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Research Article

Formulation and evaluation of orodispersible tablets of lornoxicam

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ABSTRACT

Orodispersible tablets (ODTs), also known as fast melt, quick melts, fast disintegrating have the unique property of disintegrating in the mouth in seconds without chewing and the need of water. The purpose of this investigation was to develop mouth dissolving tablets of Lornoxicam using KYRON T-314 (Polacrillin Potassium) as a novel superdisintegrant. Mouth dissolving tablets of lornoxicam were prepared by wet granulation technique using KYRON T-314 as superdisintegrant and menthol as subliming agent. The present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and patient compliance.

Keywords: KYRON T-314, Mouth dissolving tablet, Lornoxicam, Subliming agent, Superdisintegrant



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INTRODUCTION

The tablet is the most widely used dosage form because of its convenience in terms of self administration, compactness and ease in manufacturing. However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome this weakness, scientists have developed innovative drug delivery systems known as mouth dissolving tablets. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bedridden and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability and good stability made these tablets popular as a dosage form in the current market¹⁻². NSAID has been indicated for various painful indications³ and proved as effective as other NSAIDs with lower indications of gastro-intestinal adverse effects and thus, resulted in a greater compliance with treatment⁴. Lornoxicam, (2-[2-[2-(2,6 dichlorophenyl) aminophenyl] acetyl] oxyacetic acid), a nonsteroidal anti-inflammatory, analgesic and antipyretic drug used in rheumatoid arthritis, post-traumatic pain, musculo-skeletal and joint disorders⁵. Lornoxicam is practically insoluble. For poorly soluble orally administered drugs, the rate of absorption is often controlled by the rate of dissolution. The rate of dissolution can be increased by increasing the surface area of available

drug by various methods (micronization, complexation and solid dispersion).

The dissolution of a drug can also be influenced by disintegration time of the tablets. Faster disintegration of tablets delivers a fine suspension of drug particles resulting in a higher surface area and faster dissolution. Polacrillin Potassium (KYRON T- 314) is 2-methyl-2-propenoic acid polymer with divinylbenzene, potassium salt. It is a cation exchange resin used in oral pharmaceutical formulation as a tablet superdisintegrant. It appears as a cream colored, odorless and tasteless, free flowing powder⁶.

In the present study, an attempt has been made to develop mouth dissolving tablets of lornoxicam using novel superdisintegrant and to investigate the effect of subliming agent on the release profile of the drug. The fundamental principle used in the development of the fast-dissolving tablet is to maximize its pore structure. Researchers have evaluated spray dried materials⁷ and plastic materials⁸ for development of such tablets. Vacuum-drying⁹⁻¹⁴ and freeze-drying¹⁵⁻¹⁸ techniques have been also tried by researchers to maximize the pore structure of the matrix Freeze drying is cumbersome and yields a fragile and hygroscopic product. Therefore, a vacuum drying technique was adopted in the present investigation after addition of a subliming agent to increase porosity of the tablets. It is likely that a porous hydrophilic will easily pick up the disintegrating medium and break quickly.

MATERIAL AND METHODS

Materials

Lornoxicam and KYRON T-314 were obtained as a gift sample from Glenmark generics Ltd, Mumbai, India. Menthol, Magnesium stearate, Aspartame and Mannitol were purchased from local authorized dealer.

Method

Formulation of Mouth Dissolving Tablets of Lornoxicam

The orodispersible tablets of Lornoxicam were prepared using the subliming agent, menthol and KYRON T-314 as superdisintegrant, mannitol as diluent, aspartame as sweetening agent, alcoholic solution of polyvinyl pyrrolidone (PVP K-30) as binder and aerosil as flow promoter and magnesium stearate as lubricant, the composition of each batch is shown in Table 1.

Table 1: Composition of different batches of mouth dissolving tablets of lornoxicam

INGREDIENTS	QUANTITIES (mg)				
	F ₁	F ₂	F ₃	F ₄	F ₅
Lornoxicam	8	8	8	8	8
Menthol	20	20	25	25	25
Kyron T-314	20	20	20	25	25
Mannitol	145	145	135	130	130
PVP-K30	7	7	7	7	7
aerosil	3	3	3	3	3
Magnesium Sterate	2	2	2	2	2
Total	200	200	200	200	200

The raw materials were passed through a 100-mesh screen prior to mixing. The drug and other ingredients were mixed together and a sufficient quantity of alcoholic solution of PVP K-30 (10% w/v) was added and mixed to form a coherent mass. The wet mass was granulated using sieve no. 12 and regranulated after drying through sieve no. 16. Granules of the all formulations were then dried in a vacuum oven (Vertex, VT4810) at 60°C for 12 h resulting in localized drying. The final moisture content of the granules was found to be between 1-2%, which was determined using an IR moisture balance. During drying, the menthol sublimed with the formation of a porous structure on the surface of the tablet. The dried granules were then blended with talc, magnesium stearate and compressed into tablets using flat face round tooling on a Rimek-I rotary tablet machine (Karnavati Engg. Pvt. Ltd, Ahmedabad). Sublimation was performed from tablets instead of granules at 600C in selected batch (F₅).

Evaluation of formulated tablets:

Thickness

Thickness of tablet was determined by using vernier calliper (Mitutoya, Model CD-6 CS, Japan).

Hardness¹⁹

The crushing strength of the tablets was measured using a Monsanto hardness tester (Sheetal Scientific Industries, Mumbai, India). Three tablets from each formulation batch were tested randomly and the average reading noted.

Friability¹⁹

Twenty tablets were weighed and placed in a Roche friabilator (Electrolab, India). Twenty reweighed tablets were rotated at 25 rpm for 4 min. The tablets were then dedusted and reweighed and the percentage of weight loss was calculated. The percentage friability of the tablets were measured as per the following formula,

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

Weight Variation

Randomly, twenty tablets were selected after compression and the mean weight was determined.

None of the tablets deviated from the average weight by more than $\pm 7.5\%$ (USPXX).

Table 2: Evaluation of mouth-dissolving tablets of lornoxicam

Parameters	F ₁	F ₂	F ₃	F ₄	F ₅
Hardness (kg/cm ²)	3.1±0.30	3.4±0.68	2.9±0.51	3.1±0.63	3.6±0.10
Friability (%)	0.743± 0.04	0.629± 0.06	0.637± 0.05	0.688±0.04	0.574±0.04
Weight variation (mg)	204±3	199±2	203±3	197±1	200±1
Thickness (mm)	3.5±0.03	3.4±0.07	3.6±0.05	3.4±0.06	3.5±0.01
Wetting time (s)	38.2±2.5	39.3±1.5	43.6±2.2	39.1±2.0	29.4±1.5
In-vitro dispersion time (s)	68.3±2	62.1±1	56.2±2	53.7±3	41.8±2
Drug content	99.24± 3.24	98.44± 2.54	98.60±3.04	98.93±1.81	99.42±1.27
Drug release in 5min (%)	69.03±2	72.17±2	73.72±2.5	75.54±3	78.37±1.
Drug release in 30min (%)	86.81±1.2	88.11±1.6	88.73±2.5	93.26±2.7	97.25± 1.3

Wetting Time²⁰

A piece of circular tissue paper (8cm) folded twice was placed in a Petri dish (Internal Diameter = 9cm) containing 10 ml of buffer solution simulating saliva pH 6.8. A tablet was placed on the paper and the time taken for complete wetting was noted. Three tablets from each formulation were randomly selected and the average wetting time was noted. The results are tabulated in Table 2.

In vitro Dispersion Time²¹

In vitro dispersion time of prepared tablet was done by dropping the tablet in 10 ml measuring cylinder containing 6 ml of simulated salivary fluid (pH 6.8). Time required for complete dispersion of tablet was measured.

Dissolution Study

In vitro release of Lornoxicam from tablets was monitored by using 900 ml of simulated intestinal fluid, SIF (USP phosphate buffer solution, pH 7.4) at 37±0.5°C and 50 rpm using programmable dissolution tester [Paddle type, model TDT-08L, Electrolab, (USP), India]. 5 ml Aliquots were withdrawn at one minute time intervals and were replenished immediately with the same volume of fresh buffer medium. Aliquots, following suitable dilutions, were assayed spectrophotometrically (UV-1700, Shimadzu, Japan) at 378 nm.

RESULTS AND DISCUSSION

Mouth dissolving drug delivery is rapidly gaining acceptance as an important drug delivery technology. In such drug delivery, different dosage forms disintegrate rapidly in the patient's mouth within a minute and can be gulped easily without need of water. This rapid disintegration can be achieved by use of high levels of disintegrant and/or effervescent agents along with water soluble diluents. Hence, it offers increased patient compliance and convenience. Water insoluble diluents such as microcrystalline cellulose and dicalcium phosphate were omitted from the study as they are expected to cause an unacceptable feeling of grittiness in the mouth. Among the soluble diluents, mannitol was selected as diluents considering its advantages in terms of easy availability and negative heat of dissolution.

Table 2 shows that all the formulated tablets exhibited low weight variation. Addition of a subliming agent had no pronounced effect on hardness and increased friability of the tablets. The wetting time, in vitro dispersion time of the tablets were also considerably reduced in tablets (Table 2). The drug content of all the formulations was found to be between 98.4- 99.5% which was within the acceptable limits as per USP XXVII. The porous structure is

responsible for faster water uptake; hence it facilitates wicking action of KYRON T-314 in bringing about faster disintegration. Tablets with lower friability may not break during handling on machines and/or shipping. The use of a sublimation agent resulted in increased friability probably due to increased porosity. In the first few attempts (F₁-F₄), sublimation of menthol was performed from granules prior to compression into tablets. Batches F₁ to F₄ showed good mechanical integrity, but the disintegration time was a little longer than the arbitrarily chosen value of less than 50 seconds. In Batch F₅, sublimation was performed after compression rather than directly from granules. The results shown in Table 2 reveal that sublimation of menthol from tablets resulted in faster disintegration. The compaction process might have caused breakage of porous granules and subsequent reduction in porosity. The low value of wetting time and disintegration time indicate that the porosity of tablets of batch F₅ would be greater than batches F₁ to F₄.

In vitro release studies were carried out using USP XXIII tablet dissolution test apparatus paddle method at 37±10°C, taking 900 ml of simulated intestinal fluid (SIF) as dissolution medium. Speed of rotation of the paddle was set at 50 rpm. Aliquots of 5 ml were withdrawn after 1, 3, 5, 6, 8, 10, 30 min and analyzed spectrophotometrically at 274 nm. The in vitro dissolution profile indicated faster and maximum drug release from formulation F₅. Formulation F₅ prepared by direct sublimation of menthol from final tablets showed 78.37% drug release at the end of 5 min when compared to tablets prepared by sublimation of menthol from granules. The rapid drug dissolution might be due to easy breakdown of particles due to porous structure formation after sublimation of menthol and rapid absorption of drugs into the dissolution medium.

CONCLUSION

Polacrillin Potassium (KYRON T-314) is a cation exchange resin used in oral pharmaceutical formulation it swell rapidly when wetted. In the present study we used it as a novel super disintegrant and studied the effect of the effect of subliming agent on the release profile of the drug. From the outcome of this study, it can be concluded that sublimation method showed better disintegration and drug release. The prepared tablets using KYRON T-314 disintegrate within few seconds without need of water; thereby enhancing the absorption leading to its increased bioavailability. Vacuum-drying technique would be an effective alternative approach compared with the use of more expensive adjuvants in the formulation of mouth dissolving tablets.

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