DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 13(3), 565-588 (1987)

THE EFFECT OF SOME SURFACTANTS ON THE IN-VITRO PROPERTIES OF DOUBLE COMPRESSED TABLETS

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ABSTRACT

The effect of different types and concentrations of some surface active agents as well as the method of surfactant incorporation on the in-vitro 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 non-official tests. These tests include : uniformity of weight, uniformity of content, disintegration, dissolution, hardness, friability and thickness. Incorporation of a low concentration (0.2 % w/w) of surface active agents in the formulation of tablets

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decreased the disintegration time but did not affect their dissolution rate. Higher concentrations of surface active agents retarded the dissolution of tablets. Non ionic surfactants showed higher retarding effect than ionic surfactants. Changing the method of surfactant incorporation did not greatly affect the dissolution rate of tablets.

INTRODUCTION

Numerous studies have been performed to determine the effect of surfactants on drug dissolution and absorption. The incorporation of surfactants in tablets was reported to improve disintegration (1).
The incorporation of surfactants in tablets prepared by direct granulation was found to reduce their disintegration time and increase their dissolution rate (2).
The effect of docusate sodium as a clinically used surfactant on the release of chlorpheniramine maleate from a controlled-release dosage form was studied (3).

In this paper, the effect of some commonly used surfactants in tablet formulation, namely Tween 20, Brij 35, Aerosol OT and Sodium lauryl sulphate on the in-vitro properties of aspirin tablets as a model for double compressed tablets was studied.

In addition, the effect of changing the method of surfactant incorporation on the properties of these tablets was also studied.

EXPERIMENTAL

Materials

Aspirin powder (Veb Dutcher, through Al-Goumhoria Co. for Trading Medicines, Chemicals & Medical Appliances), Lactose (El-Nasr Pharmaceutical Chemicals Co., Abu Zaabal), Maize starch (Alexandria Company for Pharmaceutical and Chemical Industries), Talc (Al-Goumhoria for Trading Medicines, Chemicals & Medical Appliances), Sodium lauryl sulphate (Cambrian Chemicals, Beddington), Brij 35, Tween 20 (Atlas Chemicals Industries Inc., Wilmington, Del.), Dioctyl sodium sulphosuccinate (Alexandria Company for Pharmaceutical and Chemical Industries), Hydrochloric acid 32 % (E. Merck, Darmstadt, W. Germany), Chloroform (Analytical reagent, Mallinckrodt Inc., St. Louis, Missouri, U.S.A.) and Absolute ethanol (Riedel-De Haen AG, Seelze-Hannover) were used in this study.

Apparatus

Korsch single punch tablet machine, type EKO, Erweka, W. Germany, with 12 mm flat punch for the slugs

and 9 mm slightly concave punch for tablets; Dry granulator, type TG2, Erweka, 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 Basket rack assembly dissolution apparatus 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 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 mortar. For some formulae (Formulae 5 - 15), solutions of surface active agents in the least amount of suitable solvent were sprayed on the surface of powder. Solvents were removed by drying in an oven at 48°C for 24 hr. The mixture was compressed into flat surface tablets (slugs). The prepared slugs were crushed using a dry granulator. The obtained granules were passed through 0.8 mm sieve opening and retained on 0.63 mm sieve opening. The rest of disintegrant and lubricant

Table 1. Formulations of Aspirin Tablets

Ingredients	Amount (mg) per each tablet														
Formula No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Aspirin	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
Lactose	7.2	7.2	7.2	7.2	7.2	7.2	7.2	7.2	16	12	8	-	8	8	8
Maize starch	80	80	80	80	80	80	80	80	80	80	80	80	80	80	80
Talc	12	12	12	12	12	12	12	12	-	-	-	-	-	-	-
Aerosol OT	0.8	-	-	-	0.8	-	-	-	4	8	12	20	-	-	-
Sodium laur-yl sulphate	-	0.8	-	-	-	0.8	-	-	-	-	-	-	12	-	-
Brij 35	-	-	0.8	-	-	-	0.8	-	-	-	-	-	-	12	-
Tween 20	-	-	-	0.8	-	-	-	0.8	-	-	-	-	-	-	12

were added on the retained granules, thoroughly mixed and compressed into tablets.

For other formulae (Formulae 1 - 4), solutions of the same surfactants were sprayed on the surface of granules before compression and solvents were removed by drying in an oven at 48°C for 24 hr.

Solvents used were chloroform for dioctyl sodium sulpho succinate (Aerosol OT), 25 % ethanol for sodium lauryl sulphate and absolute ethanol for Tween 20 and Brij 35.

Evaluation of tablets

Tablets were evaluated by the U.S.P. XX official tests (4) 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° ± 0.5°C in 900 ml 0.1 N 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 $37^{\circ} \pm 0.5^{\circ}C$ 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 0.1 N HCl. Measurements 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

Surfactants are commonly used in tablet formulations. The effect of two non ionic surface active agents namely, Tween 20 and Brij 35 and two anionic surface active agents namely, Aerosol OT and sodium lauryl sulphate on the in-vitro properties of aspirin tablets as a model for double compressed tablets was investigated.

The results of tests of the uniformity of weight of the different formulae of aspirin tablets are shown in Fig. 1. The weight of tablets 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 (4). 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). The results indicated that neither the type nor the method of incorporation of surfactants affect the uniformity of weight of double compressed tablets.

The percent variation in thickness of the different formulae of aspirin tablets are shown in Table 3. The results showed that all the prepared formulae met the requirement for thickness set by King (5). Such results proved that non of the used surfactants at different concentrations 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 (6).

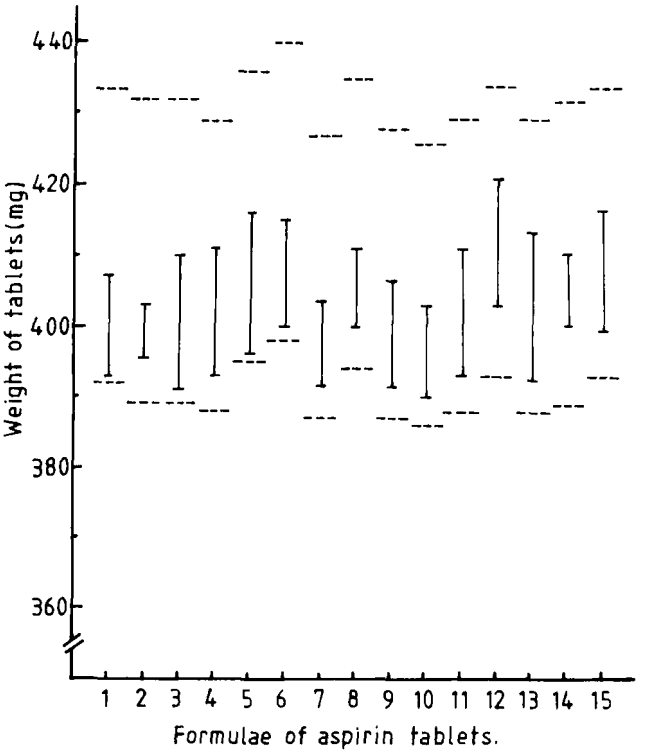

FIGURE 1.

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

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. The results indicated that all the prepared formulae fulfilled the limit for minimum hardness value of tablets set by

Table 2. Evaluation of Formulated Aspirin Tablets

Formula	S.D. of weight (mg)****	Thickness range (mm)*	Hardness range (Kg)***	Friability (%)***	H.F.R.	Disintegration time (sec)**
1	± 0.37	4.73-4.79	5.75-7.00	0.78	8.01	8.00
2	± 0.18	4.70-4.74	7.50-11.25	1.59	5.28	9.00
3	± 0.56	4.75-4.80	5.75-6.75	1.60	3.85	8.00
4	± 0.50	4.72-4.79	5.00-6.25	1.61	3.50	7.00
5	± 0.58	4.74-4.80	7.50-8.50	0.74	10.81	10.00
6	± 0.46	4.78-4.80	7.50-8.50	1.30	6.15	9.00
7	± 0.31	4.70-4.74	7.00-7.75	0.64	11.59	8.00
8	± 0.39	4.77-4.81	6.50-7.75	0.83	8.53	10.00
9	± 0.35	4.70-4.79	4.00-4.25	0.80	5.16	10.00
10	± 0.31	4.69-4.74	4.00-4.25	0.77	5.30	18.00
11	± 0.54	4.73-4.80	4.00-4.50	0.91	4.58	40.60
12	± 0.59	4.72-4.80	4.00-4.25	0.35	11.66	140.00
13	± 0.62	4.69-4.71	5.50-5.75	1.20	4.68	11.00
14	± 0.34	4.70-4.74	4.00-4.25	1.06	3.77	8.00
15	± 0.48	4.70-4.75	4.00-4.25	1.26	3.17	5.00

* 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	Standard Deviation
1	1.26	± 0.03
2	0.85	± 0.02
3	1.05	± 0.03
4	1.47	± 0.03
5	1.25	± 0.03
6	0.42	± 0.01
7	0.85	± 0.02
8	0.84	± 0.02
9	1.90	± 0.05
10	1.06	± 0.03
11	1.47	± 0.04
12	1.68	± 0.05
13	0.43	± 0.01
14	0.85	± 0.02
15	1.06	± 0.03

King (5). The results also indicated that, low concentrations of the surfactants used had no effect on the hardness of tablets (Formulae 1 - 8). On the other hand, increasing the concentration of the surfactants (Formulae 9 - 15) decreased the hardness of tablets although in preparing these tablets the machine was adjusted to give the maximum allowable pressure. Preparation of these tablets which contained higher concentrations of surface active agents at the pressure used for the preparation of the other formulae produced very soft and friable tablets. Such decrease in the hardness values due to the presence of higher concentrations of surface active agents may be due to their decreasing effect on the binding forces between the compressed particles. Changing the method of surfactants incorporation (Formulae 1 - 8) did not affect the hardness of tablets.

Friability was related to the strength of tablets. The results of friability of the formulated tablets are shown in Table 2. Gunsel and Kaning (6), secifyed a value of 0.8 % as an upper permitted value for tablet friability. Formulae 1, 5, 7, 9, 10 & 12 passed such test. Although the other formulae failed to pass this test, they could be considered acceptable as their friability values were higher by a relatively small values.

Hardness has been ass ciated with other properties such as density and porosity, all of which affect the disintegration time of tablets.

The disintegration test as specifyed in the U.S.P. XX (4), was performed on all the formulated tablets. All the prepared formulae met the U.S.P. requirement for disintegration. The results also showed that low concentration of the used surfactants (0.2 % w/w) decreased the disintegration time of tablets (Formulae 1 - 8). This decrease in disintegration time may be due to the synergistic action appeared to exist between the surfactants and starch. Surfactants increased the wettability of tablets, so allowed more rapid absorption of disintegration medium by starch, and subsequently more rapid disintegration of tablets (1).

Increasing the concentration of Aerosol OT in formulae 9 - 12 was found to retard the disintegration of such tablets. This effect may be referred to the formation of a more condensed hydrophobic film on the surface of the particles as the concentration of the surfactant was increased. This film decreased the wettability of the tablets and hence retarded their disintegration.

On the other hand, increasing the concentration of the surfactants namely, sodium lauryl sulphate, Brij 35 and Tween 20 in formulae 13 - 15 did not affect the disintegration time of tablets.

Dissolution rates of a number of pharmaeuticals were influenced by surface active agents, a process which was related to micellar solubilization (7, 8) and/or due to surface tension effect (9). Therefore, the effect of the studied surfactants on the dissolution rate of aspirin tablets was investigated.
The official monograph of aspirin in the U.S.P. XX (4), stated that not less than 80 % of the labelled amount of acetylsalicylic acid in tablets dissolves in 30 minutes. Table 4 shows that all the prepared formulae fulfilled this requirement except formula 12 which released only 77.63 % of its content within 30 minutes.

Fig. 2 shows the effect of 0.2 % w/w of different types of surfactants on the dissolution rate of aspirin tablets (Formulae 1 - 4). All these formulae contained 20 % starch as disintegrant and 3 % talc as lubricant. The dissolution rates for the different formulae containing the same concentration of different surface active agents were found to be in the following order :
formula 4 > formula 1 > formula 2 > formula 3
i.e., the studied surface active agents decreased the dissolution rate of aspirin in the following order :
Brij 35 > sodium lauryl sulphate > Aerosol OT > Tween 20.

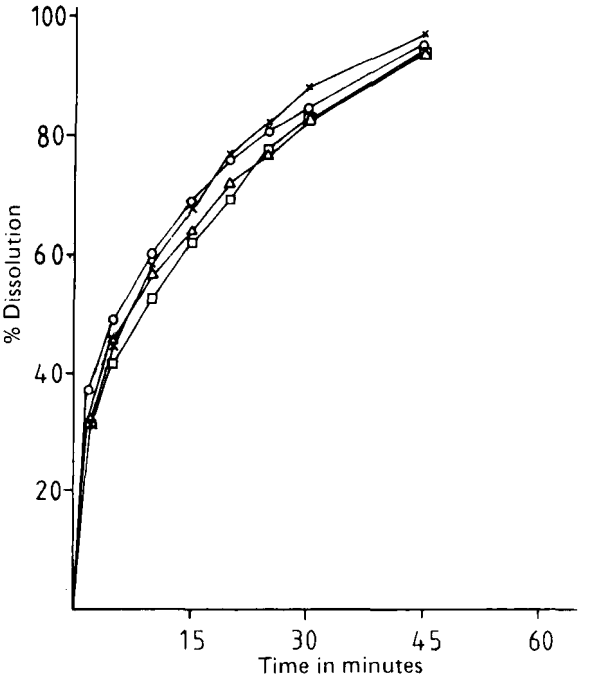

FIGURE 2. Effect of 0.2% of different surfactants sprayed on the granules on the dissolution rate of aspirin tablets in 0.1N HCl at 37°C. o—o, Aerosol-OT: Δ—Δ, sodium lauryl sulphate: □—□, Brij 35: ×—×, Tween 20:

On comparing such dissolution results with that obtained from formula 16 which contained no surface active agent, no enhancement in the dissolution rate was observed by incorporating low concentration of surfactants. The dissolution rates of formulae 1, 2 and 3 showed regular dissolution behaviour and the values of their standard deviations at t_{10} were shown in Table 4.

The effect of changing the method of incorporation

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

Formula	% Dissolved after 30 minutes ± S.D.	% Dissolved after 10 minutes ± S.D.
1	84.62 ± 0.00	59.62 ± 2.72
2	81.74 ± 1.30	56.61 ± 1.02
3	83.12 ± 0.00	52.73 ± 2.57
4	88.09 ± 8.00	58.63 ± 7.24
5	95.48 ± 4.62	69.32 ± 8.04
6	91.71 ± 1.12	68.06 ± 6.27
7	84.50 ± 1.96	58.69 ± 2.20
8	86.27 ± 4.45	57.30 ± 9.80
9	89.44 ± 0.04	65.58 ± 3.43
10	86.53 ± 2.72	62.82 ± 3.63
11	81.05 ± 2.60	57.53 ± 4.24
12	77.63 ± 3.72	51.57 ± 5.21
13	83.73 ± 2.70	55.84 ± 4.15
14	81.57 ± 1.86	57.37 ± 4.47
15	80.92 ± 2.78	58.55 ± 2.79

* Each value is the average of three tablets.

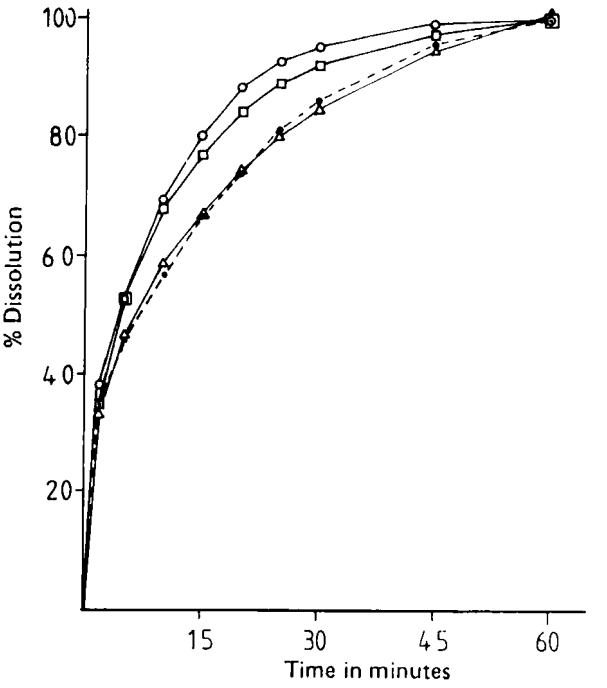

FIGURE 3. Effect of 0.2% of different surfactants sprayed on powder on the dissolution rate of aspirin tablets in 0.1N HCl at 37°C. o——o, Aerosol-oT: □——□, sodium lauryl sulphate: Δ——Δ, Brij 35: •- - -•, Tween 20.

of surfactants on the dissolution rates of aspirin tablets was studied. Fig. 3 shows the dissolution profile of aspirin tablets contained 0.2 % w/w of different surface active agents sprayed on the surface of the powder before slugging (Formulae 5 - 8) and not on the granules (Formulae 1 - 4). The results showed different dissolution rates in the following order :

formula 5 > formula 6 > formula 8 > formula 7

In addition, the results showed that spraying the surfactants on the powder enhanced the dissolution rate of aspirin on all the studied formulae except that contained Tween 20 where nearly no difference was observed. Such enhancement in dissolution may be due to the formation of a film of surfactant on the surface of powder allowing the drug to be more wetted by the dissolution medium and thereby effectively increasing the available surface area of the solid.

Although changing the method of surfactant incorporation into tablets enhanced slightly the dissolution rate of aspirin, the dissolution rate was still lower than that showed by formula 16 which contained no surfactant. Concerning the regularity of the dissolution rate of these formulae (Formulae 5 - 8), only formula 7 showed regular dissolution behaviour (standard deviation at t_{10} = 2.20).

The effect of different concentrations of surfactants on the dissolution rates of aspirin tablets was studied (Formulae 9 - 15).

The inclusion of higher proportions of surface active agents did not allow the use of 3 % w/w talc powder in these formulae as lubricant. In addition, this high concentration of surfactants will serve as a good lubricant in the absence of talc.

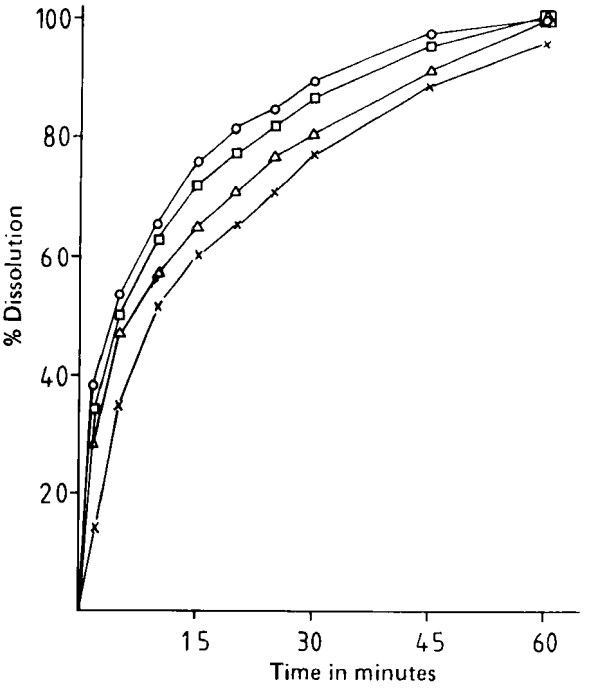

FIGURE 4. Effect of different concentrations of Aerosol-oT on the dissolution rate of aspirin tablets in 0.1N HCl at 37°C.
○—○ , 1%: □—□ , 2%: △—△ , 3%: ×—× , 5%:

Fig. 4 shows the dissolution profile of aspirin from tablets contained different concentrations of Aerosol OT (Formulae 9 - 12). The dissolution rate was found to be decreased in the following order :

formula 9 > formula 10 > formula 11 > formula 12

This rank order for dissolution means that increasing the concentration of surfactant from 1 to 5 % w/w decreased markedly the dissolution rate of aspirin.

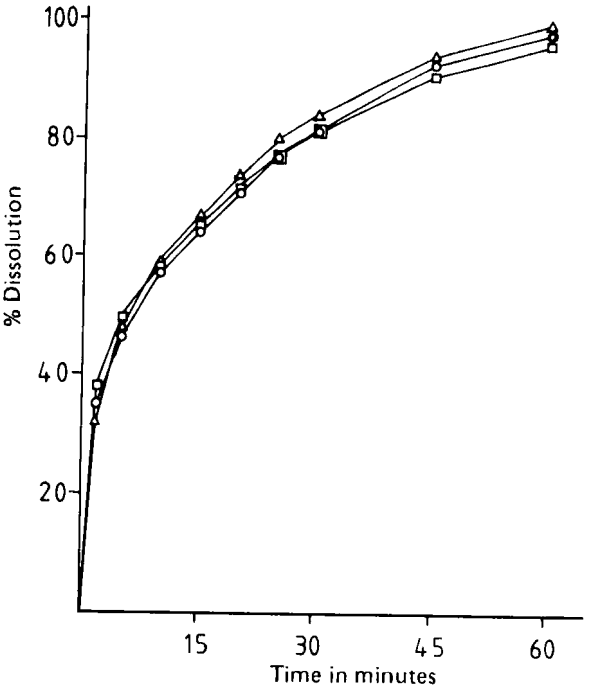

FIGURE 5. Effect of 3% of different surfactants on the dissolution rate of aspirin tablets in 0.1N HCl at 37°C.
△—△, sodium lauryl sulphate:
□—□, Brij 35: o—o, Tween 20:

This rank order for dissolution was also in a good agreement with that of disintegration, where formula 9 showed the shortest disintegration time while formula 12 showed the longest one.

Fig. 5 shows the dissolution rate of aspirin from formulae 13, 14 and 15. These formulae contained 3 % w/w of sodium lauryl sulphate, Brij 35 and Tween 20

respectively. The dissolution profile was in the following order : formula 13 > formula 14 > formula 15. Both formulae 14 & 15 failed to reach 100 % dissolution after 60 minutes. This result shows that the decreasing effect of the 3 % w/w concentration of the studied surfactants on the dissolution rate of aspirin was in the following order : Tween 20 > Brij 35 > sodium lauryl sulphate > Aerosol OT.

These results proved that non ionic surfactants (Tween 20 & Brij 35) had higher decreasing effect on the dissolution of aspirin than that of ionic surfactants (Aerosol OT & sodium lauryl sulphate) at relatively high concentration (3 % w/w).

However, in all cases the dissolution rate of aspirin was decreased by increasing the concentration of all the surfactants used in this study. Such decreasing effect may be due to a dewetting phenomenon and subsequent aggregation of the particles (10).

Finally, the aspirin content in each formula of tablets was evaluated (Table 5). All the studied formulae complied with the requirement for content uniformity (95 - 105 %) as specifyed in the official monograph of aspirin in U.S.P. XX (4).

Drying the powder or granules sprayed by solutions

Table 5. Drug Conten s of Formulate Aspirin Tablets.

Formula	% Drug Content*	Standard Deviation
1	97.00	± 0.91
2	98.20	± 0.85
3	100.00	± 1.25
4	100.00	± 2.60
5	98.24	± 0.87
6	100.00	± 0.85
7	98.24	± 1.80
8	97.00	± 0.00
9	97.00	± 0.92
10	96.00	± 1.06
11	96.00	± 1.06
12	96.00	± 0.00
13	100.00	± 1.24
14	96.00	± 1.98
15	96.00	± 1.98

* Each is the average of five determinations.

of different surfactants used in this study at 48°C for 24 hours did not affect the stability of aspirin intablets as aspirin contents in all tablets were satisfactory.

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