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DISSOLUTION RATE STUDIES ON ACETAMINOPHEN TABLETS

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ABSTRACT:
The effect of disintegrants on the dissolution rate of Acetaminophen tablets at different hardness has been investigated. It was determined that the dissolution rate is influenced by disintegrants as well as hardness for all formulations except in tablets containing Veegum as the disintegrant.

INTRODUCTION

Usually the most important process affecting drug availability in solid dosage forms is the rate of dissolution. When a drug is administered orally in solid form as a tablet, capsule or suspension or intramuscularly as a pellet or suspension one frequently finds that the rate of absorption is controlled by how fast the drug dissolves in the fluids at the absorption site. In other words dissolution rate is often the rate limiting step in the following sequence.

Solid drug	**Kd´**	**Drug in**	**Ka**	**Drug in**
in GI fluids	⟶ dissolution	Solution in GI fluids	⟶ absorption	Systemic circulation

Where Kd and Ka are rate constants for the dissolution and absorption processes, respectively.

Since the dissolution process preceeds the absorption process, any factor influencing the rate of the dissolution must influence also the rate absorption. Consequently, dissolution rate may affect the onset, intensity, and duration of biological response. Absorption from the solution proceeds much more rapidly than from the tablets. Whenever a drug is more rapidly and for more completely absorbed from solution than from some solid, it is quite likely that absorption is rate limited by dissolution process.

The present work is based on the in vitro dissolution rate of laboratory prepared Acetaminophen tablets using various disintegrants and hardness.

MATERIAL AND METHOD

It is same as reported earlier (Ahmed 1992). The dissolution test was carried out according to USP (XIX) method.

RESULTS AND DISCUSSION

The dissolution rate of Acetaminophen from control (without disintegrant) formulation at four different hardness is given in table 1. In this formulation the dissolution time of the drug as the hardness of the tablets were increased and the dissolution rate of the drug from all batches was very poor i.e. only 15.69 to 17.80% of the drug was dissolved in 40 minutes. There may be two possible reasons in the favour of this result. Firstly the formulation is without disintegrant so it took longest time to disintegrate and secondly, in this formulation the quantity of lactose was greater than the other formulations and due to better compressibility of lactose the density of the tablets were increased with increasing hardness and at the same time the porosity decreased, so that the dissolution medium could not penetrate the tablet rapidly. The dissolution pattern of this formulation at different hardness versus time is given in Fig. 1.

The dissolution rate of drug from the tablets containing 6% sodium carboxy methyl cellulose as disintegrant at four different hardness is given in table 2. It is clear from the data that the dissolution rate of Acetaminophen tablets containing sodium carboxy methul cellulose is affected by increasing the hardness of the tablets. Fig. 2 shows that the dissolution rate has decreased very sharply from hardness 2.8 to 3.7 kg/cm^2 . But for other two batches of this formulation, the decrease rate of dissolution is not very sharp by increasing hardness. During 35^{th} to 40^{th} minute of dissolution, the drug was dissolved rapidly from the tablets of hardness 3.7, 4.8 and 6.9 dg/cm^2. This result is in full agreement with the result previously obtained by Khan and Rooke (1976). They observed that the tablets containing sodium carboxy-methyl-cellulose show a slight initial increase followed by a progressive decrease in dissolution efficiency with increasing pressure. These results also confirm previous findings of Khan and Rhodes (1972, 1979). They have shown that efficiency of a swelling type disintegrant was impaired in insoluble tablet systems compacted at low pressure due to their higher porosity.

The effect of hardness on the dissolution profiles of Acetaminophen tablets containing 6% corn starch as disintegrant is shown in table 3. The result shows that the dissolution time of the Acetaminophen is slightly increased as the hardness of the tablets were increased. The maximum percentage of drug dissolved in 40 minutes was 70.9 at the hardness of 3.4 kg/cm^2 , while it was minimum i.e. 55.68% at the hardness of 5.8 kg/cm^2. The dissolution pattern is shown in Fig. 3. This result confirms the results obtained by Fassihi (1989). This result is also in full agreement with the result previously obtained by Kitazawa et al. (1975) in studying the effect of hardness on the disintegration time and the dissolution rate of uncoated caffeine tablets containing 3% w/w/ of the potato starch. It was also found by Jacob and Plein (1968) that an increase in hardness resulted in a decrease in the dissolution rate of phenobarbitone tablets but they found no correlation between dissolution rate and disintegration time. The inverse correlation between the hardness of the tablet and dissolution rate is due to the fact that as Higuchi and others (1953) showed, the density of the tablet increased with increasing hardness and at the same time, the porosity decreased so that the dissolution medium could not penetrate the tablets. The dissolution of the drug occurs only from the surface of the tablets and the rate constant for dissolution would correlate with the hardness of the tablet at this stage of the dissolution. It was also suggested that the initial hardness of the tablet still influenced the dissolution rate constant of the drug from the disintegrated particles which were small enough to pass through the screen of the basket of the disintegrated apparatus. So that hardness affects the dissolution of the tablets over all the stages of dissolution.

The dissolution rate of Acetaminophene tablets containing 6% veegum at four different hardness is listed in table 4. The result shows an unusual increased dissolution rate of the dung with increasing tablet hardness. The maximum percentage of drug dissolved in 40 minutes was 94.16% from the tablet of hardness 5.3 dg/cm^2 while the minimum drug dissolved was 78.94% in 40 minutes from the tablet of hardness 2.9 dg/cm^2. There is no correlation between the disintegration time and dissolution rate of the tablet. The reason for this phenomenon i.e. increased rate of dissolution of drug with increasing hardness of the tablet may be due to the fragmentation of veegum particles with increased compressional force and increased grain swelling as the mechanism by which veegum acts as disintegrant. The dissolution pattern of this fomulation is given in Fig. 4.

The effect of tablet hardness on the dissolution rate of tablets containing 6% Avicel PH 101 is shown in table 5. In this formulation there is an inverse relation between the hardness and dissolution rate of the tablets. Maximum amount of drug dissolved in 40 minutes is 28.3% from the tablet of hardness 3.4 dg/cm^2 while the minimum dissolved in 40 minutes is 20.15% from the tablet of hardness 5.8 dg/cm^2. Tuladhar (1982) has reported that the dissolution rate of the drug was decreased as the compressional force of the tablets, containing fine particles of the Avicel PH 101, was increased. This result may be due to the functions of the Avicel which by allowing water to enter the tablet matrix by means of capillary pores, breaks the hydrogen bonding between adjacent bundles of the cellulose microcrystals. But as the hardness of the tablets are increased the capillary pores are reduced and the penetration of dissolution medium into the tablets are decreased and ultimately there is less dissolution of drugs. This is also in agreement with the result obtained by Muti *et al.* (1985) who has reported that the use of compression forces between 500 and 2000 kg had a pronounced effect on the Acetaminophen dissolution time in tablets. These values are under the limit of B.P. (1988) a described by Acetaminophen tablets i.e. ±5%.

The uniformity of Acetaminophen content was calculated by average assay method and were found under the B.P. (1988) limit i.e. ± 5%.

Table I

Dissolution Rate of Acetaminophene from tablets of Different Hardness

Batch No.	Hardness (kg/cm^2)	Percentage drug dissolved in (min)							
		5	10	15	20	25	30	35	40
1	3.7	6.08	7.08	9.10	11.13	12.15	14.18	16.20	18.23
2	6.2	5.06	6.08	8.10	9.10	11.13	12.66	15.09	17.21
3	6.9	4.55	6.06	7.06	9.10	10.60	12.37	14.68	16.20
4	7.5	4.05	5.06	6.58	8.10	10.13	11.64	13.67	15.69

Table 2

Formulation B (Containing 6% Na-CMC)

Batch No.	Hardness (kg/cm)	Percentage drug dissolved in (mm.)							
		5	10	15	20	25	30	35	40
1	2.8	14.16	22.25	26.33	29.36	36.45	38.45	40.50	42.50
2	3.7	9.11	11.14	15.75	18.50	21.26	24.30	26.33	35.44
3	4.8	6.58	9.11	12.50	16.20	19.50	22.28	24.81	30.38
4	6.4	4.05	7.06	10.13	14.68	18.22	20.25	22.23	28.35

Table 3

Formulation C (Containing 6% Corn Starch)

Batch No.	Hardness (kg/cm^2)	Percentage drug dissolved in (win.)							
		5	10	15	20	25	30	35	40
1	3.4	24.30	34.43	47.59	52.65	58.73	63.79	68.85	70.90
2	4.4	26.33	32.40	40.50	47.00	52.50	57.00	60.50	63.80
3	5.5	16.20	26.50	31.38	42.50	49.61	53.64	57.77	60.50
4	5.8	10.13	17.21	24.30	30.88	38.13	46.58	49.61	55.68

Table 4

Formulation D (Containing 6% Veeguni)

Batch No.	Hardness (kg/cm^2)	Percentage drug dissolved in (win.)							
		5	10	15	20	25	30	35	40
1	2.9	35.40	49.30	.63.79	66.32	69.64	73.40	75.94	78.94
2	3.4	40.50	53.38	70.88	76.13	79.50	83.02	*85.05*	87.08
3	4.1	53.16	70.90	75.94	79.99	82.01	85.65	86.57	89.61
4	5.3	58.73	82.52	85.05	86.06	88.52	91.63	93.15	94.16

Table 5

Formulation **E** (Containing 6% Avicel 101)

Batch No.	Hardness kg/cm^2	Percentage drug dissolved in (min.)							
		5	**10**	**15**	**20**	**25**	**30**	**35**	**40**
1	3.4	12.15	15.18	16.20	18.16	20.25	24.33	26.33	28.35
2	4.2	9.11	10.13	14.18	16.20	20.25	22.23	24.30	26.70
3	4.8	8.1	9.11	10.13	14.30	16.66	17.21	21.00	23.28
4	5.7	6.10	8.10	10.13	11.14	14.18	16.20	18.23	20.15

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