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Design and Characterization of Fast Disintegrating Tablets of Piroxicam

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ABSTRACT: Piroxicam is an effective and selective cyclo-oxygenase COX-2 inhibitor with anti - inflammatory and analgesic properties. The poor aqueous solubility of the drug leads to variable dissolution rates. In the present study an attempt has been made to prepare fast disintegrating tablets of Piroxicam in the oral cavity with enhanced dissolution rate. The tablets were prepared with three super disintegrates i.e. sodium starch glycollate, Ac-Di-Sol and low molecular weight hydoxy propyl methylcellulose. The blend was examined for angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The tablets were evaluated for hardness, tensile strength, and drug content, friability and were found satisfactory. The disintegration time in the oral cavity was also tested. The rapidly disintegrating tablets with proper hardness, rapidly disintegrates in the oral cavity with enhanced dissolution, which is achieved by using selected superdisintegrants.

Key words: Direct compression, mouth dissolving, fast disintegration, Piroxicam

INTRODUCTION

Many patients, especially elderly find it difficult in swallowing tablets, capsules, fluids and thus do not comply with prescription, which results in high incidence of non-compliance oriented research has resulted in bringing out many safer and newer drug delivery systems. Rapidly disintegrating/dissolving tablet is one of such example, for the reason of rapid disintegration or even with saliva[2-5] . Significance of this drug delivery system includes administration without water, accuracy of dosage, ease of portability, alternative to liquid dosage forms, ideal for paediatric and geriatric patients and rapid onset of action [1-7].

Piroxicam is chemically, 4-hydroxyl-2-methyl-N-2-pyridinyl-2H-1, 2, -benzothiazine-3-carboxamide 1,1-dioxide. A selective cyclooxygenase – 2 inhibitor, used in the treatment of rheumatoid arthritis, osteo arthritis and other joint diseases.[8] The poor aqueous solubility of the drug[9] (12 mcg/mL) give rise to difficulties in the formulation rates. In the present study, an attempt had been made to prepare rapidly disintegrating tablets of piroxicam in the oral cavity with enhanced dissolution rate and hence improved patient compliance.

EXPERIMENTAL

Piroxicam was obtained as gift sample from Sehat Pharma, Gujarat-Himatnagar. Sodium starch glycol late, crosscramellose sodium (Ac-Di-Sol), microcrystalline stearate and talc were procured from SD fine chemicals, Mumbai and all other chemicals/solvents used were of analytical grade.

Preparation of Mixed Blend of Drug and Excipients

All the ingredients were passed through mesh no 60. Required quantity of each ingredient was taken for each specified formulation (depicted in the Table I) and all the ingredients were subjected to grinding to a required degree of fineness. The powder blend was evaluated for flow properties as follows.

Angle of Repose

Angle of repose was determined using funnel method[9]. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose (q) was calculated using the formula.

$= \mathrm{Tan}^{-1}(h/r)$ (1)

Bulk Density

Apparent bulk density (P_b) was determined by pouring the blend into a graduated cylinder. The bulk volume (V) and weight of the powder (M) was determined. The bulk density was calculated using the formula.

$P_b = M/V$ (2)

Tapped Density

The measuring cylinder containing a known mass of blend was tapped for a fixed time. The minimum volume (V_t) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (P_t) [9] was calculated using the following formula,

$P_t = M/ V_t$ (3)

Compressibility Index

The simplest way for measurement of free flow of powder is compressibility, a indication of the ease with which a material can be induced to flow is given by compressibility index (I)[9] which is calculated as follows,

$I= V_0-V_t/V_{bx}$ (4)

Where, V_0 is the bulk volume and V_t is tapped volume. The value below 15% indicates a powder with usually give rise to good flow characteristics, whereas above 25% indicate poor flowability.

Hausner ratio

Hausner ratio[11] is an indirect index of ease of powder flow. It is calculated by the following formula,

Hausner ratio = P_t/P_d (5)

Where P_t is tapped density and P_d is bulk density, Lower Hausner ratio (<1.25) indicates better flow properties than higher ones [12] (>1.25).

Compression of Tablets

The ingredients depicted in Table I (except talc and magnesium stearate) were mixed homogeneously and required degree of fineness was attained. Finally talc and magnesium stearate were added and mixed. The mixed blend of drug and excipients was compressed using a single punch R&D tablet punching machine to produce convex faced tablets, weighing 200 mg each with a diameter of 8 mm. A minimum of 50 tablets was prepared for each batch.

Table I: Composition of Different Batches of Rapidly Disintegrating Tablets of Piroxicam

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Piroxicam	**10**	**10**	**10**	**10**	**10**	**10**
Sodium starch glycollate	**10**	**-**	**-**	**20**	**-**	**-**
Cross carmellose sodium	**-**	**10**	**-**	**-**	**20**	**-**
L-HPMC	**-**	**-**	**10**	**-**	**-**	**20**
Mannitol	**20**	**20**	**20**	**20**	**20**	**20**
Talc	**4**	**4**	**4**	**4**	**4**	**4**
Magnesium stearate	**2**	**2**	**2**	**2**	**2**	**2**
Micro crystalline cellulose q.s	**200**	**200**	**200**	**200**	**200**	**200**

Table II: Evaluation of Mixed Blend of Drug and Excipients

Parameters	F1	F2	F3	F4	F5	F6
Angle of repose (^{0})*	**26.18 ± 1.22**	**24.26 ± 0.98**	**25.43 ± 0.82**	**25.18 ± 0.48**	**23.36 ±0.80**	**28.82 ± 0.24**
Bulk density (g/cm^3)*	**0.434 ± 0.26**	**0.445 ± 0.14**	**0.427 ± 0.34**	**0.441 ± 0.28**	**0.455 ± 0.38**	**0.415 ± 0.52**
Tapped density(g/cm^3)	**0.525 ± 0.14**	**0.538 ± 0.28**	**0.505 ± 0.34**	**0.521 ± 0.16**	**0.543 ± 0.42**	**0.501 ± 0.48**
Hausner's ratio	**1.208**	**1.207**	**1.181**	**1.180**	**1.191**	**1.205**
Compressibility index (%)	**17.29**	**17.24**	**15.40**	**15.31**	**16.16**	**17.12**

Table III: Evaluation of Tablets

Parameters	F1	F2	F3	F4	F5	F6
Weight variation (± %)*	2.5 ± 0.24	1.3 ± 0.32	1.7 ± 0.29	2.1 ± 0.42	1.5 ± 0.38	2.0 ± 0.16
Hardness (kg/cm^3)*	4.2 ± 0.56	4.3 ± 0.64	5.2 ± 0.82	4.3 ± 0.78	4.4 ± 0.64	5.6 ± 0.88
Friability (%)*	0.86 ± 0.12	0.72 ± 0.16	0.54 ± 0.08	0.88 ± 0.18	0.79 ± 0.22	0.52 ± 0.26
Tensile strength (kg/cm^2)*	9.54 ± 1.14	10.31 ± 0.86	12.10 ± 0.76	9.72 ± 0.92	9.67 ± 0.84	12.93 ± 1.28
In vivo disintegration time (sec)	37 ± 2.42	33 ± 1.64	71 ± 3.20	27 ± 1.83	25 ± 1.27	57 ± 2.78
DP_{30}#	49.56 ± 1.26	58.43 ± 2.34	51.58 ± 1.76	74.98 ± 1.44	78.05 ± 2.57	53.60 ±1.62
RDR_{10}	3.59	4.81	3.06	5.66	7.54	3.77

***n = 5, # n = 3; DP_{30}: Percent drug dissolved in 30 min; RDR_{10}: Relative dissolution rate in 10 min with pure Pirloxicam**

EVALUATION OF TABLETS

Weight Variation

Twenty tablets were selected at a random and average weight was determined. Then individual tablets were weighed and compared with average weight.

Friability

Friability of the tablets[9] was determined using Roche friability (Electrolab, Mumbai). This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Preweighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were de dusted using a soft muslin cloth and reweighed. The friability (f) is given by the formula.

$f = (1- W_0 / W) \times 100$ (6)

Where, W_0 is weight of the tablets before the test and W is the weight of the tablet after the test.

Hardness

Hardness[9] or tablet crushing strength (F_0) (the force required to break a tablet in a diametric compression) was measured using Monsanto tablet hardness tester (Sheetal Scientific Industries, Mumbai)

Tensile Strength

The tensile strength[9] (T), diameter and thickness of the tablet respectively,

$T = 2F_c/IIdt$ (7)

Drug Content

Five tablets were powdered and the blend equivalent to 10 mg of piroxicam was weighed and dissolved in suitable quantity of methanol. The solution was filtered, suitably diluted and the drug content was analyzed spectrophotometrically at 362 nm. Each sample was analyzed in triplicate.

In vivo Disintegrating Time

The time required for the tablets to disintegrate in the mouth cavity was determined by holding the tablets in mouth. The test was performed in five healthy human male volunteers in the age group of 23 to 28 years.

Dissolution Studies

In vitro dissolution studies for all the fabricated tablets and the pure drug was carried out using USP paddle method at 50 rpm in 900 mL of distilled water containing 0.25 % w/v of sodium lauryl sulphate as dissolution media, maintained at 37 ± 0.5^0.5 mL aliquot was withdrawn at the specified time intervals, filtered through whattmann filter paper and assayed spectrophotometrically. An equal volume of pre warmed (37^0 C) fresh medium was replaced into the dissolution medium after each sampling, to maintain the constant volume throughout the test. Dissolution studies were performed in triplicate.

RESULTS AND DISCUSSION

Six formulations of Piroxicam were prepared with varying concentration of the three super-disintegrants: sodium starch glycollate, cross cramellose sodium, L-HPMC and microcrystalline cellulose PH 102 was used as diluent. For each formulation, blend of drug and excipients were prepared and evaluated for various parameters as explained earlier. The powder blend was compressed using direct compression technique. Bulk density was found in the range of 0.415 – 0.455 g/cm^3 and the tapped density between 0.501 and 0.543-g/ cm^3 table II. Using these two-density data Hausner's ratio and compressibility index was calculated. The powder blends of all the formulations had Hausner's ratio of 1.2 or less indicating good flowability[11]. The compressibility index was found between 15.31 and 17.29 and the

compressibility- flowability correlation data[10] indicated a fairly good flowability of the powder blend. The good flowability of the powder blend was also evidenced with angle of repose (range of 24-29 ^{0}), which is below 40 ^{0} indicating good flowability[9].

Tablets were prepared using direct compression technique. Since the powder material was free flowing, tablets were obtained of uniform weight variations as per Pharmacopoeial specifications. The drug content was found in the range of 98.50 – 102.3% (acceptable limit) and the hardness of the tablets between 4.3 – 5.6 kg/cm^2 Table III. Friability of the tablets were found below 1 % indicating a good mechanical resistance of tablets. Tensile strength of all the tablets were between 9.54 and 12.93 Table III and all the parameters were found well within the specified limit for uncoated tablets.

The *in vivo* disintegration time (DT) of the tablets was found to be less than 60 sec., except the tablets containing 5 % L-HPMC (F3) as disintegrant (71 sec.). Moreover, tablets containing 10 % L-HPMC (F6) showed DT of 57 sec. while rest of the tablets around 30 sec. only.

The dissolution of poorly water-soluble drugs requires a dissolution medium entirely different from those used for water-soluble drugs. One of the techniques that have been useful in dissolution of insoluble drugs is the incorporation of a small amount of surfactant in the dissolution medium[13] . The use of Surfactants in the dissolution medium may be physiologically meaningful, due to the presence of natural surfactants tract. The ability of surfactants to accelerate the *in vitro* dissolution of wetting, micella solubilization, and/or deflocculation. It is easy to understand that a biorelavent medium needs similar surface-active agent as bio fluids. Studies on sodium lauryl sulphate have shown to satisfy these needs[14]. Based on these facts, dissolution of pure piroxicam and other prepared tablets were carried out in distilled water containing 0.25 % w/v sodium lauryl sulphate. All the formulations showed enhanced dissolution rate as compared to pure piroxicam. A significant increase in the percent drug dissolution and relative dissolution rate in 10 min. with pure piroxicam were observed by the formulations containing 10 % disitegrant in comparison to the 5 %. The pure drug showed only 21.88 % of dissolution in 30 min. The maximum increase in the dissolution rate with various superdisintegrants was found to be Ac-Di-Sol>SSG>L-HPMC. The preparation process in direct compressible tablets includes co grinding of all the excipients before compression, resulting in increase in the solubility due to the reduction in the effective particle size of the drug, following increase in the wetting of drug particles by the excipients and hence improved dissolution of poorly water soluble drugs[15,16]. Further the prepared formulations obeyed Hixson-Crowell cube root dissolution model[17].

It was concluded that fast disintegrating tablets of Piroxicam can be successfully prepared using selected superdisitegrants in order to improve disintegratntion/dissolution of the drug in oral cavity and hence better patient compliance and effective therapy.

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