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RESEARCH ARTICLE

Effect of Various Disintegrants on the *In-Vitro* Parameters of Drug from Dosage Form

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ABSTRACT

In this research study the effect of various disintegrants on the disintegration time of Paracetamol 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 Sodium starch glycolate, cross carmellose sodium, micro crystalline cellulose. The tablets were evaluated for weight variation, hardness, friability, disintegration time (DT) and dissolution study. Some pre-compression characteristics like bulk and tapped densities, compressional index, angle of repose, and hausner's ratio were also evaluated. 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. Disintegration time was decreased with increase of superdisintegrants whereas % drug release rate and extent were increased with increase of superdisintegrants. So it can be concluded that the immediate release tablet of Paracetamol can be formulated for emergency treatment of pain and fever. The tablet of Paracetamol can be formulated for emergency treatment of pain and fever. All formulations were evaluated for pre-compression and post-compression parameters. The hardness, friability, dissolution rate and assay of prepared tablets were found to be acceptable according to standard limits of IP official pharmacopeias.

KEYWORDS

Paracetamol, Sodium Starch Glycolate, Cross Caramellose Sodium, MCC

INTRODUCTION

Tablets for immediate release often consist of filler, a binder, lubricants and disintegrants[1.] In many cases, the disintegration time of solid dosage forms is too long to provide appropriate therapeutic effect. To improve the disintegration time, so-called disintegrants are used. In the past, non-modified disintegrants such as alginates, starches, ambrelite resins, cellulosic materials, pectins etc. were used to accelerate disintegration. Today, fast working superdisintegrants are chemically modified polymeric molecules, typically by crosslinking the organic chains.

Three classes of superdisintegrants are commonly used:

modified cellulose (croscarmellose sodium), crosslinked polyvinyl-pyrrolidone (Kollidon CL) and modified starch (Sodium Starch Glycolate). Superdisintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction which causes the

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tablet to burst or the accelerated absorption of water leading to promote disintegration Proposed mechanism for the action of disintegrants include water uptake through wicking, swelling, deformation recovery and particle repulsion[2-3].

Acetaminophen or Paracetamol is a widely used over-the-counter analgesic (pain reliever) and antipyretic (fever reducer)[4]. 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[5]. 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.

MATERIALS AND METHOD

Materials

Paracetamol, Sodium starch glycolate, cross carmellose sodium, micro crystalline cellulose and all other ingredients were obtained from S D fine Chem. Ltd.

Equipments used were Compression machine of Create company pvt ltd, Electronic balance of Citizen scales, Hardness is done by using Monsanto, Roche friabilator and Dissolution apparatus of DBK instruments, Vernier callipers

Method

Preparation of Granules

The method employed is wet granulation method for preparation of tablets. The amounts of all ingredients are mentioned in Table 1. Firstly, the active drug (Paracetamol), diluent (Starch), and the 3/4 amount of superdisintegrants, methyl paraben and propyl paraben were passed through a 20 mesh sieve and magnesium stearate were passed through a 30 mesh sieve to obtain fine particles. Paracetamol, disintegrants and superdisntegrants are mixed together for 10 mins with a mortar and pestle. The binding solution was prepared by dissolving maize starch in sufficient amount of water.

This solution was then added drop by drop to the dry mixture in the mortar. During this addition, the mixture was continuously stirred in clockwise direction which was continued for a further 10mins after all the binding solution had been added. At the end of this mixing, a uniformly mixed wet mass was obtained. The wet mass was dried in an oven for 30 mins at 60^0 C. Again dry mass was passed through a 22 mesh sieve to obtain very fine granules and were dried in a hot air oven.

Finally, these fine granules were mixed with methyl paraben, propyl paraben, sodium lauryl sulphate and after 3 minutes add Mg stearate and talc to obtain granules with the pre-requisite flow properties. All the granules were lubricated with magnesium stearate and compressed using CID-3 compression machine. The powder blend was evaluated for flow properties such as bulk density, tapped density, compressibility index, Hausner's ratio, angle of repose[6] and results are presented in Table 3.

Evaluation of Tablets

The mechanical strength of tablets is often defined as the force required fracturing a tablet across its diameter[7]. Mechanical strength is directly related to porosity and disintegration time. The packaging process and transportation of the final product requires appropriate tablet strength. To ensure tablet strength the formulations were evaluated for hardness, weight variation, thickness, friability, disintegration time and *in vitro* dissolution study.

Table 1: Composition of the Paracetamol Tablet Formulation with different disintegrating agents

S.No	Ingredients	F1	F2	F3
1	Paracetamol	500 mg	500 mg	500 mg
2	Methyl Paraben	0.255 mg	0.255 mg	0.255 mg
3	Propyl Paraben	0.595 mg	0.595 mg	0.595 mg
4	Talc	5 mg	5 mg	5 mg
5	Sodium Lauryl Sulphate	9 mg	9 mg	9 mg
6	Croscaramellose sodium	25 mg	-	-
7	Sodium Starch Glycolate	-	25 mg	-
8	Micro Crystalline Cellulose	-	-	25 mg
9	Maize Starch	305 mg	305 mg	305 mg
10	Magnesium Stearate	5.15 mg	5.15 mg	5.15 mg
Total		850 mg	850 mg	850 mg

Tablet Hardness[8]

Hardness is the crushing strength of tablet which determines the ease of handling and rigors of the transportation. For each formulation, 3 tablets were used for the study. The hardness of the tablet was determined and expressed in kg/cm^2.

Weight Variation Test

Weight variation test[9-10] was done by weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weight to the average.

Thickness

The thickness of the tablets was measured using manual Vernier Caliper, and expressed in mm.

Friability

Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Friabilator (Veego, India) was used for the purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at distance of 6 inches with each revolution. Pre weighed sample of tablets were placed in the friabilator, which was then operated for 100 revolutions. Tablets were dedusted and reweighed. The percent friability was measured using the formula:

$$\%F = \{(W - W_0)/W_0\} \times 100$$

Disintegration Time

The disintegration test on various brands of paracetamol tablets during storage was carried out according to the procedure of BP (1993) using a Manesty disintegrator. One tablet was introduced into each cylindrical glass tube of the basket-rack assembly. The assembly was suspended in the beaker containing the specified liquid. The apparatus was operated at37±1^{0}C for the specified time 30min. The assembly was removed from the liquid and the disintegration time of the tablets was noted.

Dissolution

The release rate of the tablets is determined using united state pharmacopoeia (USP) XXIV at using dissolution test apparatus II i.e paddle type. The dissolution test is performed using

900 ml of phosphate buffer (ph=7.8), at 37 +/- 2°C at 50 rpm. The tablet was introduced into the bath container containing the buffer, and paddle was rotated at 50 rpm up to 1 hour. A sample (1ml) of the solution was withdrawn from the dissolution apparatus at intervals of 5, 10, 15, 20, 25, 30 minutes. Simultaneously fresh dissolution medium is added to replace the withdrawn solution and maintain the appropriate ph. The withdrawn samples are further diluted with phosphate buffer to make up a volume of 10ml. The absorbance of the collected samples measured using UV-spectrophotometry at λmax 257 nm. The data is presented in Table 2.

Angle of Repose

The angle of repose[11] 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.

Bulk Density[12]

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[12]

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[12]

Carr's index and hausner's ratio measures the propensity of powder to be compressed and the flow ability of powder. Carr's index and hausner's ratio was calculated from the bulk and tapped density. The data is presented in **Table 3**.

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

Hausner's Ratio = Tapped density / Bulk density

RESULTS AND DISCUSSION

Paracetamol tablets were prepared by wet granulation process. The physical properties of the granules formulated with different super disintegrants for Paracetamol tablets were studied and was found to be in the prescribed limits according to I.P. The Hausner's ratio are in the range of 1.40 – 1.41 respectively which shown in Table 3. According to theoretical values as the 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 (F3) may be due to the absence of disintegrating agent. Breaking strength of all experimental tablets ranged from 4-6 kg/cm^2 and disintegration time from 1.05 min to 5.02 min.

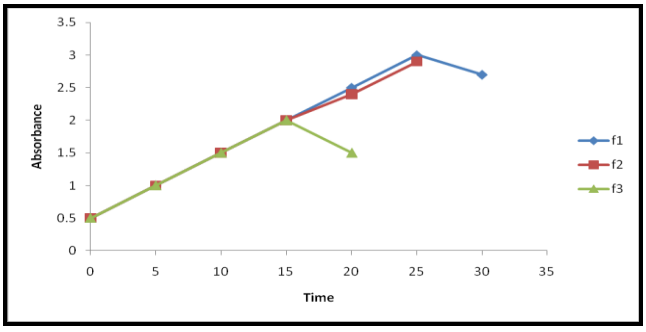

Figure 1: Dissolution profile of Paracetamol tablets prepared with different superdisintegrants

Table 2: Physical properties of Paracetamol Tablet formulated with different disintegrating agents

Parameters	F1	F2	F3
Description	White tablet	White tablet	White tablet
Theoretical wt of tablet	850mg	850mg	850mg
Weight of 10 tablets	8.46mg	8.46mg	8.46mg
Weight variation	0.84	0.83	0.84
Hardness	4.3kg/cm^2	5.4kg/cm^2	5.6kg/cm^2
Thickness	0.6mm	0.58mm	0.54mm
Disintegration Time	1min 5sec	2min 3sec	5min 2sec
Friability	0.14%	0.23%	0.28%

Table 3: Physical properties of Paracetamol granules formulated with different disintegrating agents

Test	F1	F2	F3
Description	White Powder	White Powder	White Powder
Bulk density	2.2g/ml	2.3g/ml	2.5g/ml
Tapped density	0.61g/ml	0.83g/ml	0.71g/ml
Carr's index	0.179g/ml	0.175g/ml	0.172g/ml
Hausners ratio	1.415	1.412	1.402

CONCLUSION

The *In vitro* drug release profile of all formulations was evaluated and the release studies demonstrated that the release of Paracetamol from all formulations was generally immediate. High concentration of super-disintegrants used in the formulations caused high percent release of drug, while lower concentration caused low release. For this three formulations F1, F2, F3 were prepared having the same formulation but different disintegrants for F1 containing cross carmellose sodium (Disintegrant), F2 contains sodium starch glycolate (Disintegrant), F3-containing micro crystalline cellulose (Disintegrant, filler). The results showed F1 to be a better formulation and better dissolution results compared to F2 and F3. Thus, the release characteristics were significantly influenced by the type and concentration of superdisintegrants used. Disintegration time was also governed by type and quantity of superdisintegrants. Disintegration time was decreased with the increase of superdisintegrants. Thus, the granules and tablets were found satisfactory in

terms of physical parameters, disintegration time as well as the drug release profiles from the immediate release tablets.

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