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ORIGINAL RESEARCH ARTICLE

Formulation and Evaluation of Oral Disintegrating Tablet of Lornoxicam

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ABSTRACT

The demand of oral disintegrating tablets (ODTs) has been growing especially for geriatric and pediatric patients who have difficulties in swallowing. Lornoxicam (LX) is potent enolic acid (oxicam) derivative used in the treatment of pain resulting from inflammatory diseases of joints, osteoarthritis, surgery and sciatica. The drawback of drug is, it is practically insoluble in water and so possesses poor solubility, GI absorption and bioavailability. Hence the objective of present study is to develop oral disintegrating tablet of lornoxicam using croscormellose (CM) as super disintegrating agent and it's kneading mixture with croscormellose. The kneading mixtures of lornoxicam were prepared with croscormellose in the weight ratios of 1:0.5, 1:1, 1:1.5. The mixture LX: CM (1:1.5) (KM) exhibiting highest dissolution rate was selected and tablets were prepared using this kneading mixture by wet granulation method. Various formulations were tried and ODT was selected which possessed optimum characteristics of disintegration time of 12 sec, hardness of 3.6 kg/cm^2, friability of 0.8% and cumulative percent drug release of 99.62% in 30 minutes.

Key words: Lornoxicam, ODT, croscormellose, kneading mixture.

INTRODUCTION

Oral disintegrating tablets (ODTs) are the recent developments to present viable dosage alternative for patients who have difficulty in swallowing. These are the products that disintegrate rapidly in the saliva without need of water. ODTs also are called orally disintegrating, orodisperse, mouth-dissolving, quick-dissolve, fast-melt, and rapid-disintegrating tablets and freeze-dried wafers. ODTs release drug in the mouth for absorption through local oromucosal tissues and through pregastric (*e.g.* oral cavity, pharynx, and esophagus), gastric (*i.e.*, stomach), and postgastric (*e.g.* small and large intestines) segments of the gastrointestinal tract (GIT). Lornoxicam is potent enolic acid (oxicam) derivative used in treatment of pain resulting from inflammatory diseases of joints, osteoarthritis, surgery, sciatica. It is ten times more potent than other oxicam derivatives like piroxicam and tenoxicam. Its daily dose is 8-16 mg taken before meal. Daily dose above 8 mg should be divided into two or more doses. It inhibits prostaglandin biosynthesis by blocking enzyme cyclooxygenase. It inhibits both isoforms in the same concentration range i.e. the ratio of COX1 inhibition to COX2 inhibition is 1:1. It readily penetrates into synovial fluid. Its partition coefficient (n- octanol to phosphate buffer of pH 7.4) is 1.8. It is completely insoluble in water and slightly soluble in simulated gastric fluid. It is absorbed rapidly and almost completely from g.i. tract. Maximum plasma conc. is achieved after approximately 1 to 2 hrs. The absolute bioavailability of lornoxicam is 90-95%. No first pass is observed. It is found in plasma in unchanged form & as its hydroxylated form. CYP2C9 has been shown to be primary enzyme responsible for biotransformation of it to its major metabolite 5'-hydroxylornoxicam which do not exhibit any pharmacological activity. 1/2 to 2/3 is eliminated via liver and 1/3 to 42% via kidney as 5'-hydroxylornoxicam. Combination with vit.k antagonist like warfarin increases risk of bleeding. In view of above information, we have selected lornoxicam to develop as a oral disintegrating tablet by wet granulation method by using its kneading mixture with croscormellose in the weight ratio of LX: CM (1:1.5).

PREPARATION AND EVALUATION OF KNEADING MIXTURE OF LORNOXICAM AND CROSCORMELLOSE (LX: CM) (KM):

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Preparation of kneading mixture of LX: CM (KM):

The kneading mixtures of lornoxicam-croscormellose were prepared by taking various weight ratios of LX: CM as 1:0.5, 1:1, and 1:1.5 by using kneading method. The accurately weighed amount of drug and polymer mixture were taken into mortar and triturated by adding small volume of methanol to get smooth moist mass. The mass was kneaded for 45 minutes and then dried in oven at 35˚C till constant weight is reached. The dried mass was pulverized and sifted through #100 and the collected powder fraction was stored in 30 ml glass vials.

EVALUATION OF KNEADING MIXTURE OF LX: CM:

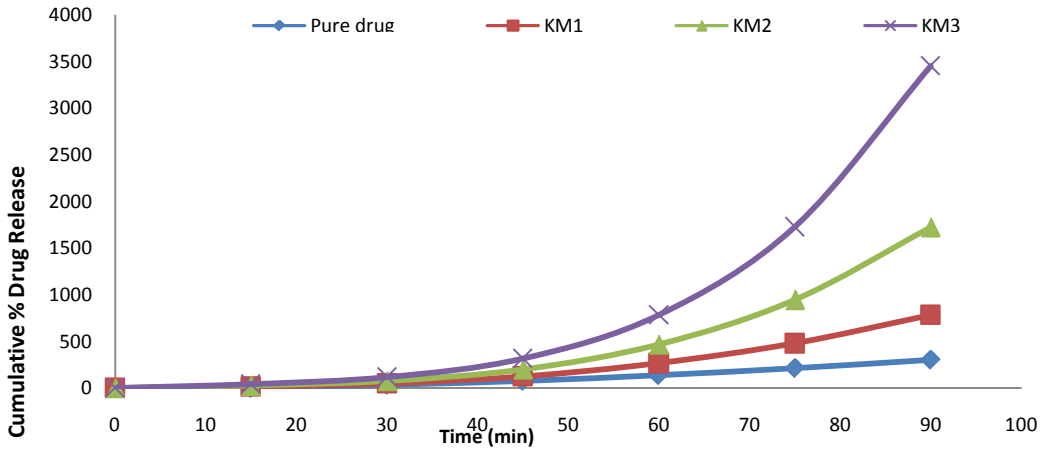
***In vitro* dissolution study:**

Dissolution studies of pure drugs and LX: CM kneading mixtures were carried out with USP dissolution testing apparatus (Paddle type) (Veego, India). The stirring speed was maintained at of 50 rpm and 900 ml of pH 7.4 phosphate buffer at 37±1˚C was used as dissolution medium. Samples of each preparation equivalent to 50 mg of drug were added to the dissolution medium. The sample aliquots each of 5 ml were withdrawn at appropriate time intervals. The initial volume of dissolution medium was maintained by replacing with 5 ml of medium to maintain sink conditions. The filtered aliquots were suitably diluted and assayed for percent drug release spectrophotometrically at λmax 374 nm. The cumulative% drug released from each of kneading mixture and pure drug is given in (**Table 1**) and presented in (**Fig 1**).

Table 1: Cumulative percent drug release of pure drug & kneading mixture KM1, KM2, KM3.

Time	Cumulative % Drug Release			
	Pure Drug	KM1	KM2	KM3
0	0	0	0	0
15	3.06	15.66	25.56	41.36
30	33.06	48.72	74.28	115.64
45	78.06	126.78	201.06	316.7
60	138.06	264.84	465.9	782.6
75	213.06	477.9	943.8	1726.4
90	303.06	780.96	1724.76	3451.16

Fig 1: Comparitive Dissolution profile of pure Lornoxicam, KM (1:0.5), KM (1:1), KM (1:1.5).



PREPARATION OF ODTS OF LORNOXICAM USING SELECTED LX: CM (1:1.5) (KM):

ODTs of lornoxicam were prepared by using selected kneading mixture, i.e. LX:CM (1:1.5) which exhibited significant improvement in the dissolution at in vitro level among all the kneading mixtures. The various formulations were tried to select the tablet with ideal characteristics of ODTs. The selected formulation that satisfied all the official parameters is given in (**Table 2**). This table is for preparing 100 tablets each of containing 8 mg of drug.

Table 2: Final formula

S No	Ingredients	Quantity taken (mg)
1	KM (1:1.5)	2000
2	MCCP	6750
3	DCP	1000
4	Maize starch	0.6
5	Talc	0.1
6	Mannitol	0.1
7	Mango Flavor	0.1
8	Croscormellose	0.2
9	Magnesium stearate	0.1

Lornoxicam and croscormellose kneading mixture (1:1.5), MCCP, croscormellose and DCP was sifted through sieve no. 30. Then the mixture was granulated by using 10% starch solution as binding agent. The wet mass was passed through #30 to get the granules. The wet granules were dried in an oven at 60̊C for about 20 minutes. To the dried granules magnesium stearate, talc, mannitol was added and mixed well. The micomeritic properties of blend were satisfactory and are shown in (**Table 3**). Then the blend compressed with 5 mm flat punches using 8 stations rotary punch machine.

Table 3: Micromeritics Properties of Prepared Blend

S No	Parameter	Result
	Angle of repose	
2	Compressibility index	16
3	Carr's index	15.62
4	Hausner's ratio	1.18

EVALUATIONS OF ODTS OF LORNOXICAM:

The prepared tablets were evaluated for hardness, disintegration friability, drug content, % drug release and weight variation and average values of each parameter is represented in (**Table 5**).

Hardness:

Five tablets collected at random and crushing strength of tablets were determined by using Pfizer hardness tester.

Disintegration test:

The disintegration time of tablet was determined by using tablet disintegration test apparatus of USP standard containing phosphate buffer of pH 7.4 as medium. Average disintegration time was found to be 12 second.

Friability test:

Friability test was carried out by using Roche Friabilator. Ten tablets were collected at random from batch and their initial average weight (W_1) was noted. Then tablets were placed in rotating chamber and subjected to combined effects of abrasion and shock with revolving plastic chamber at 100 rpm. After completion of rotations, the tablets were reweighed (W_2). The percent loss in weight or friability (f) was determined. The average percent loss was found to be 0.86%.

Estimation of Drug content:

Drug content estimation was carried out by collecting ten tablets from batch at random. These ten tablets were triturated and powder equivalent to 10 mg of drug was transferred into 10 ml volumetric flask containing methanol. This solution was sonicated for 10 minutes. Then the sample was filtered and assayed for drug content spectrophotometrically. And drug content was found to be 99.8%.

Uniformity of weight:

To perform test 20 tablets were collected at random from batch, weighed individually and average weight was determined. All tablets complies the test.

In vitro dissolution studies of tablets:

In vitro dissolution studies was carried out using USP dissolution testing apparatus (basket type) (Veego disso) using phosphate buffer of pH 7.4 as dissolution medium at 37±1˚C. The stirring speed was maintained at 50 rpm. Aliquot samples were withdrawn at various time intervals, filtered, diluted and assayed at 374 nm spectrophotometrically. The mean percent of drug dissolved calculated. The results are given in (**Table 4**) and represented in (**Fig 2**).

Table 4: Dissolution studies of prepared tablet

Time	% Drug Release	Cumulative % DR
0	0	0
5	58.12	58.12
10	87.65	145.77
15	91.79	237.56
20	92.78	330.34
25	96.92	427.26
30	99.62	526.88

Fig 2: Dissolution profile of prepared ODT of Lornoxicam.

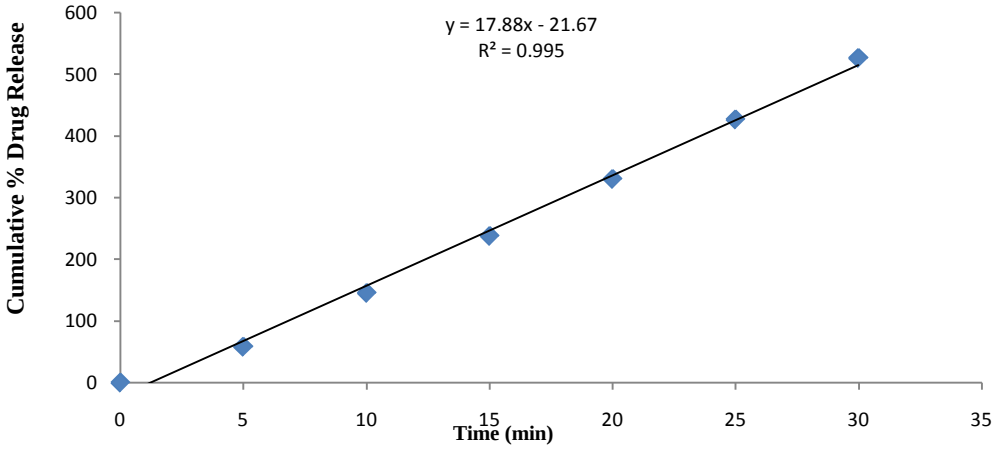


Table 5: Evaluation parameters of ODTs of Lornoxicam

S No	Parameters	Values
1	Hardness (kg/cm^2)	3.6
2	Disintegration time (sec)	12
3	Friability (%)	0.8
4	Drug content (%)	99.8
5	Average Weight (mg)	99.62
6	CPDR at 30 min (%)	99.62

Table 6: Release Kinetics Model

Time	Sq. Root of Time	Log Time	% DR	Cum. % DR	Log Cum.% DR	% Drug Remaining	Cube Root Of % Drug Remaining	Log % Drug Remaining
0	0.00	0.00	0	0	0.00	100	0.00	2.00
5	2.24	0.70	58.12	58.12	1.76	41.88	3.87	1.62
10	3.16	1.00	87.65	145.77	2.16	12.35	4.44	1.09
15	3.87	1.18	91.79	237.56	2.38	8.21	4.51	0.91
20	4.47	1.30	92.78	330.34	2.52	7.22	4.53	0.86
25	5.00	1.40	96.92	427.26	2.63	3.08	4.59	0.49
30	5.48	1.48	99.62	526.88	2.72	0.38	4.64	0.42

Fig 3: Zero order release kinetics model

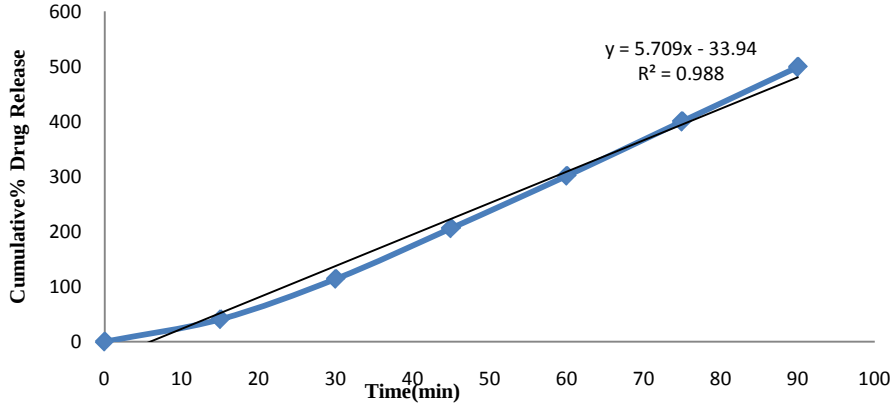


Fig 4: First order release kinetic model

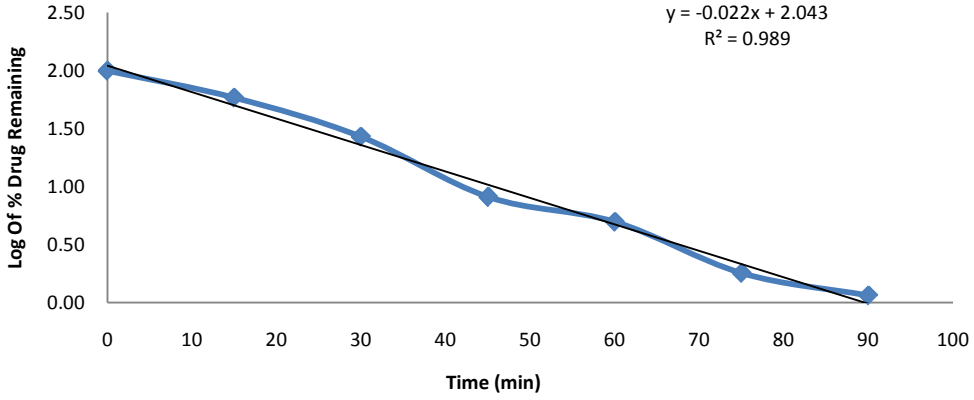


Fig 5: Higuchi release kinetics model

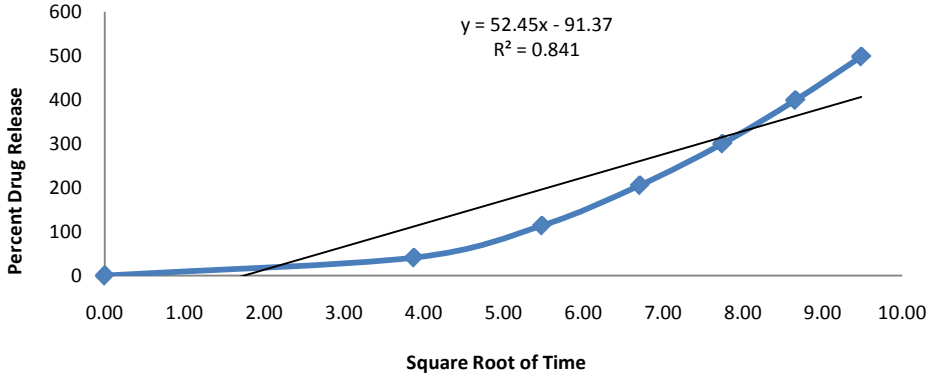


Fig 6: Krosmeyor-Peppase release kinetics model

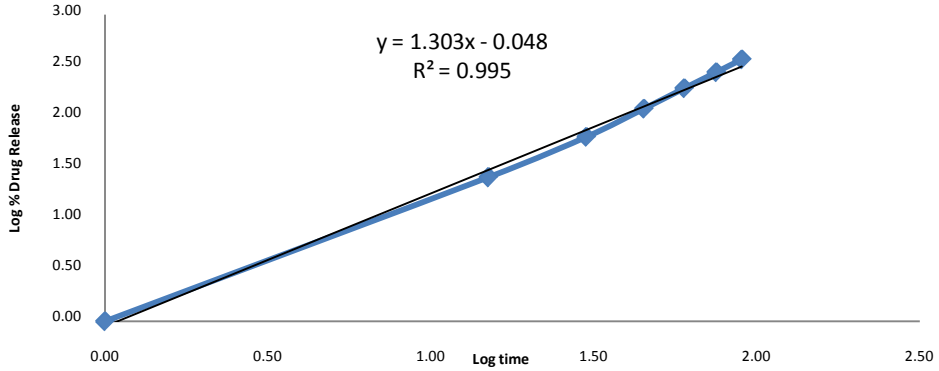


Fig 7: Hixon Crowell release kinetic model

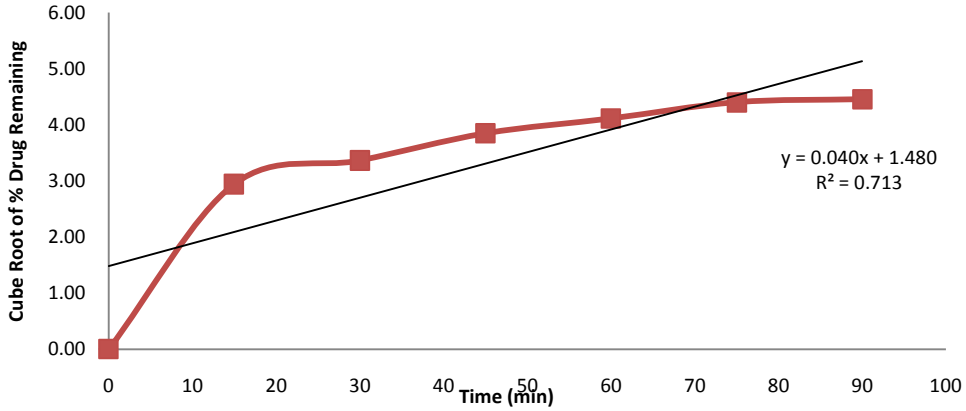


Table 7: Release kinetic models

Higuchi Model		Peppase model		Hixon Crowell model	
Line of equation	R^2 values	Line of equation	R^2 values	Line of equaton	R^2 values
Y= 52.45-91.37	0.841	Y= 1.303x-0.048	0.995	Y= 0.040x+1.480	0.713

From above release kinetic models it was found that Peppase model is best fitted for release kinetics of lornoxicam oral disintegrating tablets.

RESULTS AND DISSCUSSION

Oral disintegrating tablets of lornoxicam were prepared by using its kneading mixture with croscormellose. Firstly kneading mixtures of lornoxicam with croscormellose were prepared in weight ratios of 1:0.5, 1:1, 1:1.5. The dissolution studies were carried out for all kneading mixtures. All the mixtures showed enhanced dissolution compared to the pure drugs as shown in Table.1 and Fig.1. The pure drug released only 34.72% of drug in 90 min. The kneading mixtures of LX: CM of weight ratios 1:0.5, 1:1, 1:1.5 released 85.14%, 88.73%, and 98.84% respectively in 90 minutes. The mixture LX: CM (1:1.5) (KM) showed faster release of drug i.e.91.88% in 45 minutes which was not found with other two mixtures. Hence LX: CM (1:1.5) (KM) was selected for preparing oral disintegrating tablet of lornoxicam. The reason for enhanced dissolution of kneading mixture may be due to effective disaggregating capacity of croscormellose which is superdisintegrant. The prepared ODTs of lornoxicam compiled the official compendia by possessing hardness of 3.6 kg/cm^2, friability of 0.8%, drug content of 99.8%. And also these tablets show disintegration time of 12 second and 99.62%% of drug release in 30 minutes.

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