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Formulation and evaluation of aceclofenac fast dissolving tablets

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Abstract

The present investigation deals with development of fast dissolving tablets of aceclofenac to produce the intended benefits. Fast dissolving tablets of aceclofenac were prepared using superdisintegrants crospovidone, croscarmellose sodium and sodium starch glycolate and surfactant sodium lauryl sulfate, using the direct compression method. The tablets prepared were evaluated for thickness, uniformity of weight, hardness, friability, wetting time, *in vitro* disintegration time and *in vitro* dissolution time. The tablets disintegrated within 18 to 49 seconds. Almost 90% of drug was released from all formulations within 15 min. Stability studies of the tablets at 40±2°/75%±5% RH for 3 months showed non significant drug loss. The formulation containing 6% of croscarmellose sodium was found to give the best results. Apart from fulfilling all official and other specifications, the tablets exhibited higher rate of release.

Key-Words: Direct compression, *In vitro* dissolution and *In vitro* disintegration time, Fast dissolving, Aceclofenac, Wetting time

Introduction

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients, is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention[1].

Fast dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form.

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Their growing importance was underlined recently when European pharmacopoeia adopted the term "Orodispersible tablet" as a tablet that to be placed in the mouth where it disperses rapidly before swallowing[2]. The bioavailability of some drugs may be increased due to absorption of drug in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach[3].

Aceclofenac (2-[(2,6-dichlorophenyl) amine] phenylacetoxyacetic acid) is an orally effective non-steroidal anti-inflammatory drug (NSAID) of the phenyl acetic acid group, which possesses remarkable anti-inflammatory, analgesic and antipyretic properties. The analgesic efficacy of aceclofenac 100 mg is more prolonged than that of acetaminophen 650 mg. Aceclofenac appears to be particularly well-tolerated among the NSAIDs, with a lower incidence of gastrointestinal adverse effects[4]. Aceclofenac is practically insoluble in water. For poorly soluble orally administered drugs, the rate of absorption is often controlled by the rate of dissolution. The rate of dissolution can be increased by increasing the surface area of available drug by various methods[5]. The dissolution of a drug can also be influenced by disintegration time of the tablets. Faster disintegration of tablets delivers a fine suspension of drug particles resulting in a higher surface area and faster dissolution[6].

Objective of my study to formulate and evaluate Aceclofenac fast dissolving tablets by direct compression method and to increase the drug release profile in short duration of time. Evaluation of formulated tablets was done using various quality parameters like hardness, friability, wetting time, DT, *in vitro* dissolution study. Finally, stability study of optimized batches was performed.

Material and Methods

Materials

Aceclofenac, aspartame and croscarmellose were received as a gift sample from Stallion Lab. Pvt. Ltd., bawla, Gujarat. Sodium Starch Glycolate, crospovidone, mannitol, sodium lauryl sulfate and microcrystalline cellulose were gifted from Aura Nutraceuticals Ltd., Budasan, Gujarat.

Preparation of Fast Dissolving Tablets of Aceclofenac[7]

Different tablets formulations were prepared by direct compression technique. Drug, diluent, superdisintegrants, surfactant and sweetener were passed though sieve # 40 and magnesium stearate was passed through # 80 sieve. Required quantity of drug, and surfactant was mixed first than other excipients were mixed thoroughly. The powder was compressed using cadmach compression machine equipped with 10/32 round biconvex punches by direct compression technique. The compositions of various batches are shown in table 1.

Evaluation of Aceclofenac Fast Dissolving Tablets

Weight variation test[8]

Weight variation test was done by weighing 20 tablets individually, by using Sartorious balance (Model CP-224 S). Calculating the average weight and comparing the individual tablet weight to the average weight.

Tablet thickness[8]

The thickness was measured by placing tablet between two arms of the Varnier calipers. 5 tablets were taken and their thickness was measured.

Tablet hardness[8]

The tablet hardness, which is the force required to break a tablet in a diametric compression force. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring.

Tablet friability[8]

The friability of the tablets was measured in a Roche friabilator (Camp-bell Electronics, Mumbai). Tablets of a known weight (W_0) or a sample of 20 tablets are dedusted in a drum for a fixed time (100 revolutions) and weighed (W) again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1 %. Determination was made in triplicate.

$$\% \text{ Friability} = \frac{W_0 - W}{W_0} \times 100$$

Drug content[9-10]

Twenty tablets were taken and amount of drug present in each tablet was determined. The tablet was crushed in a mortar and the powder equivalent to 100mg of drug was transferred to 100ml standard flask. The powdered was dissolved in 5ml of methanol and made upto volume with phosphate buffer pH 6.8. The sample was mixed thoroughly and filtered through a 0.45µ membrane filter. The filtered solution was diluted suitably and analyzed for drug content by UV spectrophotometer at 274nm using phosphate buffer pH 6.8 as blank.

Wetting time[11]

A piece of tissue paper (12cmx10.75cm) folded twice was placed in a Petri dish (Internal Diameter = 9cm). 10ml of water containing Eosin, a water soluble dye , is added to petridish. A tablet is placed carefully on the surface of tissue paper. The time required for water to each upper surface of the tablet is noted as a wetting time. Determination was made in triplicate.

***In- vitro* Disintegration test**[12]

The disintegration time was measured using disintegration test apparatus. One tablet was placed in each tube of the basket. The basket with the bottom surface made of a stainless steel screen (mesh no. 10) was immersed in water bath at 37 ± 20C. The time required for complete disintegration of the tablet in each tube was determined using a stop watch. To be complied with the Pharmacopoeial standards, dispersible tablets must disintegrate within 3 min when examined by the disintegration test for tablets.

***In- Vitro* dissolution studies**[12]

In vitro dissolution studies for Aceclofenac fast dissolving tablets was carried out using USP paddle method at 50 rpm in 900 ml of phosphate buffer pH 6.8 as dissolution media, maintained at 37±0.5°C. 5 ml aliquot of the solution was withdrawn from the dissolution apparatus after suitable time intervals, and the samples were replaced with fresh dissolution medium. Absorbance of these solutions was measured at 274 nm using a shimadzu UV-1700UV/VIS spectrophotometer.

Stability study[12]

The stability study of optimized formulation (batch F9) was carried out as per ICH (International Conference on Harmonization) guidelines at 400 ºC and 75% RH using stability chamber for three month. The effects of temperature and time on the physical characteristics of tablets were evaluated for assessing the stability of prepared formulations. The samples were collected monthly and different parameters like hardness,

uniformity of weight, friability, drug content and disintegration time were studied.

Results and Conclusion

Attempt was made in the present investigation to make a fast dissolving tablet of Aceclofenac by direct compression method. Formulation was carried out using different three types of super disintegrants and optimized the concentration and hardness of the tablet to give the minimum disintegration time and get maximum drug release. To improve the in-vitro dissolution optimized the concentration of surfactant. 1.5 % concentration of surfactant used to get maximum drug release with minimum time. Since the flow properties of the powder mixture are important for the uniformity of the mass of the tablets, the flow of the powder mixture was analyzed before compression of the tablets. The results of angle of repose and compressibility index (%) ranged from (24.23±0.04º to 28.75±0.01º) and (15.22±0.04 to 23.52±0.02), respectively. The results of loose bulk density and tapped bulk density ranged from (0.36±0.04 gm/cm^3 to 0.39±0.03 gm/cm^3) and (0.46±0.01 gm/cm^3 to 0.56±0.03 gm/cm^3), respectively. The results of angle of repose (<30) and compressibility index indicates good flow properties of powder blend (Table 2).

The results of physical properties of different batches of aceclofenac fast dissolving tablets are given in (Table 3). Tablet mean thickness was almost uniform in all the formulations. The thickness varies between 3.69±0.2 mm to 3.80±0.02 mm. The prepared tablets in all the formulations possessed good mechanical strength with sufficient hardness in the range of 3.0±0.15 kg/cm^2 to 3.6±0.1 kg/cm^2. Friability values below 1% were an indication of good mechanical resistance of the tablets. All the tablets from each formulation passed weight variation test, as the % weight variation was within the Pharmacopoeial limits of ±7.5% of the weight. The weight variation in all the formulations was found to be 198.4±0.89 mg to 201.0±1.0 mg. The percentage drug content of all the tablets was found to be between 99.23±0.53 to 101.56±1.34 percent of aceclofenac which was within the acceptable limits.

The wetting time for all the formulations was performed in triplicate. The time for all formulations varied between 18±0.97 to 86±2.11 sec (Table 3). The wetting time of the tablets were also considerably reduced in tablets containing croscarmellose which may be attributed due to the wicking and swelling type of disintegrants thus facilitating the faster disintegration. The *in vitro* dissolution profile indicated faster and maximum drug release from formulation F-9 (Fig. 2).

Formulation F-9 which showed promising results, were subjected to stability studies at ambient room conditions for 3 months. After 3 months, aceclofenac fast dissolving tablets did not show any change in physical appearance or drug content. In the formulation using superdisintigrant with the concentration of 6% and hardness range of 3-4 kg/cm2, disintegration time and drug release found to be 18±0.97 seconds and 99.07±0.10% respectively within 15 minutes. Percentage friability and % drug content were found 0.64±0.01% and 99.57±0.26%, respectively and were within the acceptable limit.

In the present study, the effects of different concentrations of superdisintegrants on FDT of Aceclofenac were studies. It was found that aceclofenac tablets passes for hardness, friability, wetting time, DT, and *in vitro* dissolution profile. It was observed that when croscarmellose sodium used at 6% concentration (formulation F9) with surfactant (3 mg) % drug release was maximum in 15 minutes and disintegration time was least (18 seconds). And in stability testing of batch F9, tablets did not show any change in physical appearance or drug content. Therefore it is concluded that croscarmellose sodium can be effectively used as superdisintegrant in aceclofenac fast dissolving tablets.

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Table 1: Composition of Fast Dissolving Tablets of Aceclofenac

Ingredients (mgs)	Formulation Code (in mg)									
	T	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Aceclofenac	100	100	100	100	100	100	100	100	100	100
Mannitol	77	74	70	66	74	70	66	74	70	66
Crospovidone	-	4	8	12	-	-	-	-	-	-
Sodium starch glycolate	-	-	-	-	4	8	12	-	-	-
Croscarmellose Sodium	-	-	-	-	-	-	-	4	8	12
Microcrystalline Cellulose	7	7	7	7	7	7	7	7	7	7
Aspartame	10	10	10	10	10	10	10	10	10	10
Magnesium stearate	2	2	2	2	2	2	2	2	2	2
Surfactant	-	3	3	3	3	3	3	3	3	3
Total	200	200	200	200	200	200	200	200	200	200

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Table 2: Angle of Repose, Loose Bulk Density, Tapped Density and % Compressibility Index

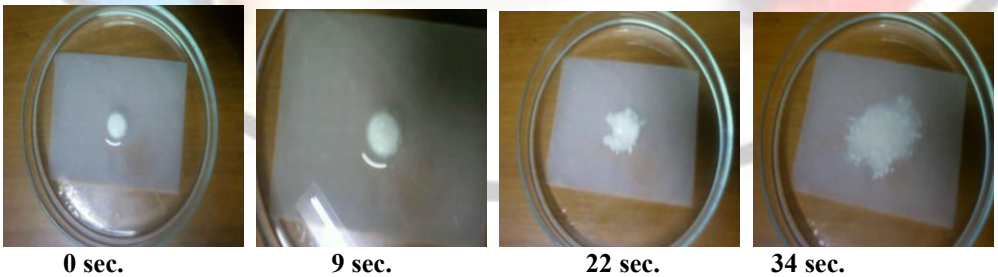
Formulation Code	Angle of Repose (θ)	Loose Bulk Density (gm/cm^3)	Tapped Bulk Density (gm/cm^3)	% Compressibility
T	25.67±0.02	0.36±0.04	0.56±0.03	23.52±0.02
F1	26.43±0.02	0.37±0.01	0.47±0.01	21.27±0.04
F2	27.35±0.02	0.39±0.02	0.49±0.02	20.40±0.03
F3	28.75±0.01	0.38±0.01	0.46±0.01	17.39±0.05
F4	26.98±0.01	0.37±0.01	0.47±0.01	21.21±0.02
F5	25.12±0.03	0.39±0.03	0.49±0.02	20.40±0.03
F6	24.53±0.04	0.37±0.03	0.50±0.02	22.91±0.02
F7	25.65±0.02	0.38±0.02	0.48±0.03	20.83±0.01
F8	24.63±0.03	0.39±0.02	0.48±0.01	18.75±0.03
F9	24.23±0.04	0.39±0.01	0.46±0.03	15.22±0.04

Each data represents Mean ±SD (n=3)

Table 4: Stability Study of Optimized Batch of Aceclofenac Fast Dissolving Tablets

Sr. No.	Time	Parameters				
		Hardness (Kg/cm^2)	Uniformity of weight	Friability (%)	Disintegration time(sec)	Drug content (%)
1	0 week	3.6±0.57	200.2±0.32	0.64±0.02	18±1.02	99.57±0.09
2	4 week	3.4±0.15	200.3±0.28	0.68±0.01	17±1.59	98.83±0.11
3	8 week	3.3±0.10	200.6±0.34	0.69±0.01	17±0.83	97.49±0.12
4	12 week	3.1±0.15	200.8±0.33	0.71±0.01	16±0.93	96.71±0.15

Each data represents Mean ±SD (n=3)



0 sec. 9 sec. 22 sec. 34 sec.

Fig. 1: Wetting time of Fast Dissolving tablet (batch F9)

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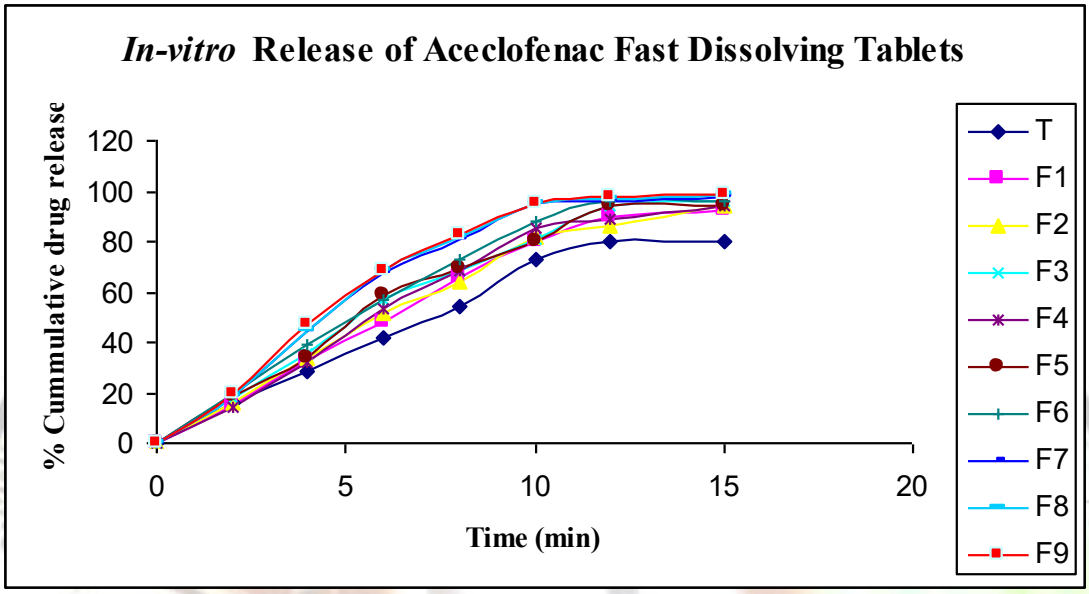

Fig. 2: Drug release study of aceclofenac Fast Dissolving tablets of different batches in pH 6.8 phosphate buffer

Table 3: Result of Evaluation Parameters of Aceclofenac Fast Dissolving Tablets

Formulation code	Parameters						
	Average weight (mg)	Thickness (mm)	Hardness	% Friability	% drug content	Wetting time (sec)	Disintegration time (sec)
T (Trial Batch)	201.0±1.0	3.79±0.03	3.3±0.05	0.76±0.03	99.69±0.54	*86±2.11*	*82±2.5*
F1	200.0±0.81	3.69±0.2	3.3±0.1	0.75±0.01	99.23±0.53	52±2.18	26±2.03
F2	200.1±0.26	3.70±0.2	3.2±0.1	0.78±0.01	99.34±0.44	51±2.33	34±1.75
F3	200.1±0.39	3.69±0.2	3.0±0.15	0.81±0.02	99.64±1.24	47±1.24	49±1.5
F4	198.4±0.89	3.80±0.02	3.3±0.15	0.76±0.01	101.56±1.34	46±1.36	29±1.23
F5	198.6±0.93	3.80±0.02	3.6±0.1	0.64±0.02	99.85±0.65	42±1.33	24±1.89
F6	200.1±0.32	3.79±0.02	3.2±0.15	0.79±0.01	98.62±0.61	39±1.28	20±1.13
F7	200.1±0.29	3.78±0.2	3.3±0.1	0.75±0.02	99.23±0.40	40±2.31	19±1.73
F8	199.4±0.43	3.79±0.2	3.2±0.05	0.71±0.01	99.41±0.56	37±1.58	19±1.25
F9	199.6±0.28	3.80±0.2	3.5±0.05	0.64±0.01	99.57±0.26	34±1.52	18±0.97

Each data represents Mean ±SD (n=3)