Research Article

Formulation, Development and *In-vitro* Evaluation of Fast Dissolving Tablet of Aceclofenac using co-processed Superdisintegrant by Direct Compression Method

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ABSTRACT

In the present reported project study, the effect of co-processed superdisintegrant was compared with synthetic super disintegrants and conventional super disintegrants in the fast dissolving tablet formulation of Aceclofenac. Aceclofenac is a potent analgesic and used in pain management. Aceclofenac directly blocks PGE2 secretion at the site of inflammation by inhibiting IL & TNF in the inflammatory cells. Aceclofenac has been demonstrated to inhibit COX activity and to suppress the PGE2 production by inflammatory cells, which are likely to be a primary source of PGE2. In the present work, 9 formulations of Fast dissolving tablets of Aceclofenac were prepared by using Synthesized Co-proceed was evaluated and compiles with the official standards, parameters and specifications. Various formulations were prepared using three types of different superdisintegrant namely- kyron T-314, sodium starch glycolate, cross carmelose sodium with three concentrations (2%, 4%, 6%) by direct compression method. The blend was evaluated for pre-compression parameters like Angle of repose , bulk density , tapped density , and then tablet evaluated post-compression parameters like thickness , drug content , hardness , weight variation , wetting time , friability , disintegration time , dissolution time, drug release study. Formulation A8 showed the lowest disintegration time and in-vitro dissolution studies recorded that formulation A8 showed 98.05% drug release at the end of 3 minutes. The best formulations were also found to be stable and optimized formulations were subjected to the stability studies as per ICH guideline and standards.

Keywords: Fast dissolving tablet, Aceclofenac, Co-proceed, sodium starch glycolate, Kyron T-314, direct compression, dissolution time.

INTRODUCTION

The tablet is most widely used dosage for because of its convenience in term of self-administration, compactness, accurate drug dose and ease in manufacturing. Over this one drawback of conventional tablet is difficulty in swallowing by pediatric and geriatric patients.[1, 2]

To beat these issues the scientists have developed novel drug delivery system that known as fast dissolving tablet. The fast dissolving defined as the tablets that dissolve in few seconds in the mouth when they come with contact saline without requirement of additional water. The advantage of FDT is onset of action, higher patient acceptance, and increased bioavailability.[3, 4]

Aceclofenac is a phenylacetic acid derivative with anti-inflammatory and analgesic properties. Double-blind comparative trials indicate that the efficacy of Aceclofenac is at least equivalent to that of ketoprofen and similar to that of indomethacin and diclofenac in patients with rheumatoid arthritis, similar to that of diclofenac and piroxicam in patients with osteoarthritis of the knee and similar to that of tenoxicam, indomethacin and naproxen in patients with ankylosing spondylitis.

Bioavailability of Aceclofenac is about 80% to 90% and its half-life is 4-4.5 h. The drug is distributed throughout the body and 90% of drug binds to plasma proteins. It undergoes rapid first-pass metabolism in the liver (approximately 95% of a dose). This leads to lower bioavailability of Aceclofenac. In order to overcome such extensive first-pass metabolism effect, so the drug is selected for fast dissolving tablet.[5-9]

MATERIALS AND METHODS

Materials

Aceclofenac was received as gift sample by IPCA labs, Mumbai, Magnesium stearate used were procured from Reckon animal health care, Jaipur , Lactose used was procured from Rescue laboratories, Jaipur, Kyron T-314 was gifted by Corel PharmaChem, Ahmadabad, Aspartame used was procured from Sweetener India, Delhi, and other reagents and chemicals used were of analytical grade.

Method

Fast dissolving tablets of Aceclofenac were prepared by direct compression method. Pure drug and excipients were passed through # 60 No. mesh. Required amount of drug and excipients were taken for every formulation according Table No. 1.

The powdered drug, Mannitol and Lactose were mixed uniformly with continuous triturating using mortar and pestle. Then required quantity of super disintegrates and aspartame taken for each formulation and mixed, finally magnesium stearate and talc powder were added and mixed well.[10, 11, 12]

The mixed blend of drug and excipients were compressed using 10 station tablet punching machine. (Shakti pharmaceuticals**)** 4 Mm punch. A Batch of 50 tablets of each formulation was prepared for all the designed formulation. Before the tablet preparation punch the mixture blend of all designed formulations were subjected to compatibility studies (IR) and pre-compression parameters like- Angle of repose, Bulk density, Tapped density, compressibility index, Hauser's ratio.[13,14,15]

Pre-formulation studies

Angle of Repose (ϑ)

Angle of repose is the maximum possible angle between the surface of the pile of the powder and the horizontal plane of the powder. When more quantity powder is added to the pile, it slides down, until the mutual friction of the particles producing a surface angle θ, is equilibrium with the gravitational force.[15, 16, 17]

The angle of repose was determined by the funnel method suggested by the scientist Newman. Angle of repose is determined by the following formula

$\tan \theta = h/r$

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

Where θ = Angle of repose
r = Radius of the cone
h = height of the cone

Bulk Density

Density is weight mass per unit volume. Bulk density is defined as the mass of the powder is divided by the bulk volume of powder and is expressed as gm/ cm^3.The bulk density of a powder primarily depends on its, particle shape, particle size, distribution and the tendency of particles to adhere together. There are two types of bulk density.[18-21]

Low bulk density

The particles are pack in such a way so as to leave large gaps between their surfaces resulting up in light powder of low bulk density.

High bulk density

Here the smaller particles shift between the large particles resulting in heavy powder of high bulk density

Tapped Density (DT)

It was the ratio of total mass of the powder to tapped volume of the powder. Volume was reported by tapping the powder for 500 times and the tapped volume was observed, if the difference between these two volumes was less than 2%. If it more than 2%, then tapping was continued for 750 times and tapped volume was noted. Tapping was continued until the difference between volumes was less than 2% in bulk density apparatus. It was expressed in g/ml and was given as following,

DT= M/Vt

Where, M is the mass of powder

Vt is the tapped volume of the powder. [22-24]

Carr's index (or) % compressibility

Carr's index indicates powder flow properties. It is expressed by percentage and is given by:

I=DT−Db/DT×100

Where, DT denotes the tapped density of the powder

And

Db is the bulk density of the powder. [25,26,27,28]

Hausner ratio

Hausner ratio is an indirect index of ease of powder flow properties. It is calculated by the following formula:

Hausner ratio=Dt/Db

Where, Dt show the tapped density.

Db is the bulk density.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25)

Evaluation of Tablet

All prepared tablets of Aceclofenac were evaluated for the following parameters as per IP guideline and standards for all the calculations are represented in the table No.3

Weight Variation

Twenty tablets of Aceclofenac formulation were selected randomly from each of the formulation and weighted individually using Citizen Digital Balance for their weight variation data. The average weight of the tablets as well as percentage deviation was calculated.[29, 30, 31]

Hardness

Hardness of the Aceclofenac tablets were measured with Monsanto tablet hardness tester for evaluation the hardness of the tablets.

Thickness

The thickness of the tablet was measured in mm by the Vernier Calipers for all the designed formulation batches.

Friability

The Friability of the Aceclofenac tablet by a sample of twenty tablets was measured using USP type Roche Friabilator. The tablets were dusted reweighed and percentage weight-loss was calculated.

%Friability = Initial Weight−Final Weight * 100/ Initial Weight

Water absorption ratio

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in small Petri-plate (ID = 6.5 cm) containing 10 ml of water. A tablet was placed on the paper and time for complete wetting of the tablet was measured in seconds. Three trials for each batch were performed and the standard deviation was also determined. The wetted tablet was weighed and water absorption ratio R, was determined by following equation

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

Where, Wa and W_b were weights of the tablets after and before study.[33, 34, 35]

Wetting Time

A piece of tissue paper (12cmX10.75cm) folded twice was placed in a small Petri dish (ID = 9 cm) containing 5ml pH 6.8 phosphate buffer, A tablet was placed on the paper and the time taken for complete wetting was observed. Three tablets from each formulation were randomly selected and the average wetting time was noted.

Disintegration Study

Disintegration time study was carried out by selecting 6 tablets of Aceclofenac and performed disintegration test (Lab India) using 900 ml distilled water at temperature ($37^0C \pm 2^0C$) [36,37,38]

Dissolution Study

The In-vitro for the dissolution study was carried out in the USP (United state pharmacopeia) dissolution test apparatus type 2 known as Paddle dissolution apparatus, used phosphate buffer as dissolution medium as 900 ml containing PH 6.8 was taken in vessel and the temperature maintained at 37 ± 0.5^0C. The speed of the paddle was set at RPM 50, then 5 ml dissolution medium was withdrawn and the same amount (5ml) of fresh medium was replenished to the dissolution medium. The calculations of the Concentration were calculated by absorbance base. The release of the drug was performed in replicates of three.

Table 1: Formulation of fast dissolving tablet of Aceclofenac

Ingredients(mg)	A1	A2	A3	A4	A5	A6	A7	A8	A8
Aceclofenac	100	100	100	100	100	100	100	100	100
Cross carmellose Sodium	4	8	12	-	-	-	-	-	-
Sodium Starch Glycolate	-	-	-	4	8	12	-	-	-
Kyron T-314	-	-	-	-	-	-	4	8	12
Aspartame	4	4	4	4	4	4	4	4	4
Flavour	4	4	4	4	4	4	4	4	4
Magnesium Stearate	4	4	4	4	4	4	4	4	4
Talc	4	4	4	4	4	4	4	4	4
Mannitol	30	30	30	30	30	30	30	30	30
Lactose	25	25	25	25	25	25	25	25	25
Sorbitol	25	21	17	25	21	17	25	24	17
TOTAL	200	200	200	200	200	200	200	200	200

Table 2: Pre-compression parameters of Aceclofenac fast dissolving tablet

Parameters→ Formulation↓	Bulk Density (mg/ml)	Tapped Density (mg/ml)	Hausners Ratio	Compressibilty Index (%)	Angle of Repose 0
A1	0.401±0.11	0.461±0.11	1.149±0.05	14.96±0.15	24.19±0.21
A2	0.421±0.15	0.471±0.24	1.118±0.09	11.87±0.23	25.32±0.15
A3	0.411±0.08	0.485±0.29	1.180±0.12	17.57±0.28	22.95±0.22
A4	0.437±0.12	0.489±0.26	1.118±0.15	11.89±0.55	23.52±0.25
A5	0.410±0.06	0.457±0.24	1.114±0.13	12.68±0.63	24.91±0.15
A6	0.449±0.10	0.516±0.21	1.149±0.21	14.92±0.89	23.19±0.14
A7	0.439±0.13	0.485±0.16	1.104±1.01	10.47±0.25	25.29±0.17
A8	0.437±0.01	0.491±0.14	1.098±1.12	12.35±0.55	24.25±0.25
A9	0.428±0.09	0.479±0.12	1.119±1.14	11.91±0.56	24.52±0.21

Table 3: Post-Compression parameters of Aceclofenac fast dissolving tablet

Parameters→ Formulation↓	Diameter (mm)	Thickness (mm)	Weight (mg)	Hardness (Kg/cm^2)	Friability (%)	Disintegration Time (Sec)
A1	4	3	204.05±0.05	3.15±0.15	0.58±0.84	44±1.44
A2	4	3	210.07±0.18	3.09±0.01	0.57±0.25	39±1.14
A3	4	3	213.01±0.11	3.13±0.99	0.67±0.17	45±1.46
A4	4	3	208.02±0.15	3.12±0.12	0.59±0.16	63±1.25
A5	4	3	198.01±0.11	3.10±0.01	0.69±0.12	59±1.52
A6	4	3	219.05±0.19	3.20±0.10	0.75±0.32	65±1.36
A7	4	3	205.01±0.17	3.15±0.05	0.62±0.13	31±1.01
A8	4	3	201.00±0.04	3.01±0.09	0.65±0.23	30±1.59
A9	4	3	198.02±0.12	3.25±0.28	0.51±0.19	33±1.58

Table 4: Drug Content in the Fast Dissolving Tablet of Aceclofenac

Parameters→ Formulation↓	Drug Content (mg / Tablet)	% Drug Content
A1	190.64±0.025	95.32
A2	192.82±0.035	96.41
A3	192.32±0.015	96.16
A4	193.34±0.041	96.67
A5	193.90±0.055	96.95
A6	193.10±0.050	96.55
A7	194.32±0.085	97.16
A8	196.10±0.051	98.05
A9	195.50±0.058	97.75

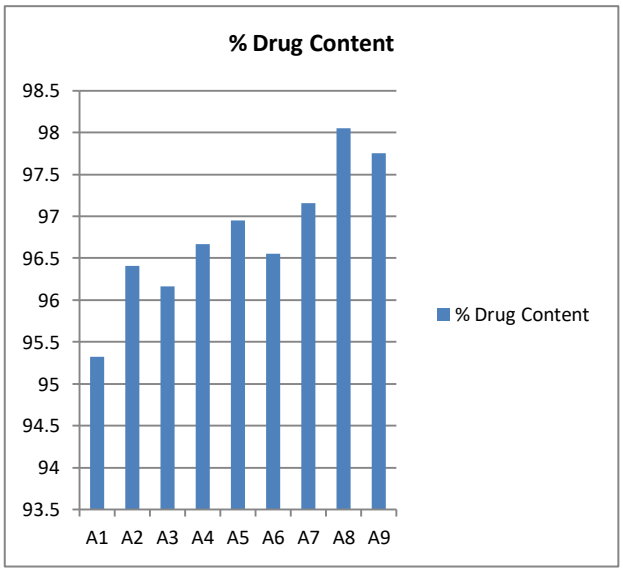

Figure 1: Drug Content in the Fast Dissolving Tablet of Aceclofenac

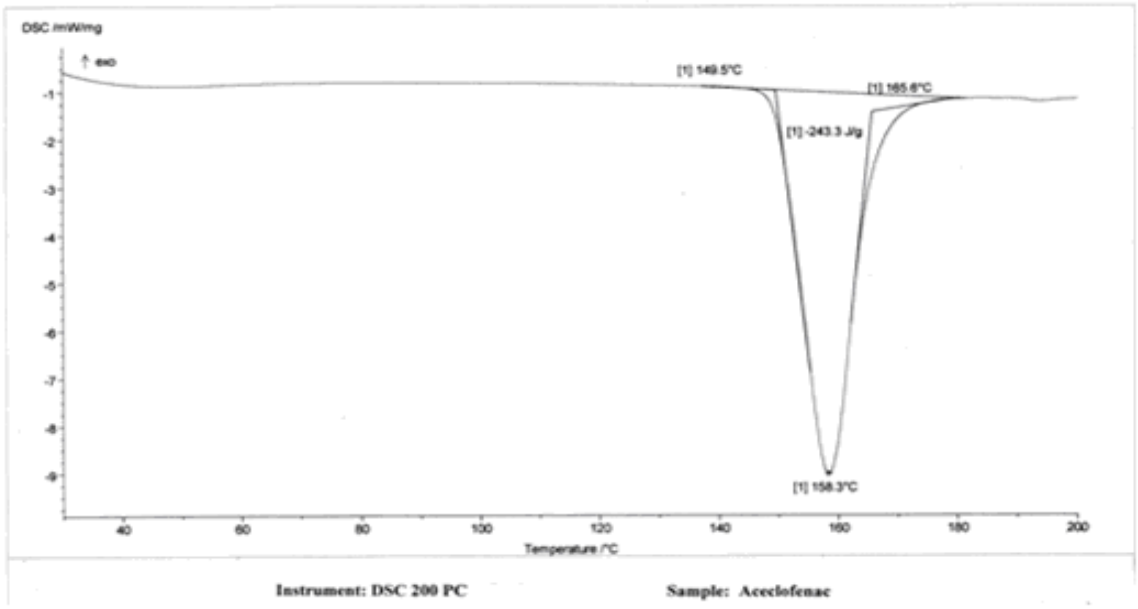

Figure 2: DSC Thermogram of Aceclofenac

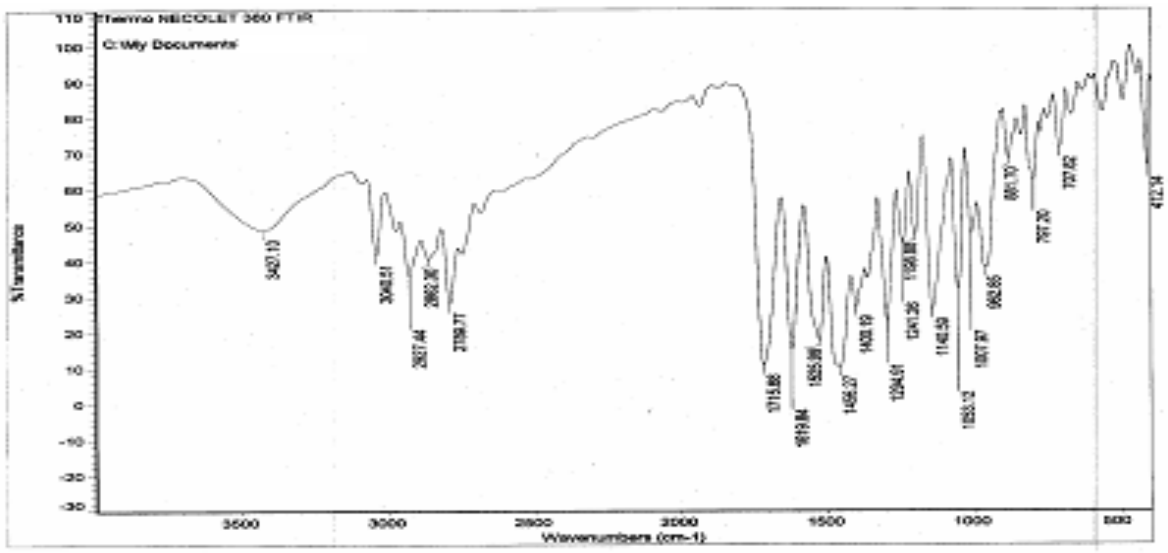

Figure 3: IR Spectra of Aceclofenac

RESULTS AND DISCUSSION

Bulk density and tapped density of powder blend has been evaluated. The angle of repose for the entire formulations blend was found to be in the range 22.95±0.22 to 25.29±0.17°. Formulations with Crosscarmelose Sodium (A1-A3) as a disintegrants showed angle of repose values ≤ 24.19±0.21°. Other the formulation Sodium Starch Glycolate containing (A4-A6) was showed angle of repose values <24.91±0.15°, (A7-A9) was showed angle of repose values ≤25.29±0.17° and indicating only fair flow property of the powder blend. Compressibility index was found to be in the range 10.47±0.25% to 17.57±0.28%. All formulations showed good flow properties. Hausner's ratio was found to be in the range 1.098±1.12 to 1.180±0.12 and that indicated that all formulation has good flow properties. The batches A8, showed low hardness and A9 higher. All parameters show weight variation, thickness, Disintegration time (sec) within standard limit. All formulation was subjected to dissolution. From all the above observations it was concluded that the formulation A8 containing Kyron T-314 4% found to be better formulation in terms of rapid dissolution and maximum percentage drug release was found 98.05%.

CONCLUSION

It can be concluded from the whole study that fast dissolving tablets of Aceclofenac drug. Co procced superdisintegrant can be used as pharmaceutical excipients for oral drug delivery. So co-procced superdisintegrant like Kyron T-314 exhibited faster drug dissolution which leads to improve bioavailability, effective therapy (Therapeutic ratio), improve patient compliance, and satisfies all the standards as fast dissolving tablet. It was concluded formulation A8 maximum percentage drug release was found 98.05, with Kyron T-314 with 4%.

From the study, it was concluded that co-procced superdisintegrant like Kyron T-314 showed better disintegrating property over the synthetic super disintegrate like, SSG(Sodium starch glycolate) CCS (Crosscarmelose Sodium).

Abbreviation Table

PGE_2	Prostaglandin E2
IL	Inter-leukin
TNF	Tumor necrosis factor
COX	Cyclooxygenase
FDT	Fast dissolving tablet
IR	Infra red

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