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Formulation and Evaluation of Orodispersible Piroxicam Tablets

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Abstract:

The demand for mouth dissolving tablets has been growing, during the last decade, especially for geriatric and paediatric patients who have swallowing difficulties. Piroxicam is a potent anti-inflammatory drug used in treatment of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis and acute gout disease. In the present work, 5 formulations of Orodispersible tablets of Piroxicam (F1 to F4) were prepared using two different superdisintegrants namely Crospovidone and sodium starch glycolate with two concentrations (3% and 5%) and a control F5 (without superdisintegrant) by direct compression method. 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 thickness, weight variation, disintegration time, hardness, friability, drug content and water absorption ratio. Formulation F1 showed the lowest disintegration time and more water absorption ratio. *invitro* dissolution studies revealed that formulation F2 showed 93.70 % percent drug release at the end of 60 minutes. The short term stability studies for the formulations showed no significant changes in disintegration time, drug content and percentage of drug released when stored at $4^0C \pm 2^0C$, 27°C ±2°C and $45^0C \pm 2^0C$ for 45 days.

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

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]. Hence the present work was aimed at increasing the rate of dissolution of Piroxicam thus providing faster rate of absorption by adding potential superdisintegrants like Crospovidone and Sodium starch glycolate in different concentrations. To mask the bitter taste of Piroxicam, aspartame was used as sweetening agent. Four formulations of orodispersible tablets of Piroxicam using two superdisintegrants namely Crospovidone (3% and 5%) and Sodium starch glycolate (3% and 5%) and a control formulation (without superdisintegrant) were prepared by direct compression method.

Experimental:

Materials:

Piroxicam was procured from Sun pharmaceuticals Ltd, Mumbai, India. Microcrystalline cellulose, Sodium starch glycolate and Aspartame were procured from Rajesh Chemicals, Mumbai, India.Mannitol was procured from Strides Arcolabs, Bangalore, India. Menthol was procured from ReachemLab. Chemicals Pvt.Ltd.Chennai. Magnesium stearate and Crospovidone were procured from Loba Chemie., Pvt. Ltd, Mumbai, India.

Methods:

Preparation of Piroxicam Orodispersible tablets [3, 4].

Piroxicam Orodispersible tablets were prepared by direct compression method according to the formula given in Table 1. A total number of four formulations (F1 to F4) of Piroxicam orodispersible tablets were prepared using two superdisintegrants namely Crospovidone and Sodium Starch Glycolate with two different concentrations (3% and 5%). 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. Required quantity of superdisintegrant and aspartame were taken for each specified formulation and mixed with the above mixture.

Table 1: Formulation Design of Piroxicam Orodispersible Tablets

S.No	Composition	F1	F2	F3	F4	F5
1	Piroxicam	20	20	20	20	20
2	Sodium starch glycolate	6	10	-	-	-
4	Crospovidone	-	-	6	10	-
5	Microcrystalline cellulose	110	106	110	106	116
6	Mannitol	54	54	54	54	54
7	Aspartame	8	8	8	8	8
8	Magnesium stearate	2	2	2	2	2
9	Menthol	qs	qs	qs	qs	qs
	Total Weight (mg)	200	200	200	200	200

F1- Sodium starch glycolate (3%); F2- Sodium starch glycolate (5%); F3- Crospovidone (3%); F4- Crospovidone (5%); F5-Control (without superdisintegrant).

Table 2: Evaluation of Powder blend

Formulation code	Angle of repose*	Bulk density* (gm/cm^3)	Tapped density* (gm/cm^3)	Compressibility Index* (%)	Hausner's ratio*
F_1	30º.92±0.021	0.372±0.015	0.431±0.075	14.79±0.064	1.16±0.038
F_2	31º.31±0.026	0.310±0.031	0.392±0.028	13.70±0.064	1.15±0.065
F_3	28º.25±0.048	0.341±0.011	0.402±0.025	14.86±.0.061	1.17±0.037
F_4	29º.51±0.022	0.332±0.018	0.403±0.035	13.24±0.036	1.12±0.069
F_5	32º.02±0.035	0.345±0.012	0.432±0.038	14.40±.0.095	1.16±0.099

*All values are expressed as mean ± standard deviation, (n= 5)

Finally magnesium stearate and menthol were added and mixed well. The mixed blend of drug and excipients were compressed using 7 mm punch on 10 stations "B" Tooling Rotatory Tablet Punching Machine to produce convex faced tablets, weighing 200 mg each (Table-1). Before tablet preparation, the mixture blend of all the formulations were subjected to compatibility studies (IR) and Precompression parameters like Angle of repose, bulk density, tapped density, compressibility index and hausner's ratio.

Evaluation of powder blend:

Angle of repose:

The angle of repose of powder blend was determined by the funnel method. The accurately weighed powder blend were taken in 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 [5]. 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.

Bulk density:

Bulk density P_b is defined as the mass of the powder divided by the bulk volume and is expressed as g/cm^3. Weighed quantity of powder blend from each formulation was taken in a measuring cylinder and the initial volume of the powder blend in the measuring cylinder was noted [6].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 Hausners ratio:

The compressibility index of the powder blend was determined by Carr's compressibility index and the Hausners ratio is calculated by using the formula [7].

Hausners ratio = Tapped density / Bulk density

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

TBD = Total bulk density, LBD = Loose bulk density

IR Spectral analysis:

It was used to study the interactions between the drug and the excipients.The KBR disk method was used for preparation of sample and spectra were recorded over the wave number 4000 to 400 cm^{-1} in a SHIMADZU FTIR (model-8400) spectrophotometer. IR spectral studies of Pure Piroxicam, Superdisintegrant and Piroxicam containing highest proportion of individual superdisintegrant were carried out [8]. If there was no change in peaks of mixture when compared to pure drug, it indicates the absence of interactions.

Evaluation of tablets:

Weight variation:

Twenty tablets were randomly selected and individually weighed [9]. 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 [10]. 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. Ten tablets were weighed and placed in the friabilator, which was then operated for 25 revolutions per minute [11]. After 100 revolutions the tablets were dusted and reweighed. The percentage friability was determined using the formula,

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

In vitro disintegration time:

The test was carried out in a disintegration apparatus using distilled water (at 37^0 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 [12].The time taken for complete disintegration of the tablet with no mass remaining in the apparatus was measured in seconds.

Wetting time and water absorption ratio:

Wetting time is closely related to the inner structure of the tablets and hydrophilicity of the excipients.

Table 3: Evaluation of Orodispersible Piroxicam Tablets

Batch Code	Weight Variation (mg)*	Thickness* (mm)	Hardness* (kg/cm^2)	Friability* (%)	Drug Content* (%)	Disinteg-ration time* (sec)	Water absorption ratio*%
F1	201±1.8	4.20±0.60	2.8±0.151	0.73±1.163	97.96±0.124	33±0.37	82.09±2.30
F2	199±1.3	4.21±0.64	2.6±0.131	0.61±0.263	98.36±0.671	36±0.63	85.25±1.05
F3	198±1.1	4.13±0.73	2.8±0.251	0.63±0.376	98.42±0.682	38±0.68	69.80±0.205
F4	200±1.6	4.12±0.75	2.7±0.108	0.59±0.421	98.60±0.612	43±1.10	73.02±1.37
F5	200±1.8	4.19±0.98	3.2±0.648	0.54±0.594	98.90±0.630	125±1.32	65.08±3.85

*****All values are expressed as mean ± standard deviation, (n= 5)

Table No 4: Dissolution studies of Piroxicam Oro-dispersible Tablet formulations

S.No	Time (min)	Cumulative % of drug release from Piroxicam Oro Dispersible tablets					
		F_1	F_2	F_3	F4	Marketed sample	F_5 (control)
1	10	53.80±0.15	57.60±0.31	46.35±0.24	57.15±0.45	65.54±0.61	44.70±0.40
2	20	61.89±0.45	66.88±045	52.65±0.28	63.55±0.32	72.72±0.33	50.19±0.26
3	30	66.92±0.30	74.42±0.41	58.52±0.21	72.70±0.31	80.30±0.64	56.04±0.36
4	40	76.07±0.31	79.51±0.25	68.50±0.32	81.90±0.21	91.17±0.26	60.21±0.47
5	50	82.82±0.35	87.75±0.21	75.01±0.58	82.85±0.27	95.55±0.28	66.05±0.38
6	60	88.70±028	93.70±0.31	87.75±0.48	89.50±0.29	99.42±0.26	71.11±0.21

All values are expressed as mean ± standard deviation, n= 5

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 in seconds. The wetted tablet was then weighed [13].Water absorption ratio was determined using the formula,

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

Where R = Water absorption ratio

Wa= Weight of tablet after wetting.

Wb= Weight of tablet before wetting.

Estimation of drug Content:

Five 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 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 [14].

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

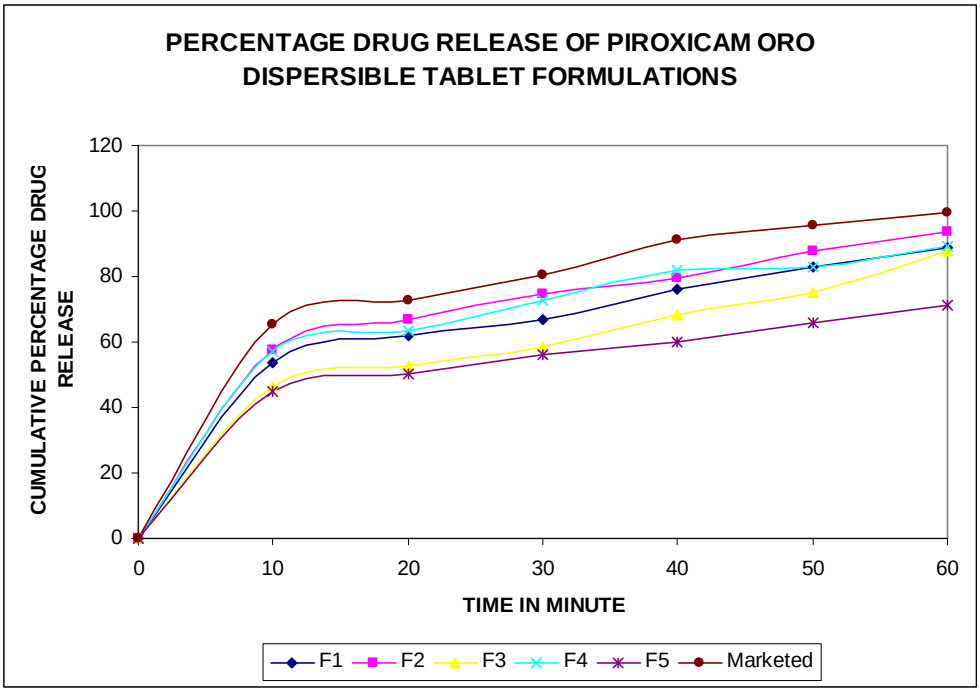

Figure 1: Comparative release profiles of Piroxicam formulations

900 ml of pH 6.8 buffer solution as a dissolution medium[15]. 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.

Kinetic Analysis [16, 17, 18, 19]:

To analyze the mechanism of drug release rate kinetics of all the formulations, the results of *invitro* release profiles were plotted in models of data treatment as follows:

1. Log cumulative percent drug remaining versus time (first order kinetic model)
2. Log Cumulative percent drug release versus time (zero order kinetic model)

Stability Studies:

The stability test was carried out to evaluate the stability of Piroxicam in formulated tablets after storing at different temperatures for 45 days. The prepared tablets were kept at three different temperatures such as 4ºC±º2C, 27°±2°C and 45°C±2°C for 45 days. Every 15 days interval, the tablets were evaluated for the drug content, disintegration time and *invitro* drug release studies [20, 21].

Results and discussion:

Orodispersible tablets of Piroxicam were prepared by direct compression method using Crospovidone (CP) and Sodium Starch Glycolate (SSG) as superdisintegrants. A total of 4 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-2). Infra-red (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-3).Tablets obtained were of uniform weight (due to uniform die fill) with acceptable variation as per IP specifications i.e. below 7.5%.The low standard deviation (S.D) values indicating efficient mixing of drug, disintegrant and excipients. . The percentage drug content of all the tablets were found in the range of 97.96± 0.124 to 98.60± 0.612 of Piroxicam, which was within the acceptable limits. Hardness of the tablets was found to be 2.6±0.131-2.8±0.251 kg/cm^2. The thickness of tablets was found to be 4.12±0.758 to 4.21±0.648mm. The result revealed that the tablets of all the formulations showed uniform thickness. In all the formulations, the friability values were less than 1% and meet the Indian pharmacopoeia (I.P) limits. The results of *invitro* 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 33 ± 0.37 to 43 ± 1.10 Seconds. The water absorption ratio for all formulations was found to be in the range of 69.80 ± 0.205 to 85.25 ± 1.05 % (Table-3).

The cumulative percentage of the drug released for formulation F2 showed better drug release of 93.70± 0.31% than F4 (89.50±0.29) and Control F5 (71.11± 0.21) at the end of 60 minutes. (Table- 4 and Figure-1). The kinetic studies revealed that the drug release from all the formulations followed first order release. Further formulation F2, F4 and F5 were subjected to stability studies for the period of 45 days at 4^0C±2^0C , 27°C ±2°C and 45^0C±2^0C and was analyzed after specific time period of 15 days interval. No significant changes were seen in drug content, disintegration time and *invitro* drug release after 45 days.

Conclusion:

The results of experimental studies of Piroxicam Orodispersible tablets proved that the Powder blend of Piroxicam showed good flow properties, tablet evaluation tests are within the acceptable limits, IR spectral analysis proved that there was no drug-excipient interaction, the kinetic studies revealed that all the formulations followed first order drug release and stability studies revealed that all the formulations were found to be stable after storing at 4^0C±2^0C , 27°C ±2°C and 45^0C±2^0C for 45 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 Crospovidone and sodium starch glycolate by direct compression method.

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References:

[1] Martindale-Extra Pharmacopoeia, The Pharmaceutical Preparations, London, 1982,28, Pg-276.

[2] Satoskar, R.S., Bhandarkar, S.D., Pharmacology and Pharmacotherapeutics, Popular prakasan Pvt Ltd, Mumbai,21, Pg-173.

[3] Vikesh Shukla., Rajashree, M.S., Bolmal, U.B., and Manvi, F.V., Formulation and Evaluation of Piroxicam Dispersible Tablets using Natural Disintegrants,The Indian Pharmacist,2007; 6,685-688.

[4] Bhagawati, S.T., Hiremath, S.N., and Sreenivas, S.A., Comparative Evaluation of Disintegrants

by Formulating Cefixime Dispersible Tablets, Indian J. Pharm. Educ. Res**,** 2005; 39, 194-197.

[5] Carr, R.L., Evaluating Flow Properties of Solids. Chem. Eng., 1965,72, 163 – 168.

[6] Shah, D., Shah, Y., and Rampradhan, M., Development and evaluation of controlled release Diltiazem hydrochloride microparticulates using cross linked poly vinyl alcohol. Drug Dev.Ind.Pharm,1977,23, 567-574.

[7] Aulton, M.E., and Wells, T.I., Pharmaceutics, The Science of Dosage Form Design, Churchill Livingstone, Vingstone, London, 1988,2, 133.

[8] Sharma, Y.R.,"Elementary Organic Spectroscopy principles and Chemical Applications", S.Chand & Co, New delhi; 2005,5,65-133.

[9] Leon Lachman., Herbert A., Liberman. and Joseph L., Kamig., The Theory and Practice of Industrial Pharmacy – Tablets; Varghese Publishing House, Mumbai, 1991,3,Pg - 318,370,300.

[10] Rippie, E., Compression of solids and compressed dosage forms. In: Encyclopedia of Pharmaceutical Technology. Swarbrick J., Marcel Dekker Inc. NY. 1990,3,149-166.

[11] Chowdary K.P.R., and Hymavathy.R. Formulation and dissolution rates studies on dispersible tablets of Ibuprofen. Indian. J. Pharm.Sci, 2000, 62,213-216.

[12] Mishra, D.N., Bindal, M., Singh, S.K., and Kumar, S.G.V., Rapidly Disintegrating Oral Tablets of Valdecoxib, Indian J.Pharm. Sci**,** 2005,67, 685-687.

[13] Yunxia, Hisakazu., Preparation and evaluation of compressed tablet rapidly disintegrating in the oral cavity.Chem Pharm Bull.1996,44,2121-2127.

[14] Vijaya, K.S.G., and Mishra, D.N., Rapidly Disintegrating Oral Tablets of Meloxicam**,** Indian Drugs.2006, 43,117-121.

[15] James Klancke., Dissolution Testing of Orally Disintegrating Tablets. Dissolution Technologies,2003,6, 6-8.

[16] Mulye, N.V., and Turco,S.J., A simple model based on first order kinetics to explain release of highly water soluble drugs from porous dicalcium phosphate dehydrate matrices, Drug.Dev.Ind.Pharm,1995, 21,943-953.

[17] Schwarz, B.J; Simonelli, A.P., and Higuchi, W.I., Drug release from wax matrices Analysis of data with first order Kinetics and with the diffusion controlled model. J.Pharm. Sci., 1998, 57, 274-277.

[18] Varelas, C.G., Dixon, D.G., and Steiner C., Zero-order release from biphasic polymer Hydrogels, J.Control .Release , 1995, 34,185-192.

[19] Colombo, P., Bettini R., and Catellani, P.L., Drug Volume Fraction Profile in the gel phase and drug release kinetics in hydroxyl Propyl methyl cellulose matrices containing a soluble drug, Eur.J.Pharm.Sci ,2003,86, 323-328.

[20] Chaudhary, P.D., Chaudhary, S.P., and Kolhe, S.R., Formulation and Evaluation of Fast Dissolving Tablets of Famotidine**,** Indian Drugs ,2005; 42, 641-649.

[21] Agarwal, S.P., and Rajesh Khanna., Physical Pharmacy, 2006,2, 242-255.