disintegration time, while formula 7 which contained 20% maize starch showed the highest dissolution profile and the shortest disintegration time. The dissolution rates of the different formulae showed regular dissolution behaviour. The standard deviations of formulae 2,5,6 & 7 at t_{10} were 2.67,1.38,2.6 and 4.24 respectively.

Finally, the drug content in the tablets of each formula 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 (10).

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