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FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLET OF LORNOXICAM

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ABSTRACT

The goal of this study was to create Lornoxicam sustained release matrix tablets in order to produce the medicine in a long-lasting form. So as to prolong its elimination time for the effective treatment of rheumatoid arthritis, and also in the management of ankylosing spondylitis, acute sciatica and low back pain. The existing examination demonstrates that use of hydrophilic and hydrophobic polymers may be successfully working for formulating sustained release matrix tablets of Lornoxicam. Optimized formulation containing HPMC K15M and xanthan gum at best ratio had successfully sustained the drug release for 24 h. Matrix tablets of optimized batch had in vitro drug release. As a result, Lornoxicam sustained release matrix tablets are effective. Biocompatible polymers were tested, analysed, and determined to be good candidates for extending the drug's release from matrix tablets.

KEYWORDS: Lornoxicam, HPMC, Sustained release, Matrix tablets.

1. INTRODUCTION

"Any drug or dosage form alteration that prolongs the therapeutic activity of the medicine" is what a sustained-release dosage form is defined as. Formulation scientists have long had a hurdle in developing oral sustained release (SR) tablets with highly water soluble medicines or bioactives.[1] Most of these medications, if not correctly designed, may be released at a rapid rate, surpassing the limit therapeutic levels and causing hazardous adverse effects. Sustained delivery of such medications ensures better drug delivery and patient compliance, increased safety and efficacy, desired release kinetics, and helps keep plasma drug concentrations within the therapeutic window for longer.[2,3] To create sustained release matrix dosage forms, several procedures have been utilised, including melt granulation,[4] melt pelletization,[5] hot melt coating,[6] Wet granulation,[7,8,9] hot melt extrusion,[10] and direct compression.[11,12] As a matrix former, a mixture of HPMC K 15M, Xanthan gum and other polymers can be used to create the tablet. Lornoxicam is a non-steroidal anti-inflammatory drug (NSAID) that serves a variety of activities in the body. After oral administration, it can be absorbed quickly and fully from the gastrointestinal tract. Lornoxicam has a 90-100 percent absolute bioavailability. No evidence of a first-pass effect has been found. It can be detected in the plasma in both its unmodified and hydroxylated forms. There is no pharmacological activity in the hydroxylated metabolite. The major enzyme responsible for Lornoxicam biotransformation has been identified as CYP2C3. Lornoxicam is excreted as an inert substance by the liver and the kidneys in roughly equal amounts. Lornoxicam inhibits prostaglandin production by blocking the enzyme cyclooxygenase, which controls the conversion of arachidonic acid to prostaglandins. Lornoxicam is most commonly used to treat osteoarthritis and rheumatoid arthritis, as well as ankylosing spondylitis, acute sciatica, and low back pain. The primary goals of this study are to confirm the drug using various analytical techniques, to investigate drug excipient compatibility, to avoid the dose and frequency of the dosage form, and to perform stability testing.[13-16]

2. MATERIALS AND METHODS

2.1 Chemicals: Lornoxicam, Hydroxypropylme thylcellulose (HPMC), Xanthan gum, guar gum, Microcrystalline Cellulose, Magnesium stearate, Talc.

2.2 Instruments: Electronic Balance, UV Spectrophotometer, FTIR Spectrophotometer, DSC, Sonicator, Stability Chamber, Tablet Dissolution Testing Apparatus, Rimek Mini Tablet Press 2, Monsanto Hardness Tester, Rotatory Flask Shaker.

2.3 Preparation of sustained release Lornoxicam tablet

Direct compression method was used for preparation of Lornoxicam tablets. The weight of Lornoxicam was taken as 8 mg/tablet in all prepared formulation batches. HPMC was used as polymeric material for preparation of matrix tablets. And Magnesium stearate at concentration

of 6% by weight of tablet was used as a lubricant. Micro crystalline cellulose (MCC) was selected as tablet diluent to maintain the constant weight of tablet as 100 mg. The powder mixtures of all above mentioned ingredients were thoroughly mixed, sieved through the 60# sieve, lubricated and then compressed into tablets using multi rotary tablet machine. And each matrix tablet contained 8 mg of lornoxicam and other pharmaceutical ingredients are as shown in (Table 1).

2.4 Preparation of matrix tablet

Tablets are prepared by direct compression technique.[17,18,19]

Table 1: Composition for sustained release matrix tablet of Lornoxicam formulation design.

Ingredients (in mg)	F1	F2	F3	F4	F5	F6
Lornoxicam	8	8	8	8	8	8
HPMC K15M	10	10	10	10	10	10
Xanthan gum	-	-	-	8	16	32
Guar gum	8	16	32	-	-	-
Magnesium Stearate	6	6	6	6	6	6
Microcrystalline cellulose	64	56	40	64	56	40
Talc	4	4	4	4	4	4
Total	100	100	100	100	100	100

3. Evaluation of preformulation parameters

3.1 Angle of Repose

The fixed funnel method was used to determine the angle of repose for each formulation's powder blend. Separately, the powder mixture was poured down the funnel until the apex of the conical pile generated just touched the funnel's tip. On the paper, this creates a pile of powder. Separately the powder mixture was poured down the funnel until the apex of the conical pile generated just touched the funnel's tip. On the paper, this creates a pile of powder. Substituting the values of the base radius and pile height into the following equation yielded the angle of repose. $\tan \theta = h/r$ (1)

Where
θ = is angle of repose.
h = is height of the heap of pile and
r = is radius of base of pile

Standards of Angle of Repose.

Angle of Repose (◦)	Type of Flow
< 25	Excellent
25-30	Good
30-40	Passable
>40	Poor

3.2 Bulk Density

The bulk density of the powder blend was evaluated by measuring the entire volume and weight of the powder in a measuring cylinder. A formula was used to compute bulk density. A formula was used to compute bulk density.
Bulk density = weight of powder/ Bulk volume (2)

3.3 Tapped Density

The tapped density was obtained by dividing the mass of a power by the tapped volume in cm3. The sample of suitable amount of powder from each formulation was carefully introduced into a 10 ml graduated cylinder. The cylinder was dropped from a height of 1 inch onto a hard wooden surface under its own weight. The tapping was repeated until there was no more change in volume, at which point the volume was determined using the equation below.
$Dt = M/V_b$ (3)

Where:
M = is weight of powder taken and
V_b = is tapped volume.

3.4 Carr's Compressibility Index

Carr's compressibility index (CCI) was calculated by using values of bulk density and tapped density as given below.
%CCI = [(TD-BD)*100]/TD (4)

3.5 Hausner's Ratio

Hausner's ratio is a number that is correlated to the flow ability of powder and powder blend. It was calculated using equation given below.
Hausner's ratio = TD / BD (5)

4. Evaluation of post formulation parameters:

4.1 Thickness

A vernier calliper was used to measure the thickness of the tablet.

4.2 Hardness

A Monsanto hardness tester was used to measure the hardness of each batch of tablets. The hardness was measured in kilogrammes per square metre (kg/cm2)

4.3 Weight variation

Weighing 20 tablets individually and comparing the individual weights to the average weight of the 20 tablets was used to determine the weight variation. And the value of weight variation test is expressed in percentage. The following formula is used
Weight Variation = (IW - AW)/AW X 100%
Where:

IW: Individual weight
AW: Average weight

Standards of Weight variation

Average weight of tablet	% deviation
≤ 80mg	±10
>80 mg – 250 mg	±7.5
≥ 250 mg	±5

4.4 Friability

The friability of 10 tablets was assessed by weighing them first and then rotating them for 4 minutes at 25 rpm in a friability tester (Roche friabilator). The remaining weight of the tablet was calculated after dusting.

% Friability = (Initial weight-final weight)/Initial weight x 100

4.5 Disintegration

The test was carried out by placing one tablet in each tube and inserting a disc into each tube. Suspend the assembly in a beaker filled with cleaned water and run the machine until the tablet completely dissolves.

5. RESULTS AND DISCUSSION

Preformulation study of Lornoxicam matrix sustained release tablet

Preformulation parameters with micromeritic properties for lornoxicam sustained release matrix tablets are as shown in Table 2.

Table 2: Micromeritic properties for lornoxicam sustained release matrix tablets.

Parameters	F1	F2	F3	F4	F5	F6
Angle of repose (Θ)	25.53	25.24	24.17	25.11	25.04	25.12
Loose bulk density (LBD) g/ml	0.401	0.384	0.325	0.332	0.337	0.254
Tapped density (TBD) g/ml	0.464	0.452	0.373	0.382	0.398	0.283
Carr's index	13.96	14.61	12.65	13.56	14.51	10.52
Hausner ratio	1.15	1.16	1.13	1.14	1.10	1.12

Physicochemical parameters for sustained release matrix tablet of Lornoxicam

Table 3: Post formulation parameters of Lornoxicam sustained release matrix tablets.

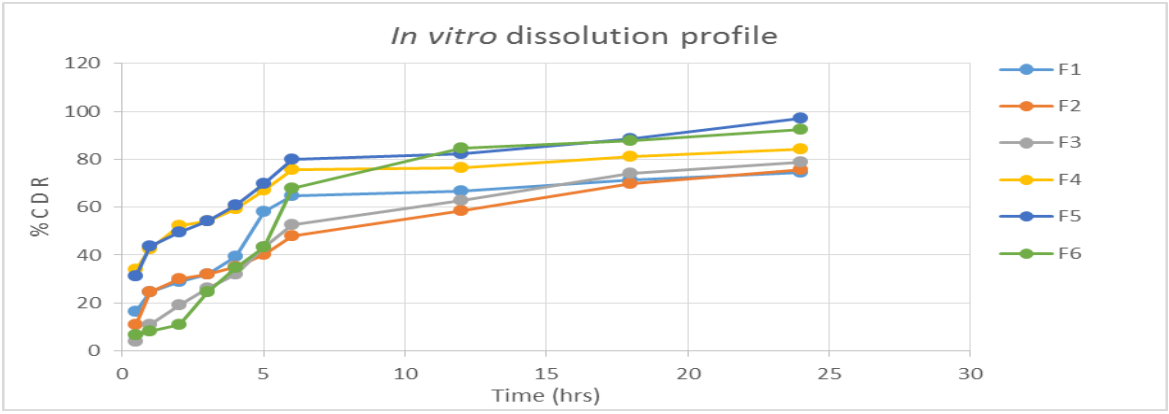
Parameters	F1	F2	F3	F4	F5	F6
Thickness ±S.D. mm(n=10)	2.43±0.02	2.51±0.04	2.54±0.02	2.51±0.03	2.46±0.05	2.55±0.03
Hardness S.D. (kg/cm2)	6.7±0.2	6.1±0.4	6.2±0.2	5.36±0.2	5.27±0.2	5.8±0.3
Average Weight variation (n=20) mg	101.4±1.50	102.62±1.67	101.51±1.42	100.35±1.34	100.27±1.59	101.22±1.60
Drug Content (%)	100.66±1.21	98.51±1.47	97.27±1.59	98.78±0.94	99.66±2.16	98.81±0.56
Friability (% w/w)	0.37±0.04	0.41±0.05	0.36±0.03	0.45±0.04	0.39±0.08	0.30±0.03

6. In Vitro Dissolution test

In-vitro dissolution studies were carried out using USP XXIII dissolution apparatus type II at50 rpm. Dissolution test was carried out for a total period of 24 hr using 0.1N HCl (pH 1.2) solution (900 ml) as a dissolution medium at 37 ± 0. 5ºC for first 2 hr and phosphate buffer (pH 6.8) solution (900 ml) solution for the rest of the period. 5 ml of sample was withdrawn at predetermined time interval of 1 hr up to 24 hr and replaced with same volume of fresh dissolution medium. The withdrawn samples were filtered and analysed by UV spectrophotometer at 376 nm using pH 6.8 as a blank. Percentage cumulative drug release was calculated.

Table 4: Cumulative % drug release.

Time (hrs.)	% CDR					
	F1	F2	F3	F4	F5	F6
0.5	16.36	10.9	4.09	34.09	31.36	6.81
1	24.65	24.61	10.93	42.5	43.84	8.22
2	28.9	30.23	19.19	52.32	49.59	11.01
3	31.93	31.87	26.16	54.26	54.21	24.76
4	39.35	35.11	31.91	59.44	60.73	34.61
5	58.28	40.25	43.41	67.1	69.69	43.39
6	64.86	47.8	52.81	75.6	79.88	67.74
12	66.81	58.63	62.72	76.36	82.09	84.54
18	71.35	69.93	74.05	80.96	88.41	87.83
24	74.55	75.85	78.63	84.22	97.08	92.51



Stability studies

The purpose of stability testing is to provide evidence on how the quality of a drug substance drug product varies with time under influence of various environmental factors such as temperature, humidity, and light are all factors that go into determining suggested storage conditions, retest intervals, and self-lives.

ICH specifies the length (duration) of study and storage conditions

Accelerated stability studies were carried out at 40 ºC ± 2 ºC / 75 % RH ±.5 % for a specific time period up to 3 months and intermediate stability studies were carried out at 30 ºC ± 2 ºC / 65 % RH ±5 % for a specific time period up to 3 months.

Table 5: Physicochemical evaluation for stability study.

Parameters	Drug content (%)	Hardness ± S.D. (kg/cm2)	Friability ± S.D. (% w/w)	Weight variation (N=20) mg	In-vitro drug release	
					At 10hr.	At 24hr.
Initial	99.48±0.91	5.1±0.3	0.36±0.05	100.40±2.81	48.59	96.85
After one month	99.28±0.44	5.0±0.4	0.36±0.08	100.38±1.34	48.06	96.83
After two months	99.27±0.41	5.0±0.5	0.36±0.01	100.38±1.12	48.01	96.42
After three months	99.27±0.67	5.0±0.5	0.36±0.03	100.36±1.22	48.02	96.26

Fourier Transform Infrared (FTIR) Spectroscopy

The formulations were subjected to FT-IR studies to find out the possible interaction between the drug and the excipients during the time of preparation. FTIR analysis of the pure drug and optimized formulation was carried out using an FTIR spectrophotometer (Bruker FT-IR - USA).

Drug – Excipient Compatibility Studies

There was no disappearance of any characteristics peak in the FTIR spectrum of drugs and the polymers used. This demonstrates that the medication and the polymers utilised have no chemical interaction. The appearance of peaks within the predicted range demonstrates that the materials used in the investigation are genuine and that no interactions occurred. Lornoxicam is also present in the physical mixture, indicating that the drug and the polymers have no interaction, confirming the drug's stability. Figures 1 and 2 show the results.

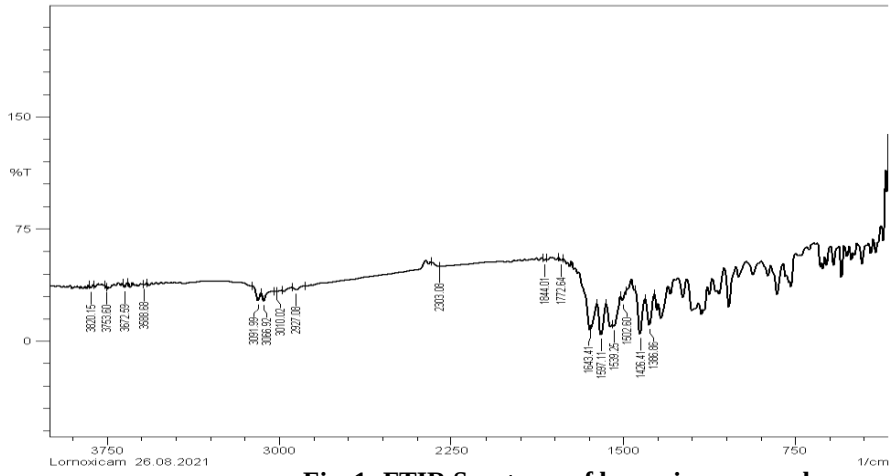


Fig. 1: FTIR Spectrum of lornoxicam pure drug.

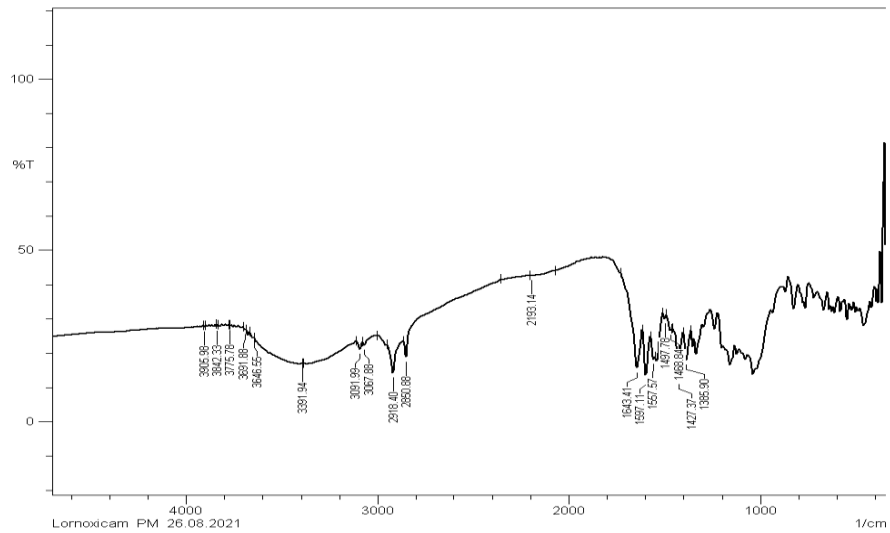


Fig. 2: FTIR Spectrum of physical mixture of drug and polymer.

Characteristic peaks of pure drug lornoxicam and optimized formulation.

Functional Group	Pure drug lornoxicam (Wave no. cm^{-1})	Optimized formulation (Wave no. cm^{-1})
OH	3588	3391
NH	3091	3091
S=O	1386	1385
C=N	1643	1597
C-Cl	750	740
C-N	1150	1225
C=O	1772	1643

SUMMARY

The present study was carried out to develop Sustained Release matrix tablets of lornoxicam using polymers such as HPMC K15M, Guar gum, and Xanthan gum and in combinations by direct compression method. And all the prepared formulations were evaluated for both pre-compressive and post compressive parameters such as angle of repose, bulk density, tapped density, Carr's index, Hausner's ratio, tablet thickness, hardness, friability, weight variation and drug content uniformity, the values obtained were found to be satisfactory and they complies with pharmacopeial standards.

CONCLUSION

The results of this study show that hydrophilic and hydrophobic polymers can be successfully combined to create Lornoxicam sustained release matrix tablets. Optimized formulation containing HPMC K15M and Xanthan gum at optimum ratio had successfully sustained the drug release for 24 h. Matrix tablets of optimized batch had in vitro drug release. By examining various preformulation parameters, it was discovered that the optimal matrix tablets of the optimized batch have a better flow property. And Matrix tablets of batch F5 had good in vitro drug substance release. F5 was selected as more optimized formulation and was further subjected or evaluated for stability study. Formulation F5 containing HPMC K15M and Xanthan gum polymer in the ratio of 3:1 and showed a maximum drug substance release of 97.08 % for 24 hours period Thus sustained release matrix tablets of Lornoxicam using biocompatible polymers were successfully formulated. Evaluated and found to be suitable candidates in extending the release of the drug from the matrix tablets.

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