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Research Article

Effect of Various Super Disintegrants on Hardness, Disintegration and Dissolution of Drug from Dosage Form

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ABSTRACT

In this study the effect of various disintegrants on the disintegration time of Acetaminophen tablets has been determined. The disintegration directly related with the hardness of the tablets. The tablets were prepared using lactose as diluent and with different levels of disintegrants like Na Cmc and Avicel. The tablets were evaluated for weight variation, hardness, friability, disintegration time (DT) and dissolution study. The tablets were prepared by using wet granulation method and were evaluated in the similar way. Percentage drug release was estimated by using UV spectrophotometry method .The hardness, friability, dissolution rate and assay of prepared tablets were found to be acceptable according to standard limits of IP official pharmacopeias.

Keywords: Acetaminophen, Sodium Cmc, Avicel

INTRODUCTION

Acetaminophen or Paracetamol is a widely used over-the-counter analgesic (pain reliever) and antipyretic (fever reducer)[1].It is commonly used for the relief of headaches, and other minor aches and pains, and is a major ingredient in numerous cold and flu remedies[2]. In combination with opioid analgesics, paracetamol could be used also in the management of more severe pain (such as in advanced cancer).The formulation of the drug product can have a significant effect on the rate of disintegration and dissolution. This includes the physiochemical properties of the active ingredients and excipients, as well as the procedures used in the production process. 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. The present investigation is based on the influence of some super disintegrants on the physical characteristics and controls of the laboratory prepared Acetaminophen tablets.

MATERIAL AND METHOD

Acetaminophen was obtained as gift sample from Threveni Chemicals, Gujarat, India. Kollidon (Signet chemicals Corporation, Mumbai), sodium-CMC (Akay organic Ltd. Tarapur, Maharashtra.), Avicel pH 101 (Saguache chloro chemicals Pvt.Ltd.Madinaguda, Hyderabad) Lactose, Mg stearate (S.D.Fine Chemicals, Mumbai, India.)

Table 1.Composition of the Acetaminophen Tablet Formulation with different disintegrating agents

S.No	Ingredients	Formula(mg/tablet)		
		F1	F2	F3
1.	Acetaminophen	500mg	500mg	500mg
2.	Kollidon	30mg	30mg	30mg
3.	Avicel 101	-	-	36mg
4.	Na CMC	-	36mg	-
5.	Mg Stearate	7.5mg	7.5mg	7.5mg
6.	Lactose	62.5mg	62.5mg	62.5mg
Total		600mg	636mg	636mg

Wet granulation method was used to prepare tablets. Different super disintegrants and the lint formulation were kept as the controlled formulation i.e. without disintegrant. And each formulation was compressed into tablets.

The required quantities of Acetaminophen, Kollidon, Mg-stearate, Avicel 101, and Lactose were weighed accurately. Acetaminophen, avicel101 and lactose were mixed in a mortar and pestle using laboratory conditions. Accurately weighed quantity of binder (kollidon) was then dispersed in IPA (Isopropyl alcohol) and stirred well. The binder solution was then slowly incorporated into the above mixed powder to obtain a damp mass. The damp mass was passed through a granulating sieve # 16 to obtain the granules. Then the granules were dried in a hot air oven at 40 ^{0}C temperature, less than the temperature of all the ingredients used. The dried granules were passed through sieve #22 in order to obtain the uniformed sized granules. All the granules were lubricated with magnesium stearate and compressed using single punch in a multistation compression machine (Cadmag), which is equipped with 8mm concave edge punches. The composition of the formulation is shown in table 1.

Physical properties of the granules formulated with different super disintegrants for Acetaminophen: [3, 4]

Angle of repose[3]

The angle of repose of powder was determined by the funnel method. The accurately weighed powder was taken in a funnel. The height of funnel (h) was adjusted in such way that the tip of the funnel just touches the apex of the heap of the powder. The powder was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone(r) was measured and angle of repose was calculated using the following equation.

$$\theta = \tan^{-1} \frac{h}{r}$$

Bulk Density[4]

An accurately weighed quantity of powder, which was previously passed through sieve # 40 [USP] was carefully poured in to graduated cylinder. Then after pouring the powder into the graduated cylinder the powder bed was made uniform without disturbing. Then the volume was measured directly from the graduation marks on the

cylinder as ml. The volume measured was called as the bulk volume and the bulk density is calculated by following formula.

Bulk density =Weight of powder/Bulk volume

Tapped Density [4]

The same measuring cylinder which was used for the bulk volume was set into tap density apparatus. The tap density apparatus was set to 300 taps drop per min and operated for 500 taps. Volume was noted as (Va) and again tapped for 750 times and volume was noted as (Vb). If the difference between Va and Vb not greater than 2% then Vb is considered as final tapped volume. The tapped density is calculated by the following formula.

Tapped density = Weight of powder /Tapped volume

Carr's index and Hausner's Ratio[4]

Carr's index and hausner's ratio measures the propensity of powder to be compressed and the flowabiltiy of powder. Carr's index and hausner's ratio was calculated from the bulk and tapped density.

Carr's index = (Tapped density – Bulk density / Tapped density) X 100

Hausner's Ratio = Tapped density / Bulk density

Evaluation of prepared Tablet: [5, 6]

The prepared tablets were subjected to hardness, Friability, Weight variation test disintegration time and *In vitro* Dissolution test.[7]

Weight Variation Test: [5, 6]

Ten tablets were selected randomly from each batch and weighed individually to check for weight variation. In all formulations, the mathematical equation for the weight variation is given by

$$\text{Highest weight variation} = \left(\frac{\text{Highest} - \text{average}}{\text{Average}} \right) \text{X } 100$$

$$\text{Lowest weight variation} = \left(\frac{\text{Lowest} - \text{average}}{\text{Average}} \right) \text{X } 100$$

Hardness[7]

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablet was determined using Pfizer hardness tester. It is expressed in kg/cm^2.Three tablets were randomly picked and hardness of the tablet was determined.

Friability Test

The friability of tablets was determined using Roche Friabilator. It was expressed in percentage (%), 10 tablets were initially weighed ($W_{initial}$) and transferred into Friabilator. The Friabilator was operated at 25 rpm for 4 min run up to 100 revolutions. The tablets were weighed again (W_{final}), the % friability was then calculated by

$$\% \text{ Friability} = \left(\frac{\text{Before Friability} - \text{After Friability}}{\text{Before Friability}} \right) \text{X } 100$$

The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

In-Vitro Disintegration Time

Further tablet were subjected for the evaluation of in-vitro disintegration time for all formulations. The disintegration of the tablets has been performed according to the I.P 1996[8].

In-Vitro Dissolution Study

For dissolution, six tablets of each formulation were taken and average of six results was considered as percentage drug release. The dissolution studies were carried out upto one hour for all the formulations using the United States pharmacopoeia (USP) apparatus II (Paddle method) taking 900 ml 0f dissolution medium. At pH 6.8 phosphate buffer, the rotational speed of the paddle was set at 50 RPM at 37 ± 0.5°C. 5 ml of aliquots was withdrawn at predetermined time interval for every 5 minutes by replacing a fresh sample of dissolution medium. The absorbance of the collected samples measured using UV-spectrophotometry at λ_{max} 257 nm.

RESULTS AND DISCUSSION

Acetaminophen tablets were prepared by wet granulation process. The physical properties of the granules formulated with different super disintegrants for Acetaminophen tablets were studied and was found to be in the prescribed limits according to I.P. The compressibility index and Hausner's ratio are in the range of 21.79 - 22.70 and 1.20 – 1.29 respectively which shown in table 2. According to theoretical values as the compressibility index is in the range of 18–23 and Hausner's ratio of less than 1.25 to not more than 1.5. Hence they indicate fair flow. The results obtained showed that the breaking strength of the tablets is directly related to the disintegration time, i.e. as the breaking strength of the tablets is increased there is also an increase in the disintegration time. Longer disintegration time of the lint formulation (F1) may be due to the absence of disintegrating agent. Values for breaking strength and disintegration times of all formulations were shown in table 3. Breaking strength of all experimental tablets ranged from 6-7 kg/cm^2 and disintegration time from 9.21 min to 29 min.

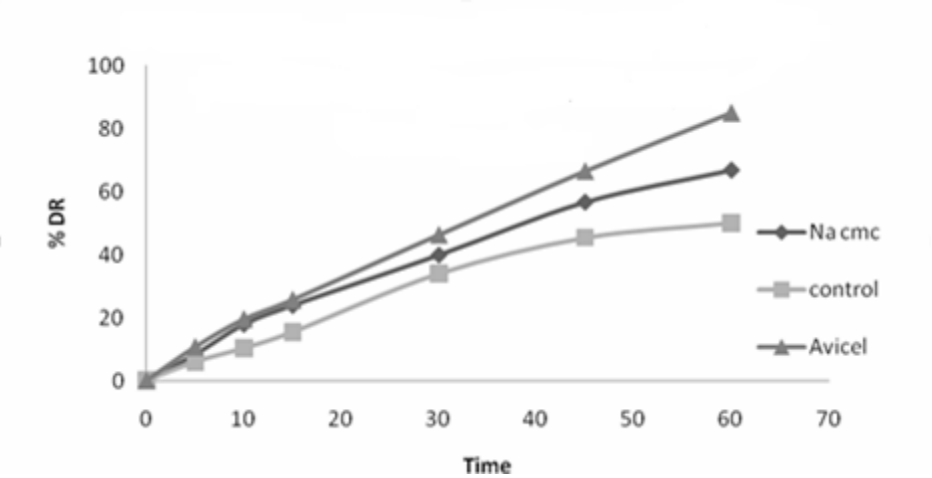
Table 2: Physical properties of Acetaminophen granules formulated with different disintegrating agents

Formulation	Angle Of Repose (degrees)	Loose bulk density(gm/ml)	Tapped Bulk density(gm/l)	Compressibility index	Hauner's ratio
F1	28	0.303	0.388	21.9	1.20
F2	25	0.305	0.390	21.79	1.27
F3	25	0.307	0.392	22.70	1.29

Table 3: Physical properties of Acetaminophen Tablet formulated with different disintegrating agents

Formulation	Weight variation (mg)	Friability (%)	Hardness(Kg/cm^2)	Drug content Uniformity(mg)	Disintegration Time (min)
F1	600±1.2	0.99	7.0	99.45±0.02	29min
F2	636±1.4	0.72	6.5	98.37±0.02	20min40sec
F3	636±1.0	0.91	6.0	98.55±0.02	9min21sec

Fig.1 Dissolution profile of acetaminophen tablets prepared with different superdisintegrants



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 micro crystals.

From the Figure 1 we concluded that lint formulation showed slower disintegration and tablets prepared with Avicel as super disintegrants showed faster disintegration (9min21sec) than tablets prepared with sodium Cmc as super disintegrants (20min 40 sec). The in-vitro release study also proves that the formulation F3 which is formulated with avicel101 as more disintegrating property than NaCMC. The results of the dissolution profile were shown in the figure1. The release rate of the drug acetaminophen was in the order of Formulation 3 >Formulation 2>Formulation 1.

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