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FORMULATION AND EVALUATION OF ACECLOFENAC FAST DISSOLVING TABLETS USING SODIUM STARCH GLYCOLATE AS SUPERDISINTEGRANT

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ABSTRACT

Fast dissolving tablets (FDT^s) are solid dosage forms that disintegrate and dissolve in the mouth either on or beneath the tongue or in the buccal cavity without water. In this study, an attempt was taken to enhance the solubility and dissolution character of Aceclofenac, a poorly water soluble non steroidal anti-inflammatory drug, by preparing FDT^s of Aceclofenac using sodium starch glycolate as superdisintegrant by direct compression method. The interaction between drug and superdisintegrant was characterized by IR spectroscopic studies. The final blend of the drug and excipients were evaluated for various precompression parameters like angle of repose, bulk density, tapped density, compressibility index, hausner's ratio and post compression parameters like thickness, hardness, weight variation, friability, disintegration time, drug content, wetting time, water absorption ratio and *in vitro* drug release study. The IR results showed no interactions between the drug and superdisintegrant used. The drug release of formulation (F_1) was 72.8±2.4% in 45 min. The results revealed that the formulation F_1 containing sodium starch glycolate (5%w/w) as superdisintegrant provided a faster drug release compared with the control formulation (F_2) prepared without superdisintegrant.

KEYWORDS: Aceclofenac, Direct compression, Fast dissolving tablets, superdisintegrant.

INTRODUCTION

Many patients express difficulty in swallowing tablets and hard gelatin capsules, tending to non-compliance and ineffective therapy. Recent advances in novel drug delivery systems (NDDS) aim to enhance safety and efficacy of drug molecules by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach is fast dissolving tablets.[1] Fast dissolving tablets are solid dosage forms containing medicinal substances which disintegrate / dissolve rapidly in oral cavity within 15-60 sec without water.[2] The bioavailability of FDT^s may be increased due to absorption of drug in oral cavity and also due to pregastric absorption of saliva containing dispersed drug thereby the amount of drug that is subjected to first pass metabolism is reduced.

Aceclofenac is a new generation Non-Steroidal Anti-Inflammatory drug used in the symptomatic treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis.[3] Aceclofenac is practically insoluble in water. Because of its poor aqueous solubility, conventional Aceclofenac dosage forms shows absorption problem and its dissolution is considered to be rate determining step in its absorption from gastro- intestinal tract**.** The present work was aimed to increase the rate of dissolution of Aceclofenac, thus providing faster rate of absorption by adding sodium starch glycolate as superdisintegrant in 5%w/w concentration. Mannitol and saccharin sodium were used as sweetening agents to mask the bitter taste of Aceclofenac.

MATERIALS AND METHODS

Materials

Aceclofenac was procured from Microlabs Pharmaceuticals, Hosur, India. Sodium starch glycolate, microcrystalline cellulose and mannitol were procured from S.d fine- chem., Pvt. Ltd, Mumbai, India. Saccharin sodium and talc were procured from Loba Chemie., Pvt. Ltd, Mumbai, India. All other reagents used were of analytical grade.

Methods

Preparation of Aceclofenac FDT^s

Fast dissolving tablets of Aceclofenac (F_1) was prepared using sodium starch glycolate as superdisintegrant in (5% w/w) concentration by direct compression method. All the ingredients were passed through mesh No: 60 separately and collected.[4] The drug, mannitol, microcrystalline cellulose and sodium starch glycolate were mixed uniformly with gentle trituration using mortar and pestle to get a uniform mixture. Finally saccharin sodium and talc

were added and mixed well. The powder blend was then compressed using 7mm punch on 10 stations "B" Tooling Rotatory Tablet punching machine to produce flat- faced tablet, weighing 200mg each at 4kg/cm^2 force. The same procedure was followed to prepare tablets of Aceclofenac without superdisintegrant (Control-F_2). Before tablet preparation, the powder blend of all the formulations were subjected to compatibility studies (IR) and Precompression parameters like Angle of repose, bulk density, tapped density, compressibility index and hausner's ratio. The composition of Aceclofenac tablet formulations were shown in Table 1.

Table 1: Composition of Aceclofenac Fast Dissolving Tablets.

S.No	Ingredients (mg)	Formulation Code	
		F_1	F_2
1	Aceclofenac	100	100
2	Sodium starch glycolate	10	_
3	Mannitol	20	20
4	Microcrystalline cellulose	61	71
5	Saccharin sodium	5	5
6	Talc	4	4
Weight of each tablet = 200mg			

PRE COMPRESSION PARAMETERS

The powder blend was evaluated for pre compression parameters like angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The angle of repose was determined by funnel method.[5] Bulk and tapped density were determined using digital bulk density apparatus. The compressibility index of the powder blend was determined by Carr's compressibility index and the Hausner's ratio was calculated by using the formula.

Hausner's Ratio = Tapped density/ Bulk density.

Carr's index (%) = [(TD-BD) / TD] ×100.

Where, BD-Bulk density, TD-Tapped density

IR Spectral Analysis

It was used to study the interactions between the drug and the excipients.[6] The KBR disk method was used for preparation of sample and spectra were recorded over the wave number 3500 to 500 cm^{-1} in a SHIMADZU FT-IR (model- 8400) spectrophotometer. IR spectral studies of Pure Aceclofenac and Aceclofenac containing highest proportion of individual superdisintegrant were carried out. If there was no change in peaks of mixture when compared to pure drug, it indicates the absence of interactions.

POST COMPRESSION PARAMETERS

Thickness

Thickness of tablets was determined using Vernier caliber.[7] Five tablets were used for the test and average values were determined. The thickness was denoted in millimeter.

Hardness

The tablets to be tested are held between a fixed and a moving jaw of hardness test apparatus (Monsanto) and reading of the indicator is adjusted to zero. The screw knob was moved forward until the tablet breaks and the out-force required for breaking the tablet was noted.

Friability

The friability of tablets were determined by using Roche Friabilator. Twenty tablets were weighed and placed in friabilator and rotated at 25 rpm for 4 min.[8] Then the tablets were taken out, dusted and reweighed. The percentage friability of the tablets were calculated by the formula,

Percentage Friability = [(Initial Weight – Final Weight)/ Initial Weight] × 100

Weight Variation Test

Twenty tablets were selected at random and average weight was determined. The individual tablets were weighed and compared with average weight.[9] Not more than two of the individual weights deviate from the average weight of tablets by more than 7.5% and none should deviate more than 2 times the percentage limit.

Disintegration Time

The disintegration test was carried out at 37 ± 2^0C in 900 ml distilled water using disintegration test apparatus.[10] One tablet was placed in each of the six tubes of the apparatus containing distilled water. One disk was added to each tube. The time taken in sec for complete disintegration of the tablets with no mass remaining in the apparatus was noted.

Estimation of Drug Content

From each formulation of Aceclofenac tablets, 10 tablets were collected randomly and powdered.[11] A quantity of powder equivalent to 100 mg of Aceclofenac was transferred into a 100 ml standard flask, dissolved in 10 ml methanol. The volume was made up to 100 ml using phosphate buffer pH 6.8. From this stock solution 10µg/ml solution was prepared. The

drug content was estimated by measuring the absorbance of the solution at 275 nm using UV-Visible double beam spectrophotometer against phosphate buffer pH 6.8 as blank.

Wetting Time and Water Absorption Ratio

Twice folded tissue paper was placed in a Petri dish having an internal diameter of 5 cm containing 6 ml of water. A weighed tablet was carefully placed on the surface of the tissue paper in the Petri dish. The time required for water to reach the upper surface of the tablet and to completely wet it was noted as the wetting time.[12] Water absorption ratio (R) was determined by the formula.

$R = 100 \times (Wa - Wb)/ Wb$

Where Wb- Weight of the tablet before wetting, Wa- Weight of the tablet after wetting.

***In Vitro* Drug Release Study**

In vitro release of Aceclofenac was studied using USP II dissolution apparatus, with 900 ml of dissolution medium maintained at 37±1°C at 50 rpm. Phosphate buffer pH 6.8 was used as a dissolution medium. 1 ml of the samples were withdrawn at suitable time intervals of 5, 10, 15, 30 and 45 min and are replaced by fresh quantity of dissolution medium. The collected samples after suitable dilution were analyzed spectrophotometrically at 275 nm against phosphate buffer pH 6.8 as blank and percentage drug release was determined.[13]

RESULTS AND DISCUSSION

Fast dissolving tablets of Aceclofenac (F_1) using Sodium Starch Glycolate (SSG) as superdisintegrant and a control formulation F_2 (without Superdisintegrant) were prepared by direct compression method. The formulations were evaluated for pre compression parameters and post compression parameters.

Precompression Parameters

The values of precompression parameters evaluated were found to be within the prescribed limits and indicated good free flowing property (Table 2).

Table 2: Pre compression Parameters

Formulation code	Angle of repose (ɵ)	Bulk density ($g/cm^{3)}$	Tapped density (g/cm^3)	Compressibility index (%)	Hausner's ratio
F_1	33.47±0.95	0.496±0.06	0.563±0.04	11.90	1.14
F_2	33.44±1.12	0.492±0.12	0.554±0.16	11.83	1.13

***All the values are expressed as mean± SD; n=3**

Infra-red spectroscopy was used as means of studying drug – excipient compatibility and confirmed by comparing undisturbed structure of IR spectra of Pure Aceclofenac with Aceclofenac containing highest proportion of superdisintegrant. It showed that IR spectrum of pure Aceclofenac and Aceclofenac containing highest proportion of superdisintegrant were similar fundamental peaks and patterns which indicated no drug excipient interaction (Figure 1 to 3).

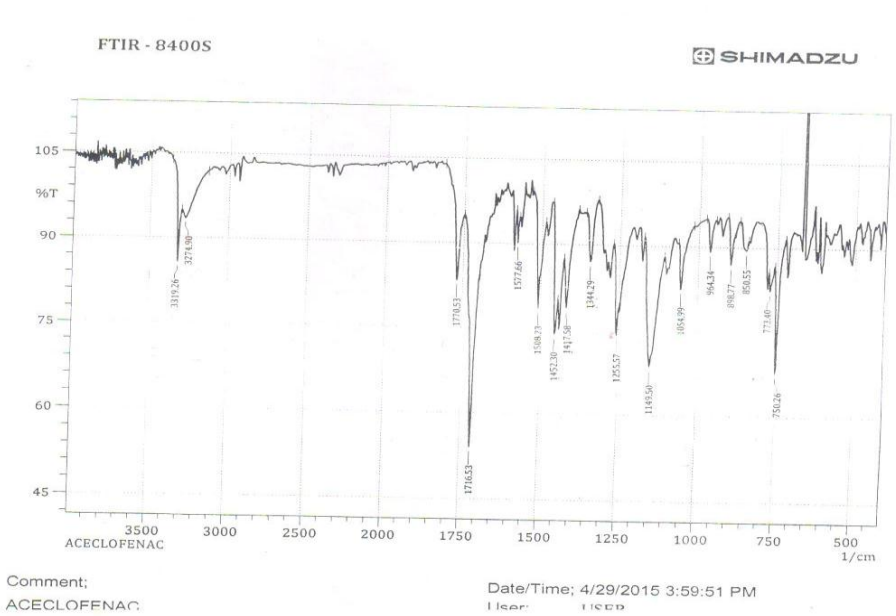

Fig 1: FT-IR Spectrum of Aceclofenac

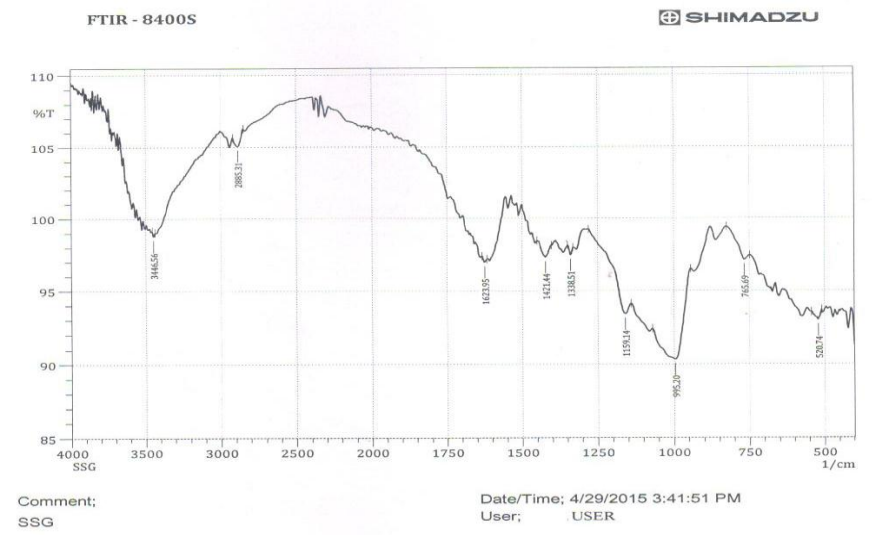

Fig 2: FT – IR Spectrum of Sodium Starch Glycolate

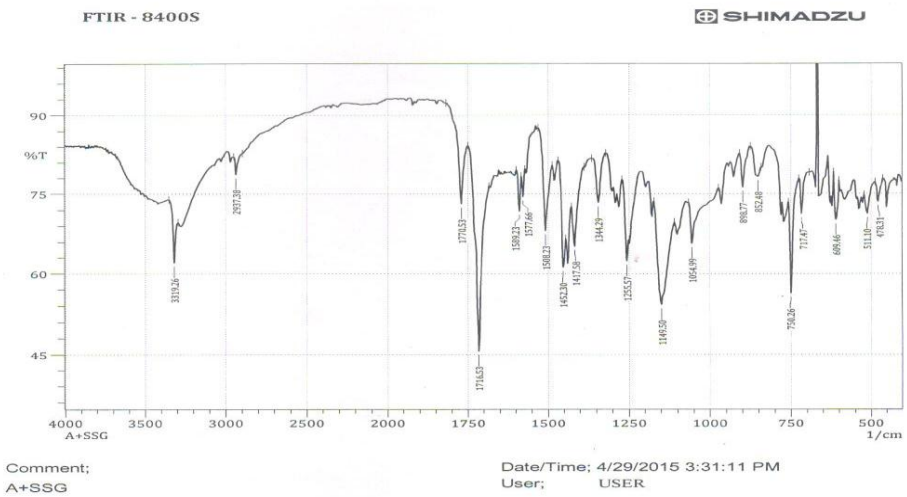

Fig 3: FT – IR Spectrum of Aceclofenac + Sodium Starch Glycolate

Post Compression Parameters

The thickness and the hardness of Aceclofenac tablet formulation F_1 and F_2 were found to be 4.2±0.06 and 4.12±0.04 mm and 3.7±1.6 and 3.6±1.32kg/cm^2 respectively. Both the formulations showed uniform thickness and hardness. Friability test was carried out using Roche friabilator. A maximum weight not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable. The friability values of Aceclofenac tablet formulation F_1 and F_2 were found to be 0.82±0.57% and 0.84±0.57%. The results revealed that both the formulations of Aceclofenac tablets passed the friability test. In weight variation test twenty tablets of each formulation were selected randomly and weighed. The actual weight of one tablet is 200 mg. So the acceptable deviation was ±7.5%. The weight variation of Aceclofenac tablets was found within the range of 197.6± 1.3 to 202.4±1.6 mg. These results revealed that the tablets obtained were of uniform weight (due to uniform die fill) with acceptable variation as per IP specifications i.e. below 7.5%.Tablets were evaluated for disintegration time in the disintegration test apparatus. The disintegration time of Aceclofenac tablet formulation F_1 and F_2 was found to be 47±1.45 and 184±2.6 sec. Formulation F_1 showed less disintegration time compared to formulation F_2 which may be due to the presence of sodium starch glycolate as superdisintegrant. The drug content of formulation F_1 and F_2 was found to be 98.62±1.9 and 99.34±2.4%. The drug content was found to be uniform in both formulations and was within the acceptable limit. The wetting time of the tablets of formulation F_1 and F_2 was found to be 42±2.4 and 86±2.6 sec. The wetting time was considerably reduced in tablets containing sodium starch glycolate as superdisintegrant compared to formulation F_2 without superdisintegrant. The water

absorption ratio of formulation F_1 and F_2 was found to be 68±2.6 and 51.25±2.3%. Formulation F_1 showed good water absorption ratio due to its swelling capacity. The results of thickness, hardness, friability, weight variation, disintegration time, drug content, wetting time and water absorption ratio of Aceclofenac tablets are given in Table 3.

Table 3: Post Compression Parameters.

Formulation code	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Weight variation (mg)	Disintegration Time (sec)	Drug content (%)	Wetting time (sec)	Water absorption ratio %
F_1	4.2±0.06	3.7±1.6	0.82±0.57	197.6±1.3	47±1.45	98.62±1.9	42±2.4	68±2.6
F_2	4.12+0.04	3.6±1.32	0.84±0.57	202.4±1.6	184±2.6	99.34±2.4	86±2.6	51.25±2.3

***All the values are expressed as mean ± SD; n = 3**

In Vitro Drug Release Studies

The percentage drug release from formulation F_1 and F_2 at the end of 45 min was found to be 72.8±2.4% and 51.12±1.7%, respectively. Formulation F_1 prepared by using sodium starch glycolate as superdisintegrant showed a better percentage of drug release when compared to formulation F_2 prepared without superdisintegrant. This may be due to easy swelling ability and wicking capacity of sodium starch glycolate compared to formulation F_2 without superdisintegrant. The delayed drug release of formulation F_2 may be due to longer disintegration time and lesser solubility in the dissolution medium. The drug release profiles of Aceclofenac tablets are shown in Figure 4.

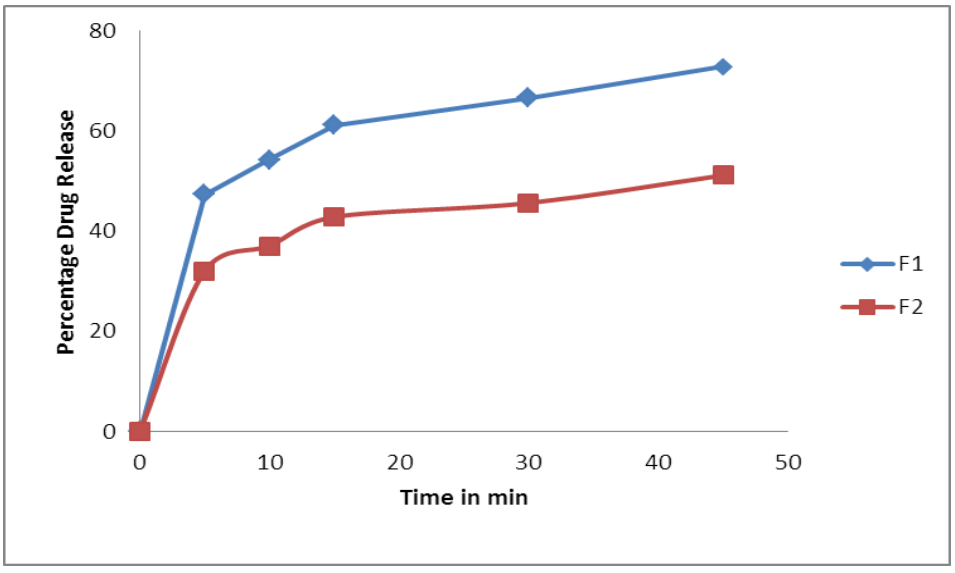

Fig 4- *In vitro* Release Profiles of Aceclofenac Formulations

CONCLUSION

The results of experimental studies of Aceclofenac tablets proved that the Powder blend of Aceclofenac showed good flow properties, tablet evaluation tests are within the acceptable limits, IR spectral analysis proved that there was no drug- excipient interaction. The formulation prepared with sodium starch glycolate as superdisintegrant showed a rapid drug release than control (without superdisintegrant) formulation and satisfied all the criteria for fast dissolving tablets. Hence the results of the above study clearly indicated that Aceclofenac can be formulated as fast dissolving tablets using sodium starch glycolate as superdisintegrant in the concentration of 5%w/w by direct compression method.

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