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FORMULATION DEVELOPMENT AND EVALUATION OF FAST DISSOLVING ACELOFENAC TABLETS

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ABSTRACT

Acelofenac (2-{2-[2, 6-Dichlorophenyl) amino phenyl} acetoxy) acetic acid] is diclofenac analog and analgesic drug with bitter taste. Acelofenac is selective COX-2 inhibitor, faster acting superior NSAIDS than other with better GI tolerability. In this study an attempt had been made to formulate fast disintegrating tablets (FDT), of acelofenac with altered taste by using (DC grade) directly compressible grade excipients to enable the formulation directly compressible with adequate mechanical strength. Superdisintegrants like crosspovidone, sodium starch glycolate (SSG), croscarmellose sodium and along with sweeting agent were used in formulation development. 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 crosspovidone and sodium starch glycolate as a superdisintigrant shows prominent disintegration time, enhanced dissolution rate.

KEYWORDS: Acelofenac, Fast dissolving tablet (FDT), Wetting time, Superdisintegrant.

INTRODUCTION

A fast dissolving drug delivery system can be defined as a dosage form for oral administration, when placed in oral cavity, rapidly disintegrates or dissolves and can be swallowed in the form of liquid.[1-2] It is difficult to swallow tablets 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 dissolve or disintegrate in the oral cavity rapidly play a vital role and are known as fast dissolving tablets. Fast dissolving tablets are also known as mouth dissolving tablets, The patients for these new fast-

dissolving/disintegrating dosage forms are pediatric, geriatric and bedridden patients. Patients with nausea, who are traveling, or who have little or no access to water are also good candidates for fast dissolving tablet (FDT).[3] The ease of administration of a 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] Aceclofenac is a newer non-steroidal anti-inflammatory drug having potent analgesic and anti-inflammatory properties. Aceclofenac is widely used in the treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. The mode of action of aceclofenac is largely based on the inhibition of prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclooxygenase, which is involved in the production of prostaglandins. The Drugs inhibits synthesis of the inflammatory cytokines interleukin (IL)-1and tumor necrosis factor and prostaglandin E2 (PGE2) production. Aceclofenac is rapidly eliminated from the body and unable to maintain therapeutic concentration at site of action. Conventionally aceclofenac is available as 100 mg tablet given by mouth required multiple daily doses twice or thrice daily to maintain adequate plasma drug concentration.[5-6] In present study, the formulation of Fast dissolving tablets of acelofenac was developed by using directly compressible grade excipients along with different superdisintegrants and their combination as per standard percentage limit.

MATERIAL AND METHODS

MATERIAL

Acelofenac was obtained as gift sample from Ranbaxy Pvt Ltd. Crosspovidone (PPXL), Sodium starch glycolate (SSG), Croscarmellose sodium (Ac-Di-Sol), Mannitol, Microcrystalline cellulose (PH102 grade), Magnesium stearate, Talc, Aspartame, were of Lobachem.

METHODS

Preformulation studies[7]

Drug - excipients compatibility study

Preformulation testing is the first step in the rational development of dosage forms of a drug substance. It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. API (active pharmaceutical ingredients)

was mixed with different excipients in a ratio of (1:1) in glass vial & kept at storage condition 40^0C at 75% RH for 1 month.

Micrometrics of Powder blend

Determination of Bulk Density, Tapped density

A known quantity of powder was poured into the measuring cylinder, carefully level the powder without compacting, if necessary and measure the bulk volume (Vo), to the nearest graduated unit. The bulk density was calculated, in gm per ml, by the formula. 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 300 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 (Carr's consolidation index)

Compressibility index is a measures of the propensity of a powder to be compressed. As such, they are measures of the relative importance of inter particulate interactions. In a free flowing powder, such interactions are generally less and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater inter particle interactions.

$$\text{Compressibility Index (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

COMPRESSION OF TABLETS BY DIRECT COMPRESSION METHOD

Weigh all the formulation ingredients and screen through sieve no. # 36. Mix all the ingredients excluding lubricant magnesium stearate because magnesium stearate is hydrophobic in nature and may retard the dissolution of formulation. Then lubricate the blend with magnesium stearate. Single punch tablet compression machine were used for compression. (Table 1).

Table 1 Formulation design of fast dissolving acelofenac tablet [9]

Composition (mg)	B_1	B_2	B_3
Acelofenac	100	100	100
Crospovidone	6	6	-
Croscarmellose Sodium (AC-DI-SOL)	5	-	6

Sodium starch glycolate	**-**	**10**	**10**
Mannitol	**112**	**112**	**112**
Dibasic calcium phosphate	**5**	**-**	**-**
Microcrystaline cellulose (PH 101)	**12**	**12**	**12**
Magnesium stearate	**3**	**3**	**3**
Talc	**4**	**4**	**4**
Aspartame	**3**	**3**	**3**
Total	**250**	**250**	**250**

EVALUATION OF TABLETS.[8-9]

Weight variation

20 tablets were randomly selected for weight variation and average weight of 20 tablets was calculated and weight of individual tablet was measured and compared with average weight.

Friability

The friability of tablets was determined using Roche friability test apparatus. About 6 tablets ($W_{initial}$) were placed into friabilator. The friabilator was operated at 25 rpm for 4 minutes or 100 rpm. The tablets were dedusted and weighed again (W_{final}). The percentage friability of tablets 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 Monsanto hardness tester. Ten tablets were randomly selected from each formulation and hardness of the same was determined. The results are expressed in average value.

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.

Disintegration test

The disintegration time of the fast dissolving tablets was determined using disintegration test apparatus.

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 fig.3.

where,

W_b = Weight of tablet before water absorption

W_a = Weight of tablet after water absorption

In-vitro dissolution rate study

Formulation B2 and B4 were studied for In-vitro dissolution rate study. Dissolution 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 276 nm (λ max of acelofenac) and drug concentration was determined from standard calibration curve fig.1. The dissolution rate studies for all designed formulations were done as shown in fig.3.

Determination of drug content

20 tablets was taken and powdered accurately. Powdered containing about 325 mg of Acelofenac 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 276 nm.

RESULTS AND DISCUSSION

The preformulation studies and evaluation parameters such as weight variation, friability, tablet hardness, thickness, disintegration time, wetting time, dissolution rate and assay for acelofenac content were found to be within pharmacopeial limit and the results were presented in table 2 and 3. The formulation consist of superdisintegrant crospovidone and SSG shows significant reduction in disintegration time in comparison to all the formulations. When crospovidone, SSG, croscarmellose sodium (Ac-Di-Sol) was used alone in the formulations, disintegration time was observed more than 1 min. furthermore. When these superdisintegrant were used in combination significant decrease in a disintegration time was noticed., wetting profile of prepared tablets shown in fig.2. Batch B1 exhibited percentage assay less than batch B2 and B3 so batch B1 was excluded for dissolution study. In vitro dissolution rate study exhibited that after 10 min formulation B2, B3 % drug release was

93.27%, 96.88% respectively. Drug content studies of selected batches shows that the drug content is within limit results are presented in table 4. Formulation B3 shows satisfactory % drug release and as shown in fig. 3. Therefore batch B3 coined as best combination of superdisintegrants for the formulation of fast dissolving tablet of acelofenac.

Table 2: Preformulation studies of blends

Parameters	B_1	B_2	B_3
Bulk density(g/ml)	0.54	0.62	0.58
Tapped density(g/ml)	0.59	0.56	0.59
Compressibility index(%)	18.6	18.4	19.5

Table 3: Evaluation of fast dissolving tablets of acelofenac batch B1-B3

Parameter	B_1	B_2	B_3
% weight variation	2.4	1.8.	2.0
Thickness(mm)	2.71	2.74	2.82
Friability (%)	0.79	0.77	0.88
Disintegration Time(sec.)	40	32	44
Hardness (kp)	4.60	4.11	4.20
Wetting time (sec.)	68	56	48

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

Batch No.	Assay (%)
B_1	95.15
B_2	98.11
B_3	98.63.

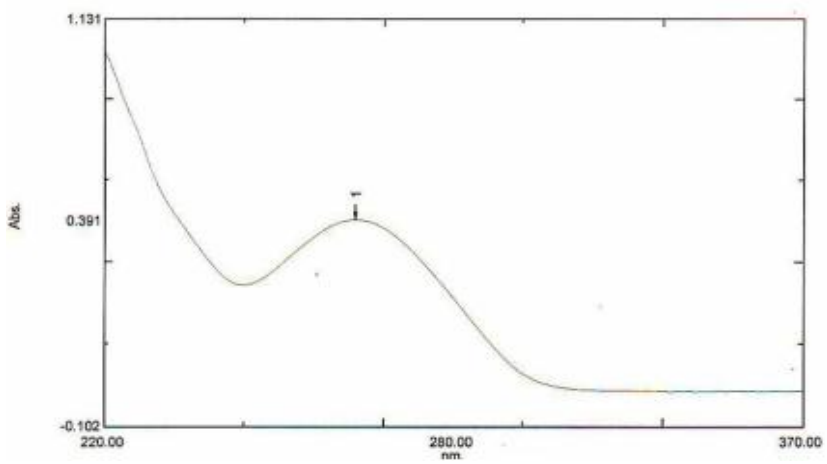

Fig. 1 Calibration curve of acelofenac

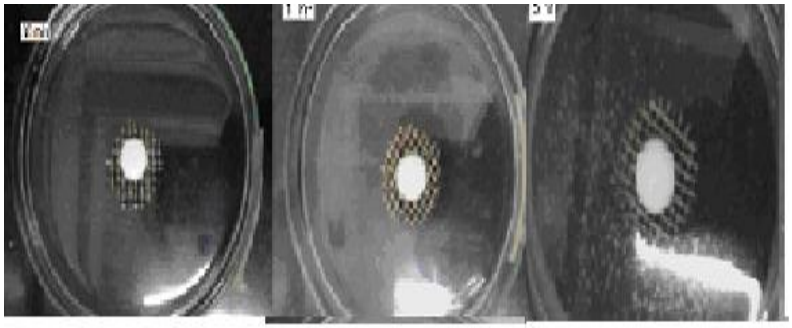

Fig. 2 Wetting profile of tablets

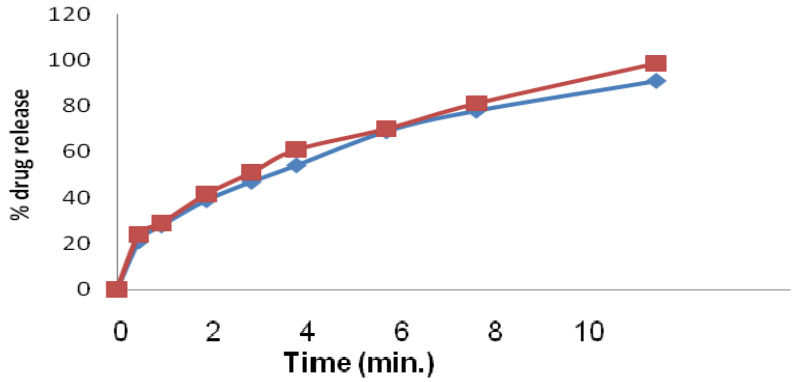

Fig. 3: Comparative study of % drug release Batch B2 and B3 of FDT of Acelofenac

CONCLUSION

The findings of present research revealed that fast dissolving tablet (FDT) of acelofenac with altered taste can be formulated by using directly compressible grade excipients and method along with superdisintegrants (crospovidone sodium starch glycolate). DC grade excipients enables the formulation compressible minimize or avoid the capping and lamination of acelofenac with adequate hardness while combination of crospovidone, SSG in different percentage enables the formulation fast dissolving simultaneously incorporation of sweeting agent mannitol and aspartame mask the bitter taste of acelofenac. The prepared fast dissolving formulations exhibited satisfactory disintegration time and enhanced dissolution rate, thus it offers patient compliance compare to conventional acelofenac tablets.

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Conflict of interest

The authors of this study declare that there is no conflict of interest in present research work.

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