

EFFECT OF DISINTEGRANTS AND HARDNESS ON THE DISINTEGRATION TIME OF ACETAMINOPHEN TABLETS

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ABSTRACT

In this study the effect of various disintegrants on the disintegration time of laboratory prepared Acetaminophen tablets at different hardness has been determined. The disintegration time was found to be directly related with the hardness of the tablets for all formulations studied except in tablets containing croscarmellose.

INTRODUCTION

The formulation of the drug product can have a significant effect on the rate of disintegration and dissolution. This includes the physicochemical properties of the active ingredients and excipients, as well as the procedures used in the production process. By specifying only the active ingredient (a general custom today) a drug product is only partially characterized. Two preparations that contain the same active ingredient in identical amounts do not always exert an identical therapeutic effect. An identical effect would occur only if the released quantity of the active ingredient was identical within an equivalent period of time.

Tablet disintegration is one part in the complex process of the release of the active ingredient from the dosage form (1, 2). Matrix tablets which release their active ingredient through dissolution in a controlled manner sometimes present their original form and do not necessarily disintegrate (3, 4).

The present investigation is based on the influence of some disintegrants on the physical characteristics and controls of test of the laboratory prepared Acetaminophen tablets.

MATERIAL AND METHOD

Wet granulation method was used to prepare tablets. These are in total 5 types of formulation. From the formulation (2) to (5) contained different disintegrants and the first formulation was kept as the controlled formulation i.e. without disintegrant. Each formulation was compressed at four different hardness (Table I). In this way twenty batches of Acetaminophen tablets were produced. Two hundred tablets were compressed at each hardness. The tablets have been tested for uniformity of weights. Diameter, thickness, friability and active ingredients. The results have been

interpreted statistically and the tablets have been found to be within limits of B.P. and U.S.P. The detail of disintegration test was described elsewhere (5).

RESULTS AND DISCUSSION

The values for breaking strength and disintegration time of the control i.e. (without disintegrant) formulation is given in table 2. Breaking strength of this formulation ranged from 3.7 to 7.5 kg/cm² and the disintegration time lies between 32.9 to 45.6 minutes. The results obtained shows that the breaking strength of the tablets directly relates with the disintegration time, i.e. as the breaking strength of the tablets were increased there was also an increase in the disintegration time. It is also observed that the disintegration time of the tablets are too long for all breaking strength of this formulation. The basic reason of this result may be due to higher amount of the lactose present in the tablet of this formulation than others and it was concluded by Shan-Yang Lin (6) that tablets containing lactose as an excipient showed an increase in tablet crushing strength with an increase in the compressional force. This might be due to better compressibility of lactose (6). Longer disintegration time of this formulation for all batches may be due to the absence of disintegrating agent.

Table 2 shows that the formulation "A" containing sodium carboxymethyl cellulose 6% as disintegrant with breaking strength ranged from 2.8 to 6.4 kg/cm² has a remarkable effect of hardness on the disintegration time. The tablets with low breaking strength has lower disintegration time while those having higher strength take longest time to disintegrate. The disintegration time of the formulation ranges from 42 to 44.6 minutes. The result shows that the disintegration times are very high for the tablets prepared with sodium carboxymethyl cellulose and there is a direct linear relation existed between the breaking strength and the disintegration time. This result is in agreement with previous findings for sodium carboxymethyl cellulose, in which when breaking strength of the tablets were increased the disintegration time was also increased (7, 8) and that of the disintegration time of the tablets containing Na-CMC as a disintegrant were very high (6).

It was also concluded (9) that although sodium carboxymethyl cellulose produces soft granules which generally compress well, but produces tablets with relatively long disintegration time.

The disintegration time and breaking strength of the formulation containing 6% corn starch as disintegrant is shown in table 2. The breaking strength of four batches of this formulation ranges from 3.4 to 5.8 kg/cm² and time of disintegration times ranges from 0.42 to 0.54 minutes. Tablet of breaking strength 3.5 kg/cm² has minimum disintegration time i.e. 0.42 minutes while those of breaking strength 5.8 kg/cm² has maximum disintegration time i.e. 0.54 minutes. The result shows that in case of corn starch disintegrant, the disintegration time relates directly with the hardness of the tablets. But the effect of hardness on the disintegration time is not very sharp i.e. there is a very little increase in disintegration time as the hardness increases. The possible reason of this may be due to poor compatibility of corn starch as reported by Susan and Spring (10).

Llyod and Joseph (11) reported that the disintegration time of sulphathiazole tablets containing corn starch as disintegrant were increased as the hardness of the tablets were increased. The same result was also reported by Ingram and Werner (12). According to them there is an increase in disintegration time with increasing hardness of the aspirin tablets containing corn starch. It was also reported by Shikifumi *et al.* (13) that the disintegration time of uncoated caffeine tablets having 3% potato starch was increased by increasing hardness. Fassihi (14) has also reported the same result for theophylline tablets containing corn starch.

The results obtained in our experiments are in agreement with those reported by the above mentioned workers (10-14).

The breaking strength and disintegration time of the tablets containing 6% veegum as disintegrant are given in table 2. The breaking strength of the tablets ranges from 2.9 to 5.3 kg/cm² and the disintegration time ranges from 0.66 to 0.73 minutes. The data shows that there are no remarkable effect of hardness on the disintegration time of the tablets containing veegum disintegrant. The tablet of hardness 2.9 and 34 kg/cm² disintegrate in almost same time i.e. 0.62 minutes. The tablets of hardness 5.3 kg/cm² took 0.73 minutes to disintegrate, here the difference of time among the tablets of four different hardness is very marginal and can be neglected. The possible reason of this may be due to the fragmentation of particles at high pressure, it is observed that veegum is an excellent disintegrant. All the tablets of this formulation were disintegrated within 0.62 to 0.73 minutes which is much shorter than the time allowed by B.P. for uncoated tablets, which is 15 minutes. The disintegration time of the tablets containing veegum as disintegrant were also determined previously by Kee-Neng *et al.* (15) and Damodaran *et al.* (16). They also suggested veegum as an excellent disintegrant. Veegum was also used as binding agent by Patel *et al.* (17) in the preparation of tablets and they concluded that the tablets prepared with veegum as binding agent disintegrate in shorter time than that Laken by tablets prepared with other binding agents. Although veegum is a very excellent disintegrating agent but its use in white tablets is limited because of the tendency for the tablets to be slightly discolored. So it is not usually used in tablets formulation.

Values for breaking strength and disintegration times of the tablets prepared with 6% Avicel pH 101 as disintegrant is shown in table 2. Breaking strength of all experimental tablets of this formulation ranged from 3.4 to 5.7 kg/cm² and disintegration time from 0.93 minutes. The data shows that there is a positive correlation between breaking strength and disintegration time of the tablets. As the hardness of the tablets were increased (here was also an increase in the disintegration time). This result is in full agreement with previously obtained by Tuladhar (18), David (19) and Fassihi (14). The basic reason of this is given (20) that Avicel has good property of compaction with compression force. As the compression force is increased there is more compactibility in the tablets containing Avicel, and it takes longer time to disintegrate.

A number of other investigators (21-25) have reviewed the applications of Avicel 101 in tablet formulations. The capillarity of Avicel explains the penetration of water into tablet, thereby destroying the cohesive bonds between particles. The hardness of the compressed tablet can

significantly affect the disintegration time by breaking down the structure of the intermolecular spaces and destroying the capillary properties.

Khan and Rhodes (26) has also reviewed the disintegration properties of dibasic calcium phosphate dihydrate tablets employing insoluble and soluble disintegrating agents. The insoluble disintegrating agents showed a greater effect when compressional forces were varied than did the soluble disintegrants.

Microcrystalline cellulose (Avicel (pH 101) exhibits very good disintegrating properties when present at a level as low as 10%. It functions by allowing water to enter the tablet matrix by means of capillary pores, which breaks the hydrogen bond between adjacent bundles of cellulose microcrystals (27). Due to high pressure the capillary pores may reduce and the disintegration time may increase.

Table 1
Formulations showing different disintegrants
(Sodium Carboxy Methyl Cellulose, Corn Starch, Veegum, Avicel 101)

		Control	Formu- lation 1	Formu- lation 2	Formu- lation 3	Form- lation 5
Acetaminophene	500.0	+	+	+	+	+
Kollidom	30.0	+	+	+	+	+
Mg stearate	7.5	+	-	-	-	-
Na-CMC	36.0	-	+	-	-	-
Corn starch	36.0	-	-	+	-	-
Veegum	36.0	-	-	-	+	-
Avicel 101	36.0	-	-	-	-	+
Lactase	62.5	+	+	+	+	+

Table 2
Disintegration time of Acetaminophene Tablets

Formulation	Batch No.	Hardness (kg/cm ²)	*Disintegration time (min.)
Control	1	3.7	31.89
	2	6.2	43.12
	3	6.9	44.12
	4	7.5	45.60
A	1	2.8	42.04
	2	3.7	44.58
	3	4.8	42.42
	4	6.4	43.33
B	1	3.4	0.42
	2	4.4	0.45
	3	5.5	0.54
	4	5.8	0.54
C	1	2.9	0.66
	2	3.4	0.67
	3	4.1	0.62
	4	5.3	0.73
D	1	3.4	0.93
	2	4.2	1.36
	3	4.8	1.88
	4	5.7	3.22

*Each reading is the average of 6 tablets.

Control = Control formulation

A = Formulation containing 6% Na-CMC.

B = Formulation containing 6% Corn Starch.

C = Formulation containing 6% Veegum.

D = Formulation containing 6% Avicel (101).

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