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Research Article

FORMULATION DEVELOPMENT AND CHARACTERIZATION OF FAST DISSOLVING ACETAMINOPHEN TABLETS

Abhishek Pandey*[1] Bhagat Singh Jaiswal[2], Manoj Sharma[3]

[1, 2, 3] School of studies in Pharmaceutical Sciences, Jiwaji University, Gwalior (M.P.)

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ABSTRACT

The aim of the present work is to formulate a tablet which disintegrate and dissolve rapidly and give its rapid onset of action. Acetaminophen is an analgesic, antipyretic drug having bitter taste. In present study an attempt had been made to formulate rapidly disintegrating tablets of acetaminophen with altered taste by using directly compressible grade excipients which makes the formulation directly compressible with adequate mechanical strength and various superdisintigrants like Crospovidone, Sodium starch glycolate, Croscarmellose sodium along with incorporating sweetening agent. The tablets were evaluated for weight variation, hardness, friability, disintegration time, wetting time, in vitro dissolution studies and drug content. It was concluded that the batch prepared by using combination of Crospovidone and Sodium starch glycolate superdisintigrants shows excellent disintegration time, enhance dissolution rate, taste masking.

KEYWORDS: Acetaminophen, Fast dissolving tablet (FDT), Superdisintigrants, Direct compression

INTRODUCTION:

Pharmaceutical technology have presented various dosage form alternatives for patients compliance who may have difficulty in swallowing solid dosage forms, particularly pediatric and geriatric patients, who are in their old age, have difficulty swallowing or chewing solid dosage forms[1]. Solid dosage forms like tablets, capsules are the most popular form among all the other dosage forms because of its convenience of compactness, easy manufacturing and self-administration. A fast dissolving drug delivery system can be defined as a dosage form for oral administration, which when placed in mouth, rapidly disintegrates or dissolves and can be swallowed in the form of liquid[2]. It is difficult to swallow tablets as well as hard gelatin capsules and also when water is not available in the case of motion sickness, allergic attacks of coughing during the common cold and bronchitis. For these reasons tablets which rapidly dissolve or disintegrate in the oral cavity play an important role and are called fast dissolving tablets. FDTs are not formulated for people who have swallowing difficulties, but also ideal for active people. Fast dissolving tablets are also called as mouth dissolving tablets, melt-in-mouth. The target populations for these new fast-dissolving/disintegrating dosage forms have generally been pediatric, geriatric, and bedridden or developmentally disabled patients. Patients with persistent nausea, who are traveling, or who have little or no access to water are also good candidates for FDT[3]. The ease of administration of fast dissolving /disintegrating tablet, along with its pleasant taste, may encourage a patient to adhere to a daily medication regimen. Although a FDT may not solve all compliance issues, it may be enough of an advance to be of therapeutic significance[4]. Acetaminophen used as an analgesic and antipyretic having bitter taste. The Acetaminophen well absorbed orally only about 1/3 is protein bound in plasma and uniformly distributed in the body plasma half-life is 2-3 hrs. Acetaminophen is not ordinarily amenable to tablet because acetaminophen crystals are very hard and brittle fracture very easily when compressed producing capping and laminating compacts[5]. In this study the formulation of fast dissolving tablets of acetaminophen was developed by using directly compressible grade excipients different superdisintigrants and their combination by using direct compression technique.

MATERIAL AND METHODS:

MATERIAL:

*Corresponding author: Abhishek Pandey |E-mail: pandey_phama@yahoo.co.in

Acetaminophen, Crospovidone (PPXL), Sodium starch glycolate, Croscarmellose sodium (Ac-Di-Sol), Mannitol, Microcrystalline cellulose (PH102), Magnesium stearate, Talc, Aspartame, Peppermint flavor from Loba Chem. All reagents are of analytical grade.

METHODS:

Pre formulation studies:

Drug - Excipients compatibility study:

The study was designed to determine compatibility of drug with different excipients. These studies were carried out in glass vials stoppers with LDPE (Low density polyethylene) plugs. API was mixed with different excipients & kept at storage condition 40^0C at 75%RH for time interval of 1 week, 2 weeks, and 3 weeks.

Physical evaluation of blend:

Physical Characterization of blend was done for Particle size distribution, Bulk Density, Tapped density and compressibility index.

Particle size distribution:

Particle size distribution of the blend was done in electronic sifter; About 20 gm. of the blend was weigh and added to sieve # 150, # 85, # 60, and # 36, with subsequent weighing of the blend in between. Time of sifting with each mentioned sieve was 2 min. / sieve.

Determination of Bulk Density, Tapped density and compressibility index:

Firstly, the graduated cylinder was tare to zero, certain quantity of powder (W) was carefully poured into the graduated cylinder and the same was weighed. Also, the volume (V_0) was noted. The graduated cylinder was then closed with lid and set into the density determination apparatus (Bulk density apparatus, Campbell electronics). The density apparatus was set for 350 taps and after that the volume (V_f) was determined. The Bulk Density, Tapped density was calculated using the following formulas:

Bulk Density = W/V_0

Tapped density = W/V_f

Where W = Weight of powder, V_0 = Initial volume, V_f =Final volume

Compressibility Index:

The compressibility index is determined by measuring both bulk density and the tapped density of a powder [6].

Compressibility Index (%)

$$= \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Formulation of tablets by direct compression method:

Weigh all the ingredients accurately and pass through sieve # 40. Mix all the ingredients geometrically except Magnesium stearate. Then lubricate the blend with Magnesium stearate. Tablets were compressed using single punch tablet machine.

Table 1 Illustrate the formulation design of tablet

Tablet composition (mg)	**B_1**	**B_2**	**B_3**	**B_4**	**B_5**	**B_6**
Acetaminophen	325	325	325	325	325	325
Crospovidone	6	-	-	6	6	-
Croscarmellose sodium (AC-DI-SOL)	-	5	-	5	-	5
Sodium starch glycolate	-	-	10	-	10	10
Mannitol	112	121	116	115	110	111
Dibasic calcium phosphate	20	-	-	-	-	-
Microcrystalline cellulose (PH 101)	-	12	12	12	12	12
Magnesium stearate	3	3	3	3	3	3
Talc	4	4	4	4	4	4
Aspartame	3	3	3	3	3	3
peppermint flavor	2	2	2	2	2	2
Total	475	475	475	475	475	475

EVALUATION OF TABLETS:

Weight variation:

Twenty tablets were randomly selected from each formulation and average was determined. Then individual tablet were weighed and individual was compared with average weight[8].

Friability:

The friability of tablets was determined using friability test apparatus About 6 tablets ($W_{initial}$) were transferred into friability test apparatus. The apparatus was operated at 25 rpm for 4 minutes or 100 revolutions. The tablets were weighed again (W_{final}) [6]. The percentage friability was calculated by using following formula

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

Hardness:

The hardness of the tablets was determined using Pfizer hardness tester Ten tablets were randomly selected from each formulation and hardness of the same was determined .The results are expressed in average value [6].

Thickness:

Twenty tablets were randomly selected from formulations and thickness was measured individually by Vernier caliper. It was expressed in millimeter and average was calculated [6].

Disintegration test:

The disintegration time of the fast dissolving tablets was determined using Disintegration test apparatus. The operation was performed on 6 tablets in triplicate[6].

Wetting time:

Five circular tissue papers of 10 cm diameter are placed in a Petri dish with a 10 cm diameter. Ten millimeters of water-containing Eosin, a water-soluble dye, is added to Petri dish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time [8].

In-vitro dissolution rate study:

In-vitro dissolution rate study was done by using USP Type I apparatus which was rotated at 150 rpm. Phosphate buffer pH 7.2 (900 ml) was taken as dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5°c. Aliquots of dissolution medium were withdrawn at specific time interval and it was filtered. Absorbance of filtered solution was determined by Spectrophotometer at 249 nm and drug concentration was determined from standard calibration curve. The dissolution rate studies for all designed formulations were done as presented in table 2 and shown in fig.1

Determination of drug content:

20 tablets was taken and powdered accurately. Powdered containing about 325 mg of acetaminophen was taken and shake it with 60ml methanol in 200ml volumetric flask and dilute to volume with methanol. 5ml of this solution was taken and diluted up to 100ml with methanol and absorbance was noted at 249 nm[7].

RESULTS AND DISCUSSION:

The compositions of different batches are described in table 1. The pre formulation studies and evaluation parameters like weight variation, friability, hardness, thickness, disintegration time, wetting time, dissolution rate and assay for drug content were found to be satisfactory and results were presented in table 2 and 3.

The formulation containing crospovidone and sodium starch glycolate shows sufficiently decrease in disintegration time (i.e. 30 sec.) among all the formulation. When crospovidone, sodium starch glycolate, croscarmellose sodium was used alone in the formulations, disintegration time was noticed more than 1min. furthermore, when combination of superdisintigrants was used, significant decrease in a disintegration time was achieved. In vitro dissolution rate study shows that after 10 min formulation B4 – B6 % drug release 90.27%, 94.98%, 97.76% respectively. Drug content studies were done on selected batches and results are presented in table 4 which shows that the drug content are within limit. As fast dissolution formulation B5 shows satisfactory % drug release and disintegrating time as shown in fig. 1 and 2. Thus the formulation batch B5 can be said as best combination of superdisintigrants for fast dissolving tablet of acetaminophen.

Table 2: Pre formulation studies of Blends

Parameters	B_1	B_2	B_3	B_4	B_5	B_6
Bulk density(g/ml)	0.62	0.52	0.58	0.51	0.61	0.58
Tapped density(g/ml)	0.62	0.62	0.61	0.63	0.62	0.58
Compressibility index (%)	16.1	19.4	16.4	20.6	19.4	20.5

Table 3: Evaluation of fast dissolving tablets of acetaminophen of different batches

Parameter	**B_1**	**B_2**	**B_3**	**B_4**	**B_5**	**B_6**
% weight variation	1.7	2.1	2.0	2.1	1.5	2.1
Thickness(mm)	3.76	3.60	3.66	3.72	3.70	3.81
Friability (%)	0.94	0.66	0.78	0.77	0.72	0.85
Disintegration Time(sec.)	74	67	72	43	30	47
Hardness (kp)	4.0	4.6	4.60	4.40	4.21	4.30
Wetting time (sec.)	70	75	62	66	58	49

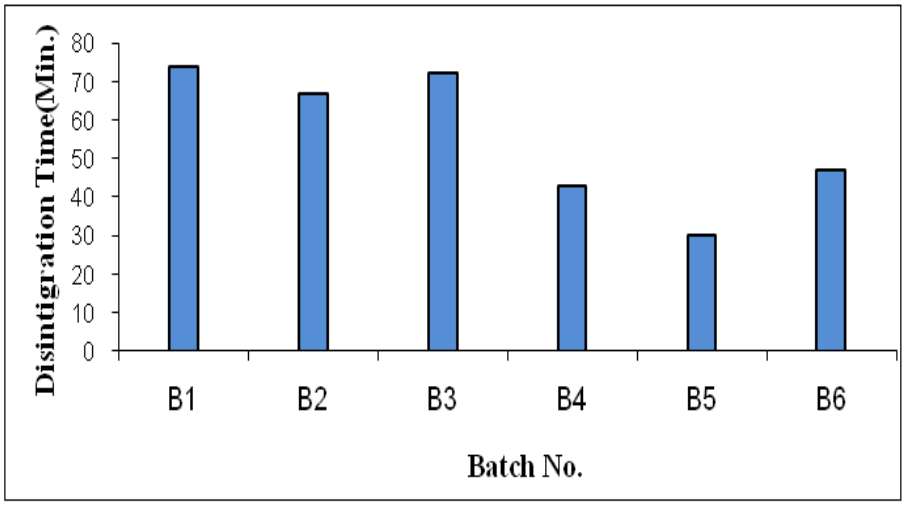

Fig 1: Disintegration time (min.) of various batches containing different superdisintigrants

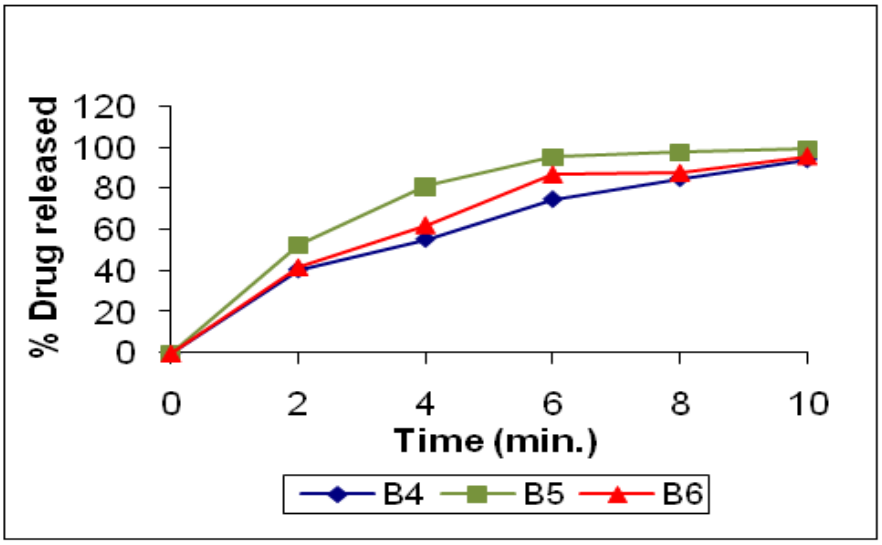

Fig. 2: Comparative study of % drug release of FDT of acetaminophen

Table 4: Drug content studies of fast dissolving tablets of acetaminophen

Batch No.	Assay (%)
B_4	94.35
B_5	97.21
B_6	98.00

CONCLUSION:

The present investigation revealed that fast dissolving tablet with altered taste of acetaminophen can be formulated by using direct compression method by incorporating directly compressible grade excipients along with suitable superdisintigrants Crospovidone Sodium starch glycolate. directly compressible grade excipients makes the formulation compressible and avoid the capping and lamination of acetaminophen with adequate mechanical strength while combination of Crospovidone, Sodium starch glycolate in different concentration enables the formulation fast dissolving simultaneously addition of sweetening agent mannitol and aspartame alter the bitter taste of drug. The proposed fast dissolving formulations exhibit satisfactory characteristics of disintegration time and enhanced dissolution and thus provide ease of patient compliance compare to conventional formulation of acetaminophen.

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