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Research Article

FORMULATION AND EVALUATION OF FAST DISSOLVING PIROXICAM TABLETS USING DIFFERENT SUPER DISINTEGRANTS

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ABSTRACT

In the recent past Fast Dissolving Tablets (FDT) has gained much attention as a preferred alternative to conventional oral dosage forms such as tablets and capsules. FDT is a solid dosage form that disintegrates and dissolves in the mouth without the assistance of water. In the present work, 10 formulations of fast dissolving tablets of piroxicam (F1 to F9) using three different superdisintegrants namely crospovidone, sodium starch glycolate and pregelatinized starch with three different concentrations (3%, 4% and 5%) and a control F10 (without superdisintegrant) were analysed. The final blend of the drug and excipients were evaluated for powder flow properties, bulk density, tapped density, compressibility index and hausner's ratio. All the formulations were evaluated for weight variation, disintegration time, hardness, friability, wetting time and water absorption ratio. Formulation F3 showed the lowest disintegration time and more water absorption ratio. *In vitro* dissolution studies revealed that formulation F3 showed better drug release at the end of 30 minutes. The stability studies for the formulation F3 showed no significant change in disintegration time, drug content and percentage of drug released when stored at $45^0C \pm 2^0C$/ 75% RH for a period of 90 days. These results revealed that the formulation F3 containing crospovidone (5%) as superdisintegrant was better one which satisfied all the requirements necessary for fast dissolving tablets.

Keywords: Direct compression, Fast dissolving tablets, Superdisintegrant, Piroxicam, Crospovidone.

INTRODUCTION

Piroxicam is a potent anti-inflammatory drug. It is used in treatment of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis and acute gout disease[1] . It has prolonged half life of about 45hrs [2] . It is poorly water soluble drug and when administered orally it may cause bioavailability problems due to its poor solubility and dissolution rates in biological fluids [3]. The present work was aimed to increasing the dissolution rate of piroxicam, thus providing faster rate of absorption by adding potential superdisintegrants like crospovidone, sodium starch glycolate and pregelatinized starch in the formulations. Mannitol was used as sweetening agent to mask the bitter taste of piroxicam. The FDT of piroxicam may overcome problems such as difficulty in swallowing, inconvenience in administration while travelling and patient's acceptability[4]. The bioavailability of FDT may be increased due to absorption of drugs in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover, the amount of drug that is subjected to first pass metabolism is less when compared to preparation without superdisintegrant. The main criterion for FDT is to disintegrate / dissolve rapidly in oral cavity with saliva within 15-60 seconds without the need of water[5].

MATERIALS

Piroxicam was procured from Amaratal and Co. Chennai, India. Crospovidone, Magnesium stearate and Talc were procured from Loba Chemie., pvt. Ltd, Mumbai, India. Sodium starch glycolate, microcrystalline cellulose and Mannitol were procured from S.d fine-chem., Pvt. Ltd, Mumbai, India. Pregelatinized starch was procured from paxmy speciality chemicals, Mumbai, India.

METHODS

Preparation of Piroxicam FDTs

The formulations of FDTs of piroxicam were prepared by direct compression method. A total of 10 formulations (F1 to F9) of fast dissolving tablets of Piroxicam using three different superdisintegrants namely Crospovidone, sodium starch glycolate and pregelatinized starch with three concentrations (2%, 3% and 5%) were prepared. A control tablet was also prepared without any superdisintegrant (F10). All the ingredients were passed through mesh no.60 and collected separately. The drug, superdisintegrant, mannitol and microcrystalline cellulose were mixed uniformly with gentle trituration using mortar and pestle to get a uniform mixture. Finally magnesium stearate and talc were added to the mixture and mixed well. The tablets were compressed using 12 mm flat- face surface punch tablet compression machine to get tablet of 400 mg weight (Table-1)[6-7]. Before tablet preparation, the mixture blend of all the formulations were subjected to precompression parameters like bulk density, tapped density, compressibility index and hausner's ratio.

Evaluation of Powder Blend

Angle of repose[8]

The angle of repose for powder blend was determined by the funnel method. The accurately weighed quantity of powder blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the heap of the powder blend. The powder blends were allowed to flow through the funnel freely onto the wooden surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation:

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

Where 'h' and 'r' are the height and radius of the cone respectively.

Bulk density[9]

Bulk density P_b is defined as the ratio for mass of the powder to the bulk volume and is expressed as g/cm^3.Weighed quantity of powder blend from each formulation was taken in a measuring cylinder separately and the initial volume of the powder blend in the measuring cylinder was noted. This was calculated by using the formula

$$P_b = M / V_b$$

Where, P_b - Bulk density, M - Weight of the sample in g,V_b- Final volume of the blend in cm^3.

Tapped density

It is the ratio of total mass of the powder to the tapped volume of powder. The volume was measured by tapping the powder blend for 500 times. Then the tapping was done for 750 times and the tapped volume was noted. Tapped density was calculated by using the following formula

$$P_t = M / V_t$$

Where, P_t-Tapped density, M - Weight of the sample in g, V_t -Tapped volume of blend in cm^3.

Compressibility index and Hausner's ratio[10]

The compressibility index of the powder blend was determined by Carr's compressibility index and the Hausner's ratio. It is calculated by using the formula

Hausner's ratio = Tapped density / Bulk density

Carr's index (%) = [(TBD-LBD) x 100] / TBD

TBD = Total bulk density, LBD = Loose bulk density

Evaluation of Tablets

Weight variation[7]

Twenty tablets were randomly selected and individually weighed. The average weight of tablets was calculated. Then the individual weight was compared with that of average weight and the amount of weight variation was determined.

Hardness[11]

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 force required for breaking the tablet was noted.

Friability[12]

Friability test was performed by using Roche friabilator. Ten tablets were weighed and placed in the friabilator, which was then operated for 25 revolutions per minute. After four minutes (100 revolutions) the tablets were dusted and reweighed. The percentage friability was determined using the formula,

Percentage friability = Initial weight - Final weight × 100/ Initial weight

In vitro disintegration time[13]

The test was carried out in a disintegration test apparatus using distilled water (at 37^0 C ± 0.5^0 C) as disintegration medium. A tablet was placed in each of six tubes of the apparatus and one disc was added to each tube. The time taken for complete disintegration of the tablet with no mass remaining in the apparatus was measured.

Wetting time and water absorption ratio[6]

Wetting time is closely related to the inner structure of the tablets and hydrophilicity of the excipients. A piece of tissue paper, folded double, was placed in a Petri plate containing 6 ml of distilled water. A preweighed tablet was placed on the paper and the time for complete wetting of the tablet was measured. The wetted tablet was then taken out and weighed. Water absorption ratio of this tablet was determined by using the formula,

$$R = (W_a - W_b)/Wa \times 100$$

Where R = Water absorption ratio

W_a= Weight of tablet after wetting.

W_b= Weight of tablet before wetting.

Estimation of drug Content[14]

Ten tablets from each formulation were weighed individually and powdered. The Powder equivalent to 20mg of Piroxicam was weighed and dissolved in 10ml of methanol and chloroform in equal ratio (according to I.P 2007) and the volume was adjusted to 100ml with pH 6.8 buffer. From this solution 1 ml was taken and made up to 100 ml using pH6.8 buffer and the solution was analyzed at 333nm by UV–visible spectrophotometer using pH6.8 buffer as the blank.

***Invitro* drug release**

Invitro dissolution studies for all the formulated tablets of Piroxicam was carried out using USP II paddle method at 50 rpm in 900 ml of pH 6.8 buffer solution as a dissolution medium[13]. The dissolution medium was maintained at 37±0.5^{0}C.10ml of sample was withdrawn at 10 minutes intervals of time. 10 ml of buffer solution (pH 6.8) was replaced to maintain the constant volume throughout the experiment. The samples were suitably diluted and the percentage of drug released from each formulation was measured at 333 nm using UV–visible spectrophotometer.

Stability Studies[15]

The stability test was carried out to evaluate the stability of Piroxicam in formulations (F3, F6 and F9). The prepared tablets were kept at 45^{0}C ± 2 ^{0}C 75% RH for 90 days. Every 30 days interval, the tablets were evaluated for drug content, disintegration time and *in-vitro* drug release studies.

RESULTS AND DISCUSSION

In the present study of piroxicam, FDTs were prepared with three superdisintegrants such as crospovidone, sodium starch glycolate and pregelatinized starch at various concentrations (3%, 4% and 5%) by direct compression method. Also one control batch (F10) was prepared without any superdisintegrant (Table-1).

Table 1: Formulation Design of Piroxicam Fast Dissolving Tablets.

Sr. No	Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	Piroxicam	100	100	100	100	100	100	100	100	100	100
2	Crospovidone	12	16	20	_	_	_	_	_	_	_
3	Sodium starch glycolate	_	_	_	12	16	20	_	_	_	_
4	Pregelatinized starch	_	_	_	_	_	_	12	16	20	_
5	Mannitol	10	10	10	10	10	10	10	10	10	10
6	Microcrystalline cellulose	258	254	250	258	254	250	258	254	250	270
7	Talc	10	10	10	10	10	10	10	10	10	10
8	Magnesium stearate	10	10	10	10	10	10	10	10	10	10

- Formulations Fl, F2 and F3 contains crospovidone as superdisintegrant in 3%, 4% and 5% concentrations.
- Formulations F4, F5 and F6 contain sodium starch glycolate as superdisintegrant in 3%, 4% and 5% concentrations.
- Formulations F7, F8 and F9 contain pregelatinized starch as superdisintegrant in 3%, 4% and 5% concentrations.
- Formulation F10 is control tablets (without superdisintegrant).

The final blend of the drug and excipients were evaluated for powder flow properties, Bulk density, Tapped density, Compressibility index and Hausner's ratio. The values of pre-compression parameters evaluated were found to be within the prescribed limits and indicated good free flowing property (Table-2).

Table 2: Evaluation of Piroxicam Powder blend

Formulation Code	Angle of Repose*	Bulk Density* (g/cm^3)	Tapped Density* (g/cm^3)	Compressibility Index*(%)	Hausner's Ration*
F1	32.45±0.68	0.21±0.01	0.21±0.03	13.34±O.63	1.12±0.01
F2	33.62±0.82	0.19±0.03	0.23±0.02	12.63±0.74	1.15±0.03
F3	33.80±0.95	0.19±0.02	0.23±0.03	11.67±0.23	1.14±0.07
F4	33.92±0.59	0.20±0.03	0.20±0.01	12.19±0.93	1.11±0.04
F5	33.54±0.59	0.18±0.02	0.22±0.02	11.38±0.58	1.12±0.08
F6	33.01±0.91	0.18±0.01	0.21±0.01	11.48±0.83	1.13±0.03
F7	32.96±1.01	0.19±0.02	0.21±0.01	12.21±0.85	1.13±0.07
F8	32.87±0.97	0.18±0.03	0.21±0.03	11.93±0.17	1.15±0.05
F9	33.60±0.70	0.20±0.03	0.22±0.02	11.84±0.24	1.12±0.03
F10	33.44±0.62	0.19±0.01	0.21±0.02	11.21±0.11	1.13±0.02

*All values are expressed as mean ± standard deviation, n=3

The data obtained of post-compression parameters such as hardness, friability, weight variation, amount of drug content, disintegration time, wetting time and water absorption ratio are shown in (table-3).

Table 3: Evaluation of piroxicam Fast Dissolving Tablets.

Formulation	Weight Variation* (mg)	Hardness* (kg/cm2)	Fria Bility* (%)	Drug Content* (%)	Disin Tegration Time* (sec)	Wetting time* (sec)	Water Absorption Ratio* (%)
F1	0.397±0.003	4.02±0.23	0.93±0.37	97.74±0.63	38±0.98	10±1.63	53.64±3.76
F2	0.399±0.001	4.11±0.64	0.87±0.31	99.64±0.38	41±1.02	9±1.74	59.12±1.23
F3	0.399±0.002	4.05±0.37	0.89±0.31	98.96±0.83	44±1.12	11±1.21	55.48±4.85
F4	0.398±0.002	4.13±0.28	0.95±0.36	98.12±0.26	37±0.74	8±1.85	61.64±4.32
F5	0.398±0.001	3.98±0.83	0.92±0.33	98.27±0.27	39±1.23	8±1.64	57.21±3.75
F6	0.399±0.005	4.02±0.73	0.92±0.37	97.23±0.12	38±1.06	9±1.12	62.63±7.73
F7	0.398±0.002	3.96±0.92	0.90±0.32	99.16±0.23	42±1.32	13±2.21	59.87±4.64
F8	0.399±0.006	4.05±0.39	0.88±0.36	98.63±0.29	48±0.93	7±1.98	56.54±3.63
F9	0.398±0.001	4.02±0.63	0.93±0.32	98.73±0.24	39±1.72	9±1.92	59.12±4.21
F10	0.399±0.003	4.08±0.38	0.91±0.35	98.21±0.74	43±1.63	11±1.54	60.63±3.64

*All the values are expressed as mean ± standard deviation (n=3)

The hardness was found to be in the range of 3.96±0.92 to 4.13±0.28 kg/cm^2 in all the formulations indicating good mechanical strength with an ability to withstand physical and mechanical stress conditions, while manufacturing and handling the dosage form. In all the formulations, the friability values were less than 1% and meet the United States pharmacopoeia (U.S.P) limits. All the tablets passed weight variation test as the percentage weight variation was within the U.S.P limits. (Table-3). The weight of all the tablets was found to be uniform with low standard deviation (S.D) values indicating efficient mixing of drug, disintegrants and excipients. The percentage drugs content of all the tablets were found in the range of 97.23±0.12 to 99.64±0.38 of piroxicam, which was within the acceptable limits. The results of *invitro* disintegration time and wetting time of all the formulations were found to be within the prescribed limits and satisfied the criteria of fast dissolving tablets. The values were found to be in the range of 37±0.74 to 48±0.93 sec and 7±1.98 to 13±2.21 seconds, respectively. The water absorption ratio for all formulations was found to be in the range of 53.64±3.76 to 62.63±7.73 % (Table-3).It was observed that when crospovidone was used as disintegrant, the tablets disintegrated rapidly within less time due to easy swelling ability of crospovidone when compared to that of other tablets prepared by using sodium starch glycolate, pregelatinized starch as superdisintegrants and control (without superdisintegrant). Among the formulations, F3 containing crospovidone 5% was found to be the best as it showed good hardness, least weight variation, optimum friability, least wetting time, least disintegration time and more water absorption ratio which is an ideal characteristic of a fast dissolving type tablet (Table-3).Further formulations F3, F6 and F9 were subjected to stability studies for the period of 90 days at $45^0C \pm 2^0C$ / 75% RH and was analyzed after specific time period of 30 days interval. No significant changes were seen in drug content, disintegration time and *invitro* drug release after three months. (Table-4 and Table-5)

Table 4: Percentage of drug release from formulations F3, F6 and F9 after stored at $45^0C \pm 2^0C$ 75% RH for 90 days

Time	Percentage Drug Release								
	F3			F6			F9		
	30 days	60 days	90 days	30 days	60 days	90 days	30 days	60 days	90 days
10 MIN	38.73±0.67	40.72±0.36	39.63±0.53	35.03±0.42	37.87±0.53	37.47±0.27	31.93±0.97	29.82±0.64	29.32±0.53
20 MIN	67.12±0.85	69.63±0.12	70.73±0.88	53.73±0.77	55.78±0.12	53.64±0.78	49.72±0.53	47.65±0.43	46.94±0.63
30 MIN	95.34±0.66	95.26±0.42	97.09±0.51	89.82±0.73	89.52±0.42	91.34±0.63	87.47±0.73	90.63±0.12	90.98±0.22

*All the values are expressed as mean ± standard deviation (n=3)

Table 5: Drug Content and Disintegration time of formulations F3, F6 and F9 after stored at $45^0C \pm 2^0C$ 75% RH for 90 days.

Fornmulation	Percentage drug content			Disintegration time (Sec)		
	30 days	60 days	90 days	30 days	60 days	90 days
F3	99.12±0.63	99.68±0.23	99.32±0.42	30.21±0.72	29.43±0.12	29.71±0.64
F6	97.73±0.12	98.52±0.72	98.42±0.11	32.43±0.23	31.93±0.91	30.62±0.06
F9	97.10±0.53	97.23±0.41	97.68±0.59	35.09±0.34	34.05±0.62	34.27±0.37

*All the values are expressed as mean ± standard deviation (n=3)

Overall results indicated that formulation F3 was better, which satisfied all the criteria as a fast dissolving tablet.

CONCLUSION

The present investigation thus indicated that FDTs of piroxicam can be prepared by direct compression method using three superdisintegrants crospovidone, sodium starch glycolate and pregelatinized starch. The formulations prepared with superdisintegrants showed a rapid drug release than control (without superdisintegrant). The formulation F3 containing 5% crospovidone as superdisintegrant showed a better percentage of drug release when compared with formulations F6 and F9 which contains 5% sodium starch glycolate and 5% pregelatinized starch as superdisintegrant. Hence crospovidone was found to be a better superdisintegrant for the formulation of piroxicam Fast Dissolving Tablets.

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