ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES Knowledge to Innovation

Vol 8, Issue 6, 2015

ISSN - 0974-2441

Research Article

FORMULATION AND STABILITY INDICATING ANALYSIS OF ORODISPERSIBLE TABLET OF PIROXICAM

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Received: 09 July 2015, Revised and Accepted: 24 August 2015

ABSTRACT

The main object of this research work is to develop and studying the stability analysis of orodispersible tablet of piroxicam. Five formulations of orodispersible tablets of piroxicam (F1-F4) were prepared using two different superdisintegrants namely crospovidone and sodium starch glycolate with two concentrations and a control F5 (without superdisintegrant) by direct term stability studies for the formulations showed no significant changes in disintegration compression method. The precompression and post compression study of piroxicam and excipient were carried out. The short time, drug content and percentage of drug released when stored at 4°C±2°C, 27°C ±2°C, and 45°C±2°C for 15 days.

Keywords: Orodispersible, Stability, Piroxicam, Anti-inflammatory, Direct compression, Superdisintegrant.

INTRODUCTION

Orodispersible tablet system can be defined as a tablet that disintegrates and dissolves rapidly in saliva within few seconds without need of drinking water or chewing. In spite of tremendous development in drug delivery technology, the oral route remains perfect route for administration of therapeutic reagents because of the low cost of therapy, ease of administration, accurate dose, self-medication, pain avoidance, leading to high level of patient compliance. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability not require water for oral administration, have a pleasing mouth feel, have an acceptable taste masking property make these tablets popular as a dosage form of choice [1,2]. Piroxicam is a potent anti-inflammatory drug. It is used in the treatment of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and acute gout disease. It has prolonged the half-life of about 45 hrs. Piroxicam has pKa about 6.3. 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. Hence, the present work was aimed at increasing the rate of dissolution of piroxicam thus providing a faster rate of absorption by adding potential superdisintegrants such as crospovidone (CP) and sodium starch glycolate (SSG) in different concentrations. To mask the bitter taste of piroxicam, saccharin sodium was used as the sweetening agent. Four formulations of orodispersible tablets of Piroxicam using two superdisintegrants namely CP and SSG and a control formulation (without superdisintegrant) were prepared by direct compression method.

MATERIALS

The drug piroxicam was a generous gift sample from Concept Pharmaceuticals Pvt. Ltd., Aurangabad. SSG, CP, mannitol, magnesium stearate, saccharine sodium, microcrystalline cellulose were supplied S.D. Fine Chemicals (Mumbai). Other reagents and organic solvents used were of analytical grade.

METHODS

Orodispersible tablets of piroxicam were prepared by direct compression method by using superdisintegrant SSG, CP together with a binding agent like microcrystalline cellulose. Magnesium stearate was used as lubricants.

Preparation of mouth dissolving tablet

Piroxicam orodispersible tablets were prepared by direct compression method according to the formula given in Table 1. A total number of four formulations (F1-F4) of piroxicam orodispersible tablets were prepared using two superdisintegrants namely CP and SSG with two different concentrations [1-3]. A control tablet was also prepared without any superdisintegrant (F5). All the ingredients were passed through mesh No. 60 separately and collected. The drug, mannitol, and microcrystalline cellulose were mixed uniformly with gentle trituration using mortar and pestle to get a uniform mixture. The required quantity of superdisintegrant and saccharin sodium were taken for each specified formulation and mixed with the above mixture and compressed on a 8 station tablet machine (Jaguar JM-D) equipped with round 8-mm punches [4,5].

Table 1: Formulation of piroxicam orodispersible tablets by design expert

S. No.	Composition	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)
1	Piroxicam	20	20	20	20	20
2	SSG	15	5	5	15	-
3	CP	5	15	5	5	-
4	Microcrystalline cellulose	100	100	110	90	120
5	Mannitol	51	51	51	51	51
6	Saccharin sodium	7	7	7	7	7
7	Magnesium stearate	2	2	2	2	2
8	Menthol	q.s	q.s	q.s	q.s	q.s
	Total	200	200	200	200	200

CP: Crospovidone, SSG: Sodium starch glycolate

Drug excipient interaction study

Fourier transform infrared spectroscopy (FTIR)

It was used to study the interactions between the drug and the excipients. The KBR disk method was used for the preparation of sample and spectra were recorded over the wave number 4000 to 400/cm in a BRUKER FTIR spectrophotometer. IR spectral studies of Pure Piroxicam, superdisintegrant and piroxicam containing the highest proportion of individual superdisintegrant were carried out. If there was no change in peaks of the mixture when compared to the pure drug, it indicates the absence of interactions.

Evaluation of powder blend [6]

The blend were characterized by their micromeritics properties, such as, bulk density, tapped density, Carr's compressibility index, Hausner ratio, and flow property.

Bulk density

The bulk density was obtained by dividing the mass of powder by the bulk volume in cm^3. The sample of about 10 cm^3 of powder was carefully introduced into a 25 ml graduated cylinder. The cylinder was dropped at 2-second intervals onto a hard wood surface three times from a height of 1 inch. The bulk density of each formulation was then obtained by dividing the weight of the sample in grams by the final volume in cm^3 of the sample contained in the cylinder. It was calculated using equation given below:

$D_f = M/Vp$

Where, D_f=Bulk density,
M=Weight of samples in grams,
Vp=Final volumes of granules in cm^3.

Tapped density

The tapped density was obtained by dividing the mass of powder by the tapped volume in cm^3. The sample of about 10 cm^3 of powder is carefully introduced into a 25 ml graduated cylinder. The cylinder was dropped at 2-second intervals onto a hard wood surface 100 times from a height of 1 inch. The tapped density of each formulation was then obtained by dividing the weight of the sample in grams by the final tapped volume in cm^3 of the sample contained in the cylinder. It was calculated using equation given below:

$D_o = M/Vp$

Where, D_o=Bulk density,
M=Weight of samples in grams,
Vp=Final tapped volumes of granules in cm^3.

Table 2: Relationship between % compressibility and flow ability

% Compressibility	Flow ability
5-15	Excellent
12-16	Good
18-21	Fair to passable
23-35	Poor
33-38	Very poor
>40	Extremely poor

Carr's index

The percentage compressibility of microspheres was calculated according to equation given below:

$$\% \text{ Compressibility} = \frac{D_o - D_f}{D_o} \times 100$$

Where, D_f=Bulk density, D_o=Tapped density

Hausner ratio

The Hausner ratio of a microsphere was calculated according to equation given below:

Hausner ratio= D_o/D_f

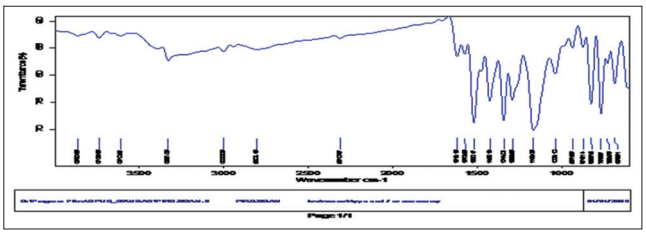

Fig. 1: Infrared spectra of drug

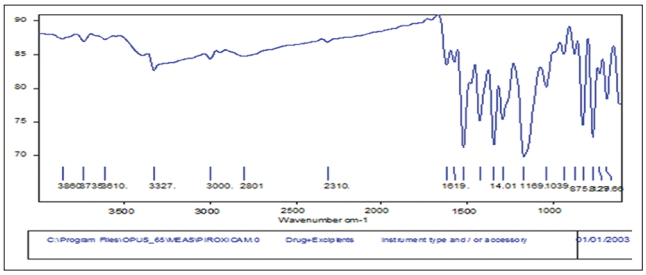

Fig. 2: Infrared spectra of drug + excipient

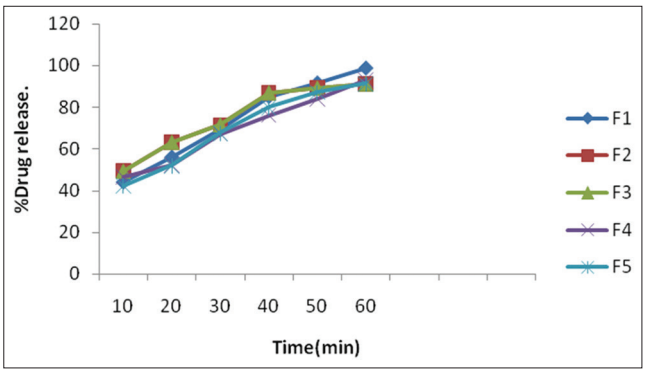

Fig. 3: Percentage drug release profile of piroxicam formulation

Table 3: Evaluation of powder blend

Batch code	Angle of response	Bulk density (g/cm_3)	Tapped density (g/cm_3)	Compressibility index (%)	Hausner's ratio*
F1	30°.11±0.031	0.327±0.075	0.357±0.012	14.95±0.021	0.896±0.045
F2	31°.11±0.022	0.314±0.045	0.392±0.025	11.30±0.036	0.874±0.032
F3	30°.99±0.039	0.320±0.041	0.363±0.063	14.41±0.065	0.893±0.047
F4	30°.58±0.042	0.314±0.056	0.373±0.051	14.67±0.028	0.869±0.063
F5	32°.23±0.037	0.325±0.049	0.360±0.089	14.54±0.087	0.880±0.098

*Each sample was analyzed in triplicate (n=3)

D_o=Tapped density,
D_f=Bulk density.

Angle of repose

The angle of repose of powder blend was determined by the funnel method. The accurately weighed powder blend was taken in the 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 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.

Evaluation of tablets [6-9]

Weight variation

20 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.

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 force required to break the tablet was noted.

Friability

Friability test was performed using Roche friabilator. 10 tablets were weighed and placed in the friabilator, which was then operated for 25 revolutions per minute. After 100 revolutions, the tablets were dusted and reweighed. The percentage friability was determined using the formula:

$$\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

In vitro disintegration time

The test was carried out in a disintegration apparatus using distilled water (at 37°C±0.50°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 in seconds.

Wetting time

Wetting time is closely related to the inner structure of the tablets and hydrophilicity of the excipients. The wetting time of the tablets was measured using a simple procedure. Five circular tissue papers of 10-cm diameter were placed in a Petri dish with a 10-cm diameter. 10 ml of water containing methylene blue, a water-soluble dye was taken in the Petri dish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablets was noted as the wetting time.

***In vitro* drug release [10,11]**

In vitro dissolution studies for all the formulated tablets of piroxicam was carried out using an electrolab paddle method at 50 rpm in 900 ml of pH 6.8 buffer solution as a dissolution medium. The dissolution medium was maintained at 37°C±5°C. 10 ml 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 a ultraviolet-visible spectrophotometer.

Stability studies [1]

The stability test was carried out to evaluate the stability of piroxicam in formulated tablets after storing at different temperatures for 15 days. The prepared tablets were kept at three different temperatures such as 4°C±2°C, 27°C±2°C, and 45°C±2°C for 15 days. Every 5 days interval, the tablets were evaluated for the hardness, disintegration time and in vitro drug release studies.

RESULTS AND DISCUSSION

Orodispersible tablets of piroxicam were prepared by direct compression method using CP and SSG as superdisintegrants. A total of four formulations (F1-F4) and a control formulation F5 (Without Superdisintegrant) were designed. The values of precompression parameters evaluated were found to be within the prescribed limits and indicated good free flowing property (Table 3). IR spectroscopy was used as means of studying drug-excipients compatibility and confirmed by comparing undisturbed structure of IR spectra of Piroxicam, which indicated no drug-excipients interaction.

The data obtained of post-compression parameters such as hardness, thickness, friability, weight variation, amount of drug content, disintegration time and water absorption ratio are shown in Table 4. Tablets obtained were of uniform weight (due to uniform die fill) with acceptable variation as per Indian Pharmacopoeia (IP) specifications, i.e., below 7.5%. The low standard deviation values indicating efficient mixing of drug, disintegrants, and excipients. The hardness of the tablets was found to be 3.2±0.123-3.1±0.175 kg/cm^2. The thickness of tablets was found to be 4.11±0.62-4.20±0.61 mm. The result revealed that the tablets of all the formulations showed uniform thickness. In all the formulations, the friability values were <1% and meet the IP limits. The results of *in vitro* disintegration 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 31±0.35 to 42±0.51 seconds. The percentage of the drug released for formulation F1 showed better drug release of (98.64±0.64) than F4 (93.79±0.59) and control F5 (91.45±0.57) at the end of 60 minutes (Table 5 and Fig. 2). Further formulation F1, F4, and F5 were subjected to stability studies for the period of 15-day at 40°C±20°C, 27°C±2°C, and 45°C±20°C and were analyzed after specific time period of 5-day interval. No significant changes were seen in disintegration time and *in vitro* drug release after 15 days.

CONCLUSION

The results of experimental studies of piroxicam orodispersible tablets proved that the powder blend of piroxicam showed good flow

Table 4: Evaluation of orodispersible piroxicam tablets

Batch code	Weight variation (mg)*	Thickness* (mm)	Hardness* (kg/cm^2)	Friability* (%)	Disintegration time* (seconds)	Wetting time (seconds)
F1	199.7±0.9	4.18±0.58	3.2±0.123	0.75±0.314	31±0.35	20±0.52
F2	198.1±1.2	4.20±0.61	2.7±0.152	0.55±0.235	34±0.39	13±0.23
F3	200.8±1.6	4.15±0.39	3.2±0.163	0.84±0.386	39±0.37	23±0.36
F4	200.3±1.8	4.11±0.62	3.1±0.175	0.44±0.863	42±0.51	21±0.34
F5	200.7±1.1	4.17±0.75	3.5±0.169	0.54±0.172	139±0.45	12±0.58

*Each sample was analyzed in triplicate (n=3)

Table 5: Dissolution studies of piroxicam oro-dispersible tablet formulations

Batch code	% Drug release (time in minutes)					
	10	20	30	40	50	60
F1	44.00±031	56.61±0.45	69.93±036	85.32±0.56	91.54±0.21	98.64±0.64
F2	49.21±0.67	63.07±0.24	71.45±0.37	86.75±0.74	89.12±0.23	91.23±0.11
F3	49.21±0.67	63.07±0.24	71.45±0.37	86.75±0.74	89.12±0.23	91.23±0.11
F4	46.32±0.11	52.13±0.36	67.12±0.33	76.32±0.47	84.39±0.56	93.79±0.59
F5	42.10±0.35	51.87±0.24	67.54±0.98	79.89±0.84	87.17±0.77	91.45±0.57
Marketed sample	54.63±0.11	62.56±0.33	71.87±0.51	88.54±0.61	94.79±0.96	99.79±0.37

*Each sample was analyzed in triplicate (n=3)

Table 6: Stability study at 4°C±2°C

Batch code	Hardness			Disintegration time (seconds)			*In-vitro* drug release		
	5 days	10 days	15 days	5 days	10 days	15 days	5 days	10 days	15 days
F1	3.1±0.13	3.2±0.23	3.7±0.47	30±0.25	32±0.45	32±0.25	98.44±0.61	98.61±0.64	97.64±0.36
F2	2.4±0.12	2.7±0.52	2.5±0.42	33±0.49	34±0.59	34±0.49	91.23±0.31	91.33±0.11	91.43±0.19
F3	3.1±0.23	3.2±0.13	3.9±0.21	40±0.57	39±0.57	38±0.42	91.53±0.51	91.33±0.11	90.23±0.41
F4	3.6±0.25	3.1±0.22	3.3±0.21	44±0.11	43±0.61	42±0.61	93.39±0.49	92.59±0.59	93.69±0.50
F5	3.2±0.19	3.5±0.51	2.7±0.19	141±0.15	140±0.15	139±0.75	91.46±0.37	90.45±0.57	91.55±0.24

*Each sample was analyzed in triplicate (n=3)

Table 7: Stability study at 27°C±2°C

Batch code	Hardness			Disintegration time (seconds)			*In-vitro* drug release		
	5 days	10 days	15 days	5 days	10 days	15 days	5 days	10 days	15 days
F1	3.2±0.23	2.2±0.50	2.7±0.11	31±0.35	36±0.55	34±0.45	97.44±0.52	98.61±0.34	98.74±0.86
F2	2.6±0.17	3.7±0.45	2.5±0.49	39±0.39	32±0.69	35±0.42	92.63±0.32	91.33±0.81	91.43±0.56
F3	3.9±0.14	2.2±0.41	2.9±0.52	41±0.37	40±0.57	36±0.41	91.33±0.21	91.33±0.47	90.83±0.33
F4	3.2±0.37	2.1±0.82	3.6±0.21	43±0.41	41±0.61	32±0.83	93.49±0.42	92.59±0.54	93.11±0.52
F5	3.7±0.29	3.3±0.22	2.7±0.10	142±0.15	138±0.15	141±0.65	92.46±0.64	90.45±0.56	91.35±0.12

*Each sample was analyzed in triplicate (n=3)

Table 8: Stability study at 45°C±2°C

Batch code	Hardness			Disintegration time (seconds)			*In-vitro* drug release		
	5 days	10 days	15 days	5 days	10 days	15 days	5 days	10 days	15 days
F1	3.5±0.23	2.1±0.43	2.7±0.68	30±0.67	35±0.95	31±0.26	97.43±0.47	98.69±0.74	98.14±0.26
F2	2.4±0.12	3.6±0.55	2.5±0.36	39±0.56	32±0.87	38±0.72	92.32±0.51	91.53±0.23	91.43±0.33
F3	3.9±0.24	2.2±0.31	2.9±0.73	41±0.37	44±0.30	39±0.42	91.73±0.56	91.56±0.78	90.43±0.56
F4	3.2±0.55	2.2±0.17	3.6±0.35	43±0.41	41±0.54	37±0.45	93.54±0.43	92.37±0.23	92.29±0.44
F5	3.6±0.68	3.4±0.14	2.7±0.96	142±0.15	139±0.59	141±0.25	92.66±0.26	90.68±0.45	91.65±0.39

*Each sample was analyzed in triplicate (n=3)

properties, tablet evaluation tests are within the acceptable limits, IR spectral analysis proved that there was no drug excipient and stability studies revealed that all the formulations were found to be stable after storing at 4°C±2°C, 27°C±2°C, and 45°C±2°C for 15 days. The drawbacks of the conventional dosage forms of Piroxicam can be minimized by piroxicam orodispersible tablets. The formulations prepared with superdisintegrant showed a rapid drug release than control (without superdisintegrant) formulation. Thus, the results of the above study clearly indicated that piroxicam may be formulated as orodispersible tablets using two superdisintegrants CP and SSG by direct compression method.

ACKNOWLEDGMENT

The authors are thankful to Concept Pharma, Aurangabad for providing the gift sample of piroxicam and also thankful to management of Amrutvahini College of Pharmacy, Sangamner for providing all facilities to carry out this research work.

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