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Formulation and evaluation of lornoxicam of sustained release matrix tablets

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ABSTRACT

The major objective of the present research work is to prepare and evaluate sustained release matrix tablets of lornoxicam using hydroxyl propyl methyl cellulose (HPMC K15M). It is practically insoluble in water and aqueous fluids. Sustained release formulation is needed for lornoxicam because of its short biological half-life of 3.0-5.0 h. To study and evaluate the effect of two solubilizers namely polyvinyl pyrollidine PVP K30 and poly ethylene glycol (PEG 400) on the aqueous solubility of lornoxicam. Lornoxicam sustained release matrix tablets were formulated by employing hydroxyl propyl methyl cellulose (HPMCk15M) as matrix former, poly ethylene glycol (PEG400) as solubilizer, lactose or dicalcium phosphate as diluent for lornoxicam by wet granulation process. All the tablets prepared were evaluated for hardness, disintegration time and dissolution rate. Lornoxicam SR tablet equivalent 220 mg was used in each case. The solubility of lornoxicam was found to be 4.36, 40.76, and 38.36 mg/100ml respectively in water and water containing 2% PEG 400 and 2% PVP. Formulations F1, F2, F3, and F4 contain 50% HPMC K15M as release retardant. Formulations F1 and F2 contain lactose and DCP respectively as diluents, Formulations F3 and F4 contain PEG 400 at 5% strength as solubility enhancer, Tablets containing lactose as diluent gave relatively rapid release when compared to those containing DCP. All Formulations F1-F4 gave very slow release, about 20-35% in 24 hrs diluent. Formulations F5 and F6 were prepared employing HPMC K15M. Drug release from these formulations was very rapid and complete within 6 h in the case of F5 and within 10 h in the case of F6. Formulations F7 and F8 were prepared using 25% and 40% HPMC K15M, Lornoxicam release from the commercial SR tablets was slow and extended over a period of 18-20 h. Lornoxicam release from formulation F7 was slow and spread over 16 h. Drug release from formulation F7 was nearly similar to that from commercial formulation. Hence formulation F7 is considered as the best SR formulation of Lornoxicam. The FTIR spectra of lornoxicam and its formulated tablets in HPMCK15M, lactose and DCP were obtained with FTIR Spectrophotometer.

Keywords: Lornoxicam, HPMC K15M, PEG 400, Wet granulation method and sustained released tablets

INTRODUCTION

Tablets may be defined as solid pharmaceutical dosage forms containing drug substances with or without suitable diluents and prepared either by compression or molding methods. The basic rationale of a sustained drug delivery system is to optimize the biopharmaceutic, pharmacokinetic and pharmacodynamic properties of a drug in such a way that its utility is maximized through reduction in side effects and cure or control of condition in the shortest possible time by using smallest quantity of drug administered by the most suitable route[1].

Types SR dosage forms

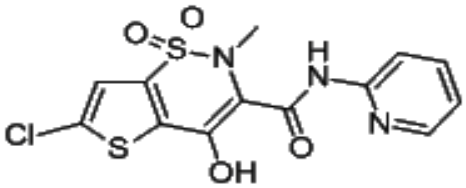
There are different types of SR dosage forms, they are,

i. Dissolution controlled system
ii. Diffusion controlled systems
iii. Biodegradable combination of both dissolution and diffusion systems
iv. Osmotic systems
v. Ion exchange resin system
vi. Pro-drug
vii. Swelling and expanding systems
viii. Floating systems
ix. Bio-adhesive systems[2].

DRUG PROFILE

The Chemical name is, (2-[2-[2-(2,6 dichlorophenyl) aminophenyl] acetyl] oxyacetic acid)/ 6-chloro-4-hydroxy-2-methyl-N-2-pyridinyl-2H-thieno-[2,3-e]-1,2-thiazine-3-carboxamide 1,1-dioxide.

Structure



Molecular Formula: $C_{13}H_{10}C_lN_3O_4S_2$
Molecular Weight: 371.82
Therapeutic Category: Anti- Inflammatory and Analgesic agent.
Melting Point: 225 -230^{0}C
Half life: 3-5hr[3,4,5].

MATERIALS AND METHODS

Formulation of Lornoxicam Sustained Release Tablets

Lornoxicam sustained release matrix tablets were formulated employing hydroxyl propyl methyl cellulose (HPMCk15M) as matrix former and poly ethylene glycol (PEG400) as solubilizer for lornoxicam as per the formulae given in table 01.

Table.1: Formulae of Lornoxicam SR Tablets Prepared

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8	PURPOSE
Lornoxicam	18	18	18	18	8	8	8	8	API/NSAID
PEG400 (5%)	-	-	11	11	11	11	11	11	Solubilizer
HPMCk15M	110	110	110	110	11	22	55	88	Polymer
Lactose	92	-	81	-	181.2	170.2	141.2	104.2	Diluent
Di-calcium phosphate	-	92	-	81	-	-	-	-	Diluent
Talc	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4	Lubricant
Magnesium stearate	4.4	4.4	4.4	4.4	4.4	4.4	4.4	4.4	glidant
Total weight (mg)	220	220	220	220	220	220	220	220	

Preparation of Lornoxicam Sustained Release Matrix Tablets

Lornoxicam, hydroxypropyl methyl cellulose (HPMCK 15M), polyethylene glycol (PEG400), lactose or dicalcium phosphate were mixed thoroughly in a dried mortar and granulated with water (qs). The water was added and mixed thoroughly to form a dough mass. The mass was passed through mess no.12 to obtained wet granules. The wet granules were dried at 60^{0}c .The dried granules were passed through mess no.16 to break the aggregates. Lubricants (talc and magnesium stearate) were passed through mess no.80 on to the dried granules

and blended in a closed poly ethylene bag. The tablet granules were compressed in to tablets on a Cadmach 16 station rotary tablet punching machine[6].

RESULTS

Table.2. Precompression evaluation parameters for formulated tablets of f1 to f8

Evaluation parameters	F1	F2	F3	F4	F5	F6	F7	F8
Bulk density (gm/cm)	0.75	0.73	0.75	0.73	0.70	.80	.79	.82
Tapped density (gm/cm)	0.81	0.80	0.82	0.81	0.77	.89	.87	.90
Carr's index (%)	7.40	8.75	8.53	10.97	9.09	10.11	9.19	8.88
Angle of repose (Degree)	21.80	24.70	19.2	25.1	21.80	22.2	29.68	25.1

Table.3. Post-Compression Evaluation Parameters For Formulated Tablets Of F1 To F8

Evaluation parameters	F1	F2	F3	F4	F5	F6	F7	F8
Weight varation (mg)± SD	220±.550	219±.990	220±.890	219±.990	219±.820	220±.890	219±.990	220±.780
Hardness(kg/cm^2)	7.890±.110	8.55±.450	7.580±.420	8.55±.45	8.33±. 67	7.580±.420	8.55±.45	7.580±.420
Friability (%)	.45	.54	.60	.46	.54	.46	.54	.55

Table.4.Drug Release Profiles of Lornoxicam SR Tablets Prepared

Time (hrs)	Percent Drug Released(($\bar{X}$ ± s.d) (n=3) F1	F2	F3	F4	F5
0	0	0	0	0	0
0.5	1.92±0.18	2.16±0.50	4.24±1.68	2.35±0.29	78.12±8.18
1	2.25±0.39	2.66±0.63	4.77±1.55	2.66±0.25	85.05±1.18
1.5	2.90±0.30	3.38±0.61	5.37±1.35	3.24±0.25	87.95±1.53
2	3.88±0.62	4.27±0.81	6.14±1.94	3.81±0.40	89.57±2.27
3	4.96±0.54	5.35±0.72	7.12±2.04	4.53±0.07	91.35±2.96
4	6.47±0.57	6.14±0.29	8.49±1.94	5.71±0.74	95.06±1.02
5	6.88±0.11	6.88±0.20	9.33±1.78	6.67±0.18	97.47±0.67
6	7.72±0.46	7.65±0.78	10.98±2.75	7.65±0.27	100.03±0.03
7	9.23±0.93	8.59±0.33	11.89±2.25	8.39±0.42	100.0±0.00
8	9.52±0.61	9.04±0.36	12.83±2.52	9.50±0.25	
9	10.22±0.70	9.86±0.14	14.29±2.79	10.53±0.04	
10	12.13±1.13	10.29±0.14	15.40±2.87	11.18±0.14	
11	12.59±0.77	11.22±0.79	16.45±2.44	12.35±0.50	
12	14.15±0.80	11.97±0.54	18.63±1.15	14.58±1.13	
14	16.14±0.92	13.09±0.47	19.50±2.46	15.83±0.99	
16	18.13±0.97	15.11±2.19	20.38±2.13	17.43±1.30	
18	20.77±0.46	16.91±2.35	22.59±2.66	19.54±1.18	
20	22.64±1.11	20.19±1.91	24.60±1.71	20.77±1.74	
22	25.16±2.75	20.96±1.03	28.11±2.81	21.87±0.94	
24	26.35±2.94	21.65±1.26	31.20±1.47	22.42±0.54	

TIME (hrs)	Percent Drug Released(($\bar{X}$ ± s.d)			
	F6	F7	F8	COMMERCIAL
0	0	0	0	0
0.5	72.69±2.5	4.63±1.1	4.74±.1.0	6.63±0.3
1	77.36±2.1	6.94±0.1	6.32±1.0	9.17±0.2
1.5	78.72±1.7	12.44±2.3	8.26±2.2	14.22±0.8
2	80.78±1.3	18.77±2.3	8.71±2.3	18.37±1.8
3	83.04±1.2	33.40±3.0	9.68±2.7	34.29±2.0
4	85.28±1.8	45.83±2.1	11.98±3.0	46.80±1.7
5	87.15±1.4	57.83±1.1	15.80±2.4	58.48±1.7
6	88.93±0.7	59.55±2.2	18.52±1.8	59.04±1.9
7	90.46±1.2	62.30±2.8	24.25±2.2	64.56±2.7
8	91.93±1.4	73..23±2.8	25.69±1.6	75.91±1.3
9	93.04±1.0	84.44±1.6	26.73±2.7	82.90±2.7
10	94.09±1.0	85.25±2.5	27.70±2.3	84.98±2.8
11	95.52±0.5	90.35±1.5	30.88±1.4	87.36±2.1
12	98.52±1.1	97.28±1.4	31.66±2.4	92.13±2.1
14	100.10±0.0	99.21±2.2	32.68±2.8	94.40±2.6
16	100.00±0.0	100.80±1.6	33.63±3.0	97.46±2.1
18	93.04±1.0		34.70±2.8	100.09±0.1
20	94.09±1.0		35.47±1.0	
22	95.52±0.5		36.32±1.3	
24	98.52±1.1		37.23±1.8	

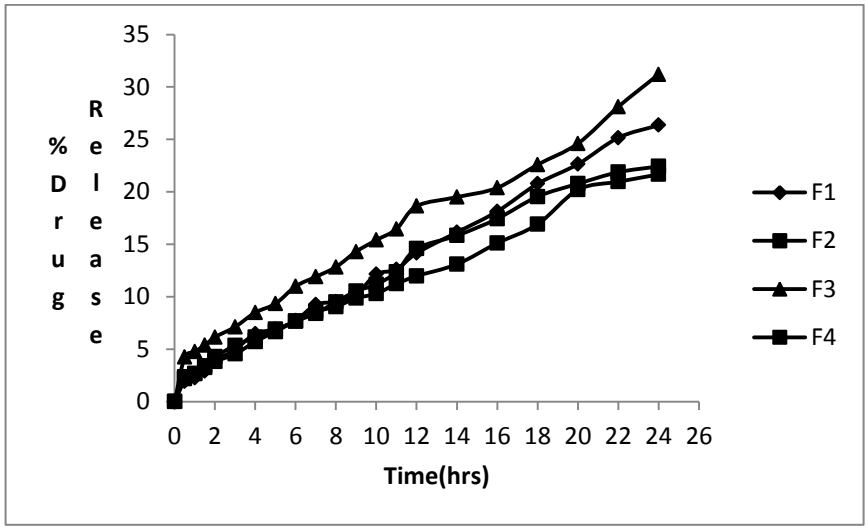


Fig.1.Zero Order Plots of Drug Release of Lornoxicam SR Tablets

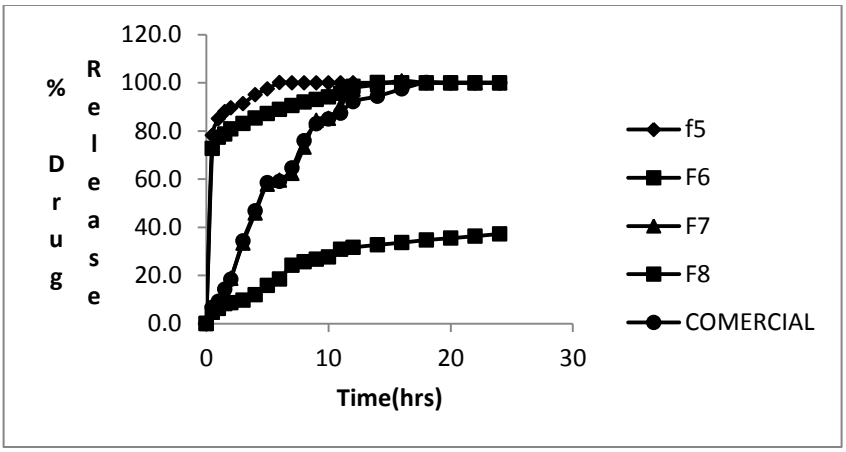


Fig.2. Zero Order Plots of Drug Release of Lornoxicam SR tablets

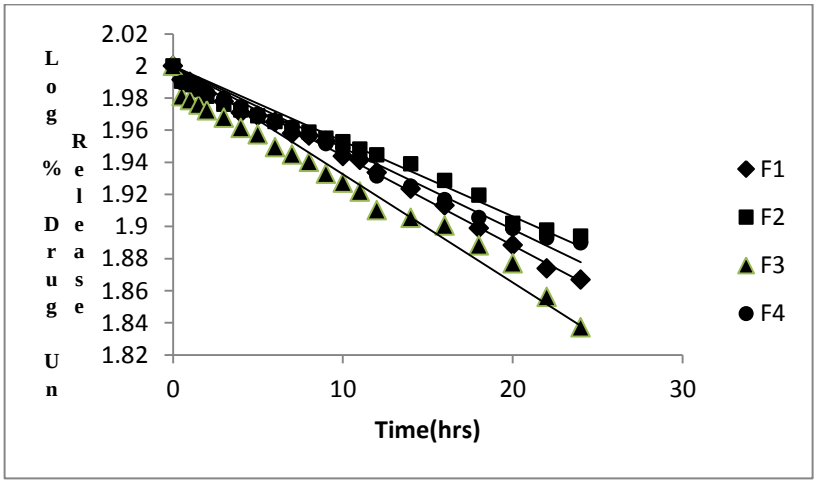


Fig.3. First Order Plots of Drug Release of Lornoxicam SR Tablets

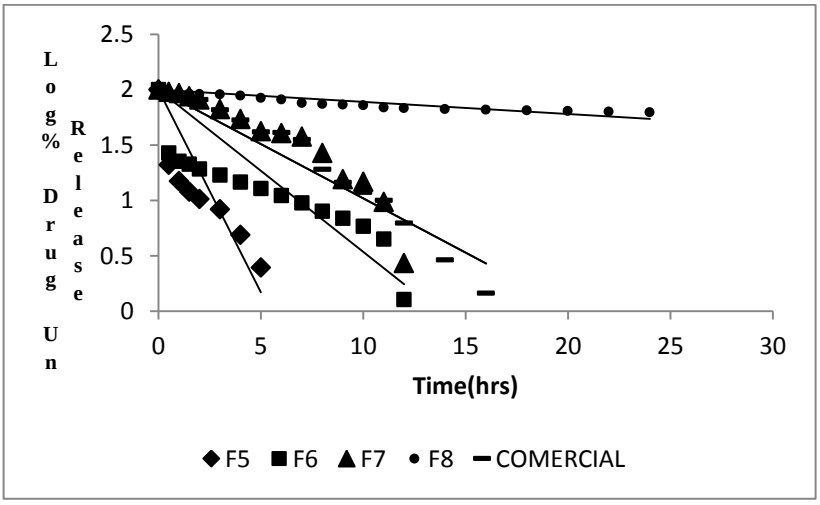


Fig.04. First Order Plots of Drug Release of Lornoxicam SR Tablets

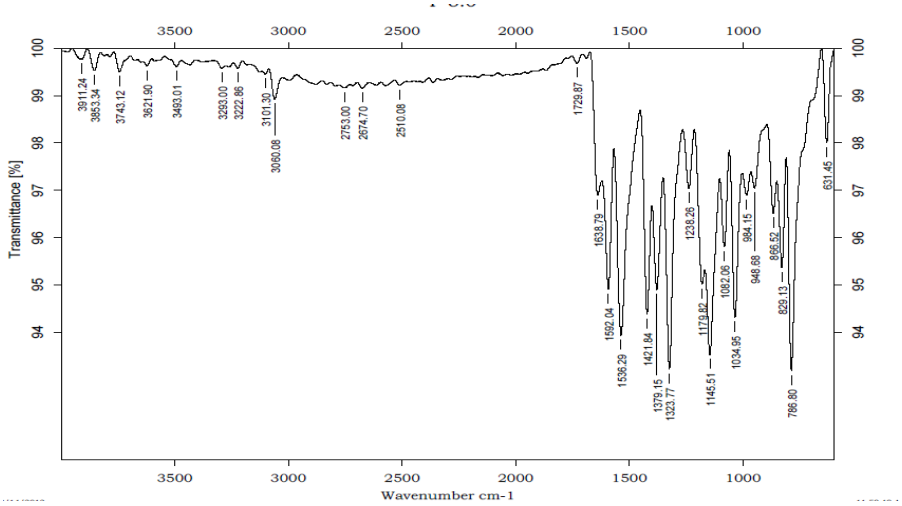


Fig.05. FTIR Spectrum of Lornoxicam

DISCUSSION

Lornoxicam SR tablets were prepared as per the formulae given in Table.1 Formulations F1, F2, F3, F4, contain 50% HPMC K15M as release retardant. Formulations F1 and F2 contain lactose and DCP respectively as diluents. Formulations F3 and F4 contain PEG 400 at 5% strength as solubility enhancer. Lornoxicam release from these tablets was very slow and spread over more than 24 h. Tablets containing lactose as diluent gave relatively rapid release when compared to those containing DCP as diluent. Lornoxicam release rate was found to be increased when PEG 400 was included in the formulation as solubility enhancer.

Formulations F1-F4 gave very slow release, about 20-35% in 24 hrs and hence these formulations are considered not suitable for sustained release of lornoxicam. Formulations F5 and F6 were prepared employing HPMC K15M respectively at 5% and 10% strength with a view to improve drug release from the matrix tablets. Drug release from these formulations was very rapid and complete with in 6 h in the case of F5 and within 10 h in the case of F6. For comparison drug release from one commercial SR formulation of lornoxicam [Lorasid] was also studied. Lornoxicam release from the commercial SR tablets was slow and extended over a period of 18-20 h.

Formulations F7 and F8 were prepared using 25% and 40% HPMC K15M respectively. They also contain lactose as diluent and PEG 400 as solubility enhancer. Lornoxicam release from formulation F7 was slow and spread over 16 h. Drug release from formulation F8 was again very slow and was only about 37% in 24 h. Hence the formulation F8 is also considered not suitable.

A comparison of the release profiles of the formulated and commercial SR tablets indicated that a drug release from formulation F7 was nearly similar to that from commercial formulation. The similarity of the release profiles of formulation F7 and commercial SR tablet was compared .Hence formulation F7 is considered as the best SR formulation of lornoxicam. Thus the results of study indicated that lornoxicam SR tablets could be formulated employing HPMC K15M [25%] as release retardant and matrix former, PEG 400 [5%] as solubility enhancer and lactose as diluent.

CONCLUSION

The aqueous solubility of lornoxicam was markedly enhanced by PVP K30 and PEG 400. A 9.34 and 8.79 fold increase in the solubility of lornoxicam was observed with PEG 400 and PVP K30 respectively at 2 % w/v concentration. PEG 400 gave higher enhancement in the solubility of lornoxicam. Lornoxicam release from the formulated SR tablets was very slow and spread over more than 24 h. Tablets containing lactose as diluent gave relatively rapid release when compared to those containing DCP as diluent. Lornoxicam release rate was found to be increased when PEG 400 was included in the formulations as solubility enhancer.

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