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Research Article

FORMULATION AND EVALUATION OF FAST DISPERSIBLE TABLETS OF ACECLOFENAC USING DIFFERENT SUPERDISINTEGRANT

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ABSTRACT

Convenience of administration and patient compliance are gaining significant importance in design of dosage form. Fast dispersible tablets disintegrate either rapidly in water, to form a stabilized suspension, or disperse instantaneously in the mouth to be swallowed without the aid of water. Aceclofenac, a non-steroidal antiinflammatory drug, is used for posttraumatic pain and rheumatoid arthritis. Fast dissolving tablet of aceclofenac were prepared by direct compression method after incorporating superdisintegrants croscarmellose sodium, crospovidone and sodium starch glycolate. Nine formulation having superdisintegrant at different concentration (10, 15, 20 mg) level were prepared. Effect of superdisintegrant on wetting time, dispersion time, drug content and *in vitro* release has been studied. Tablet containing cross carmellose sodium showed excellent in vitro dispersion time and drug release as compared to other formulation. After study of nine formulations F3 shows short dispersion time with maximum drug release in 30 min. It is concluded that fast-dispersible aceclofenac tablets could be prepared by direct compression using superdisintegrants.

Keywords: Aceclofenac, Superdisintegrants, Fast dispersible tablets, Dissolution test

INTRODUCTION

Aceclofenac, a nonsteroidal antiinflammatory drug (NSAID) has been indicated for various painful indications and proved as effective as other NSAIDs with lower indications of gastro-intestinal adverse effects and thus, resulted in a greater compliance with treatment[1,2]. Aceclofenac is practically insoluble. For poorly soluble orally administered drugs, the rate of absorption is often controlled by the rate of dissolution[3]. The rate of dissolution can be increased by increasing the surface area of available drug by various methods (micronization, complexation, solid dispersion) [4].

Many patients find it difficult to swallow tablets and hard gelatin capsules and thus do not comply with prescription. This results in high incidence of noncompliance and ineffective therapy[5]. The proper choice of superdisintegrant and its consistency of performance are of critical importance to the formulation development of fast dispersible tablets[6]. The objective of the present study is to develop fast dispersible tablets of aceclofenac and to study the effect of functionality differences of superdisintegrants on the tablet properties as well as to improve the patient compliance without compromising the therapeutic efficacy.

MATERIALS AND METHODS

Materials

Aceclofenac (Glenmark Pharmaceuticals Ltd. Nasik, India). Croscarmellose sodium, Sodium starch glycolate, Crospovidone and Microcrystalline cellulose (Intas Pharma, Ahmadabad, India), Aspartame (Ranbaxy, New Delhi, India) were obtained. Other materials and solvents used were of analytical grade.

Preparation of tablets

Fast dispersible tablets containing 100 mg of aceclofenac were prepared by direct compression method and the various formulae used in the study are shown in [Table 1]. All the ingredients without magnesium stearate and talc were mixed uniformly followed by addition of magnesium stearate and talc. The prepared powder blend was evaluated for various parameters like bulk density, tapped density, angle of repose, compressibility index and Hausner ratio. After evaluation of powder blend the tablets were compressed with a ten-station rotary punch-tableting machine (Rimek Mini Press-1) using 7 mm flat punches set.

Evaluation of powder blends [4,7-9]:

Bulk density

Apparent bulk density (ρb) was determined by placing presieved drug excipients blend into a graduated cylinder and measuring the volume (Vb) and weight (M) "as it is".

$$\rho b = M/Vb$$

Tapped density

The measuring cylinder containing a known mass of blend was tapped for a fixed number of taps. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (ρt) was calculated using following formula.

$$\rho t = M/ Vt$$

Table No 1: Table shows Formulation of Fast Dispersible Tablet of Aceclofenac.

Ingredients (mg/tablet)	Formulations								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Aceclofenac	100	100	100	100	100	100	100	100	100
Croscarmellose Sodium	10	15	20	---	---	---	---	---	---
Crospovidone	---	---	---	10	15	20	---	---	---
Sodium Starch Glycolate	---	---	---	---	---	---	10	15	20
Microcrystalline cellulose	40	40	40	40	40	40	40	40	40
Mannitol	34	29	24	34	29	24	34	29	24
Aspartame	10	10	10	10	10	10	10	10	10
Talc	4	4	4	4	4	4	4	4	4
Magnesium Stearate	2	2	2	2	2	2	2	2	2
Total	200	200	200	200	200	200	200	200	200

Angle of repose

Angle of repose (α) was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (*h*) was obtained. The radius of the heap (*r*) was measured and angle of repose was calculated.

$$\alpha = \tan^{-1} (h/r)$$

Compressibility index

The simplest way of measurement of free flow property of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by % compressibility which is calculated as follows:

$$C = (\rho t - \rho b) / \rho t * 100$$

ρt - Tapped density, ρb - Untapped bulk density

Hausner's ratio

Hausner's ratio is an index of ease of powder flow; it is calculated by following formula.

$$\text{Hausner's ratio} = \rho t \backslash \rho b$$

ρt - Tapped density, ρb - Untapped bulk density

Table 2: Table Shows Evaluations Powder Blend

Parameters	Formulations								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Bulk density (gm/cm^3)	0.434±0.04	0.439±0.05	0.449±0.04	0.425±0.02	0.416±0.03	0.425±0.04	0.421±0.05	0.425±0.03	0.430±0.04
Tapped density (gm/cm^3)	0.470±0.05	0.476±0.03	0.487±0.04	0.465±0.03	0.459±0.05	0.465±0.01	0.459±0.02	0.470±0.06	0.481±0.03
Angle of repose	24.33±0.03	24.15±0.02	24.09±0.03	25.67±0.01	26.34±0.02	25.78±0.04	24.13±0.01	25.82±0.02	24.49±0.03
% Compressibility	7.65	7.77	7.80	8.60	9.36	8.60	8.27	9.57	10.60
Hausners ratio	1.082	1.084	1.084	1.094	1.103	1.094	1.090	1.105	1.118

Evaluation of tablets

All the tablets were evaluated for different parameters as hardness, friability, drug content, wetting time, *In vitro* dispersion time, and *In vitro* dissolution study.

Hardness [8, 10]

For each formulation, the hardness of tablets was determined using the Fizer hardness tester (Cadmach, India)

Friability test [8, 10]

Twenty tablets were weight and placed in the Roche friabilator (Electolab, Mumbai) and apparatus was rotated at 25 rpm for 4 min. after revolution the tablets were dusted and weighed. The friability is given by the formula:

$$F = (1- Wo/W) \times 100$$

Where, Wo is the weight of the tablets before the test and W is the weight of the tablet after the test.

Drug content [11]

Two tablets were powdered and the blend equivalent to 200 mg of aceclofenac was weighed and dissolved in suitable quantity of phosphate buffer of pH (7.4). The solution was filtered, suitably diluted and the drug content was analyzed spectroscopically at 274 nm. Each sample was analyzed in triplicate.

Wetting time [12, 13]

A piece of tissue paper (10.75×12 mm).folded twice was placed in a culture dish (d=6.5 cm) containing 6 ml of water. A tablet was put on the paper and the time for complete wetting was measured.

***In vitro* dispersion time [14]**

Tablet was added to 10 ml of phosphate buffer solution (pH 7.4) at 37±0.5°C. Time required for complete dispersion of a tablet was measured.

***In vitro* drug release [15, 16]**

In vitro drug release of aceclofenac from fast dissolving tablets was determined using USP Dissolution Testing Apparatus II (Paddle type) (Disso2000, Labindia).The dissolution test was performed using 900 ml of phosphate buffer (pH 7.4) at 37 ± 0.5^{0}C. The speed of rotation of paddle was set at 100 rpm. At a predetermined time interval (5 min); 5 ml samples

were withdrawn, filtered through Whatman filter paper. Absorption of solution was checked by UV spectrophotometer at 274 nm and drug release was determined from standard curve.

Table 3: Table Shows Evaluations of Tablets

Parameters		Formulations								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
Hardness (kg/cm2)		3.81	3.89	3.92	3.42	3.48	3.50	3.66	3.68	3.71
Friability (%)		0.352	0.357	0.361	0.291	0.293	0.293	0.426	0.426	0.428
Drug Content (%)		99.31	99.42	99.60	98.86	99.23	99.56	99.43	99.34	99.12
Wetting Time (sec)		57.43	57.56	56.23	54.46	55.56	54.54	59.35	59.45	56.37
Dispersion Time(min)		28.31	24.10	23.34	31.56	33.47	35.42	33.35	29.25	29.41
% drug release	5	42.67	62.81	71.69	38.26	59.54	64.67	31.47	53.96	60.71
(min)	30	89.39	94.76	99.21	87.98	95.79	95.56	92.67	88.87	83.64

RESULT AND DISCUSSION

For each designed formulation, blend of drug and excipients was prepared and evaluated for micromeritic properties shown in Table-2. Bulk density was found to be between 0.416±0.03 and 0.449±0.04 gm/cm^3 and tapped density between 0.459±0.05 and 0.487±0.03 gm/cm^3 for all Formulations. From density data % compressibility was calculated and was found to be between 7.65% and 10.60%. Angle of repose was found to be in the range of 24.13±0.02 and 26.34±0.02. Hausner ratio was found below 1.118. All the formulation shows the good blend properties for direct compression and hence tablets were prepared by using direct compression technology.

As the tablet powder mixture was free flowing, tablets produced were of Hardness (3.50- 3.92 kg/cm ^{2}) and friability loss (0.291-0.428 %) indicated that tablets had a good mechanical resistance. Drug content was found to be high (≥98.86%) in all the tablet formulations. Thus wetting times of tablets was found to be crospovidone ≤ croscarmellose sodium ≤sodium starch glycolate. While dispersion time was found croscarmellose sodium ≤ sodium starch glycolate ≤ crospovidone. The influence of superdisintegrants on the dissolution of aceclofenac from the tablets is shown as below. The drug release in 5 min and 30 min increased with increase in the level of croscarmellose sodium. However values decreased with increase in the level of sodium starch glycolate. While values did not change proportionally with increase in the level of crospovidone shown in fig 1, 2 and 3. Out of nine formulations F3 formulation is best shows drug release 99.21 in 30 min shown in fig 3.

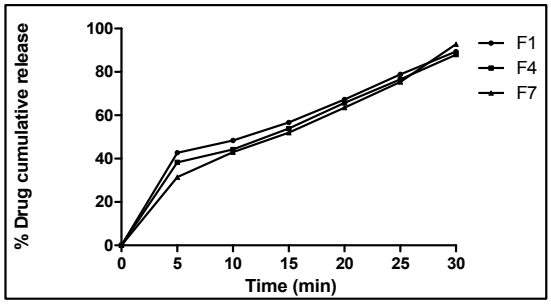

Fig. 1: Figure Shows % Cumulative Drug Release of Formulation F1, F4 and F7

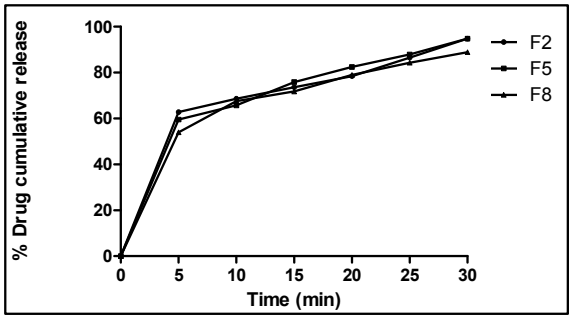

Fig. 2: Figure Shows % Cumulative Drug Release of Formulation F2, F5 and F8

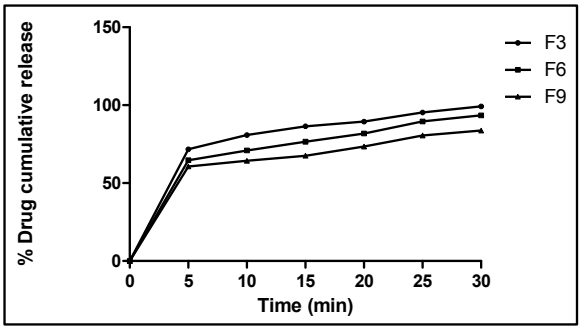

Fig. 3: Figure Shows % Cumulative Drug Release of Formulation F3, F6 and F9

CONCLUSION

In the present study, 3 disintegrants representing each of the 3 main classes of superdisintegrants differed in their ability to disintegrate model tablets into their primary particles when used at the same w/w percentage concentration. Such a difference can potentially affect drug dissolution. The dissolution parameters were consistent with dispersion times of croscarmellose sodium and sodium starch glycolate containing tablets, while not consistent with crospovidone.

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