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FORMULATION DEVELOPMENT AND EVALUATION OF SUSTAINED RELEASE TABLETS OF LORNOXICAM

Abhishek Pandey*[1] and Sanket Singhal[2]

[1]School of Studies in Pharmaceutical Sciences, Jiwaji University, Gwalior (M.P.).

[2]A.R.A. College of Pharmacy, Dhule, Maharashtra.

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***Corresponding Author**
Abhishek Pandey
School of Studies in Pharmaceutical Sciences, Jiwaji University, Gwalior (M.P.).,

ABSTRACT

Lornoxicam is a non-steroidal anti-inflammatory drug, Lornoxicam has short half-life (3-5 hr.), makes the development of sustained-release (SR) forms extremely advantageous, lornoxicam is weak acid having pKa 5.1, it has pH dependent solubility, characterized by poor solubility in low pH condition present in stomach, which consequently leads to a delayed onset of its analgesic action. Formulation of sustained release tablet is effective approach for non- steroidal anti-inflammatory drug (lornoxicam) for maximum pain relief with prolong drug concentration due to sustained release from tablet matrix. Different formulations (F1- F8) were designed with HPMC (K4M and K100), MCC, PVP k30, magnesium stearate and talc. Pre and post compression parameters for all formulations were studied. Batch F8 selected as optimized batch on the basis of dissolution profile.

KEYWORDS: Lornoxicam, Sustained release, Dissolution, HPMC.

INTRODUCTION

Oral route of drug administration is the most important method of administering drugs for systemic effects. Nevertheless, it is probable that at least 90% of all drugs used to produce systemic effects are administered by the oral route. When a new drug is discovered, one of the first questions a pharmaceutical company asks is whether or not the drug can be effectively administered for its intended effect by the oral route.

Tablet represents unit dosage forms in which one usual dose of drug has been accurately placed. They are provide the greatest ease of swallowing with least a tendency for hang-up

above the stomach, especially when coated, provided that tablet disintegration is not excessively rapid. Tablets are compressed of two or three tablets of granulation compressed together. They have the appearance of a sandwich because the edges of each tablet are exposed.[1] Extended Release systems were introduced three decades ago. Extended release, extended action, prolonged release, controlled release, timed release, depot and repository dosage forms are the terms used to identify drug delivery system that are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. Expressions such as "prolonged action", & "Sustained release" have also been used to describe extended release dosage form.[2-3] Lornoxicam is a non-steroidal anti-inflammatory drug, Lornoxicam has short half-life (3-5 hr.), makes the development of sustained-release (SR) forms extremely advantageous, but Lornoxicam is weak acid having pKa 5.1, it has pH dependent solubility, characterized by poor solubility in low pH condition present in stomach, which consequently leads to a delayed onset of its analgesic action. Formulation of sustained release tablet is effective approach for non- steroidal anti-inflammatory drug for maximum pain relief. Extended release dosages forms cover a wide range of prolong action preparation that provides continuous release of their active ingredient for a specific period of time.[4] By prescribing sustained release system, it is possible to achieve several therapeutic advantages like Frequency of doses reduced. Patient compliance can be improved, and drug administration can be made more convenient. The aim of the present research work was to develop sustained release tablet of lornoxicam to maintain its prolong drug concentration due to sustained release from tablet matrix.

MATERIAL AND METHODS

MATERIAL

Lornoxicam was obtained as gift sample from Ajanta Pharmaceuticlas Pvt Ltd. HPMC, Microcrystalline cellulose, PVP k 30, Magnesium stearate, Talc were of Lobachem.

METHODS

Drug - excipients Interaction Study[5]

Preformulation testing is an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. It is the first step in the rational development. Physical mixtures of drug and excipients were filled in the prewashed vials and

sealed. The sealed vials were kept at 40°C at 75% RH for 1 month relative humidity for 30 days in stability chamber.

Evaluation of physical properties[6]

Angle of repose

The angle of repose was determined by the funnel method. The accurately weighed powder was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder. The powder was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured.

The bulk density and tapped density (TBD) of drug, polymers and excipients were determined. 2 gm of powder was introduced into a 10 ml calibrated measuring cylinder. After noting down the initial volume, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 seconds intervals.

Compressibility

The compressibility index of all ingredients were determined by following equations.

Formulation of tablet

The Sustained Release was achieved by means of a polymeric matrix for which the tablet is formed. Sustained release tablet tends to swell and slowly erode rather than disintegrating. Formulation and development of Lornoxicam Sustained release tablet involves following steps.

Manufacturing of Lornoxicam Sustained Release Tablet[7-9]

- Sifting of active material.
- Melting of hydrophobic polymers on hot water bath & heating of drug in tray dryer.
- Addition of active material to melt of polymer with continuous stirring.
- Solidifying melted mixture at room temperature.
- Screening of solidified mass- granulation.
- Addition of excipients-sifting of excipients and addition to granules of step 5.
- Lubrication – sifting of lubricants and blending with granules of step 6.
- Compression of lubricated granules of step 7**.**

Table.1 Composition of Lornoxicam Sustained Release Tablet.

Composition	Quantity in mg							
Lornoxicam	12	12	12	12	12	12	12	12
MCC	157	152	162	167	172	182	167	172
HPMC K4M	90	90	85	60	60	50	40	40
PVP K30	5	10	15	15	15	15	15	15
Purified Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
HPMC K100M	-	-	-	10	15	25	30	25
Talc	2	2	2	2	2	2	2	2
Mg.Sterate	4	4	4	4	4	4	4	4
Total	450	450	450	450	450	450	450	450

Evaluation of sustained release tablet[10-12]

Weight variation test

According to the official test, 20 tablets were weighed individually and collectively. Average weight per tablet was calculated from the collective weight. Then the weights of the individual tablets were compared with the average weight to determine weight variation.

Friability and hardness

For each formulation, the hardness of 6 tablets was determined using the Monsanto hardness tester. In The Roche friabilator the weight of tablets was noted initially (W1) and placed in a friabilator for 4 min/ 100 rpm. The tablets were reweighed and noted as (W2). The difference in the weight is noted and expressed as percentage.

Thickness

The thickness of the tablets was determined using a vernier caliper. 20 tablets from each batch were used.

Drug content

Ten Tablets were weighed individually, crushed, and the drug was extracted in phosphate buffer ph 7.4. The solution was filled through a 0.45 um Millipore filter and drug content was determined by UV spectroscopy after a suitable dilution with reference to calibration curve.

In-vitro dissolution parameter (Table.2).

Dissolution medium	pH 6.8 phosphate buffer
Dissolution medium volume	1000ml
Apparatus	USP Type-II,Paddle
Speed	100 rpm
Temperature	37oC
Sampling time interval (hour)	1, 3,6,10

RESULT AND DISCUSSION

Precompression parameter of sustained release tablet blend.

Precompression parameters like angle of repose, loose bulk density, tapped bulk density, compressibility index, and hausner's ratio of all batches of lornoxicam was represented in table 3**.**

Table: 3 Precompression parameters of sustained release tablet

Batch	Angle of Repose (θ)	LBD (g/mL)	TBD (g/mL)	Compressibility Index (%)	Hausner's Ratio
SR1	28.6	0.167	0.182	8.24	1.08
SR2	28.36	0.160	0.179	12.09	1.14
SR3	27.86	0.167	0.181	8.50	1.19
SR4	28.7	0.167	0.200	9.12	1.09
SR5	28.89	0.159	0.220	10.00	1.07
SR6	29.88	0.180	0.201	11.1	1.11
SR7	30.76	0.178	0.198	12.1	1.12
SR8	30.67	0.178	0.198	12.1	1.12

Evaluation of Sustained release tablets

Weight variation of tablet was found within limit (460 ± 5%). Friability of bi-tablet tablet 0.1% was found less than 1% except in batch F1 & F2 due to less binder. Hardness was found 9.0-9.5, in batch F1 & F2 hardness is less (5.0-6.5) and thickness variation was found less than 5% variation. Content uniformity of lornoxicam in bi-tablet tablet was found between 92 -99% respectively. Batch F7 and F8 were selected to obtained for dissolution study on the basis of drug content uniformity among them batch F8 exhibited desired release profile. (Table 4 and 5).

Table. 4 Properties of Sustained release tablet

Sr. NO	Weight Variation (mg) *	Thickness (mm) *	Hardness (Kp) †	Friability (%)†	Drug Content Uniformity (%)
F1	460±1.3	7.0±0.03	5.0±0.60	1.12±1.1	92.0±1.1
F2	461±2.1	5.4±0.04	6.5±0.50	1.00±0.9	97.0±1.2
F3	459±1.3	6.1±0.09	9.12±1.20	0.1±0.12	95.0±1.1
F4	460±1.1	5.7±1.8	9.3±0.89	0.12±0.1	97.0±1.1
F5	462±1.1	6.0±1.1	9.5±0.55	0.13±0.2	96.0±1.3
F6	460±1	5.9±1.4	9.4±0.98	0.14±0.1	97.0±0.4
F7	460±2.7	6.0±1.8	9.3±1.20	0.12±0.3	99.0±1.0
F8	459±2.0	6.1±1.8	9.1±1.12	0.12±0.2	99.0±0.9

Table: 5 Cumulative % Drug Release Lornoxicam from Bi-tablet Tablet

TIME (hr)	F7	F8
0	0	0
1	21.12±1.7	24.10±1.4
2	28±1.3	29±1.1
4	39.0±1.3	41.6±1.1
6	47.0±1.1	51.0±1.6
8	54.2±1.11	60.9±1.2
12	69.0±1.1	70.0±1.0
16	78±1.1	81±1.3
24	97.0±1.1	98.0 ±1.1

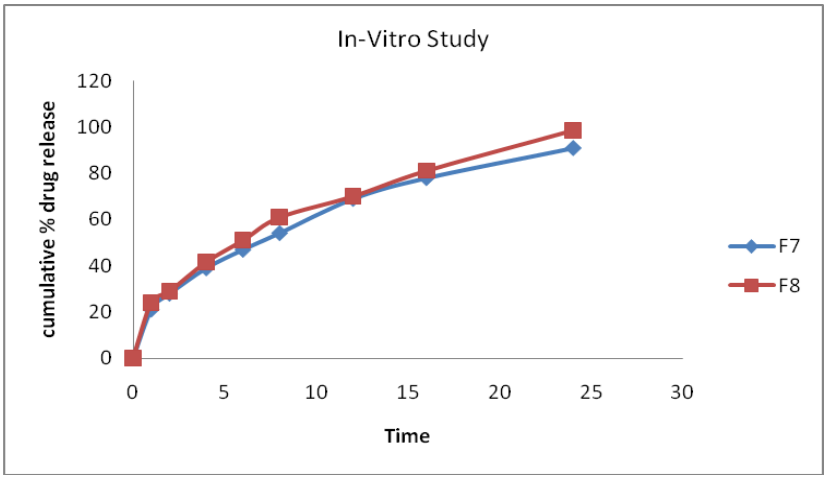

Fig.1 In-vitro drug release study of sustained release tablet Batch F7 and F8

Drug release study

The zero-order rate describes the systems where the drug release rate is independent of its concentration. Figure.2 shows that cumulative amount of drug release vs. time for zero-order kinetics.

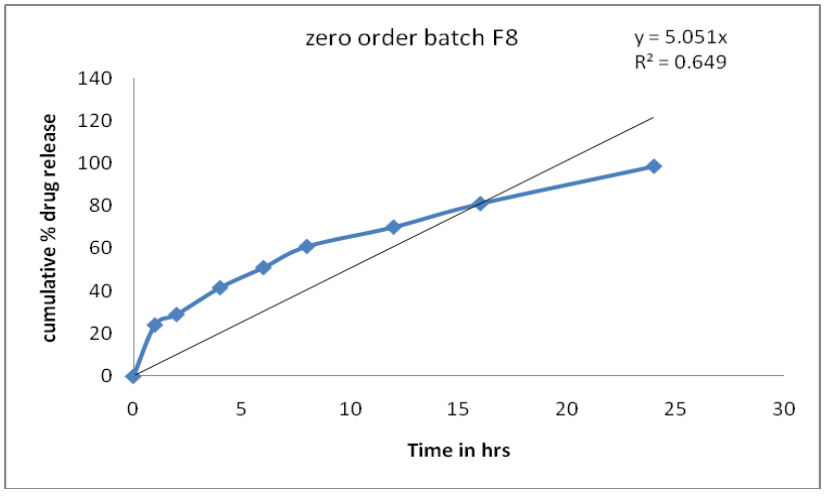

Figure. 2 Zero order plot (cumulative amount drug release vs. time)

The first order Equation which describes the release from systems where the release rate is concentration dependent, is illustrated by figure 3, shows the log cumulative percent drug remaining vs. time.

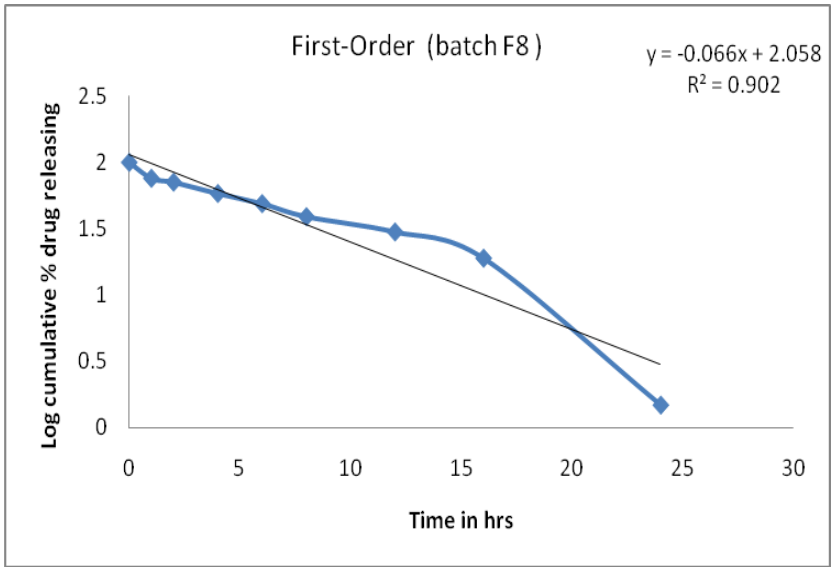

Figure: 3 First order plot (cumulative amount drug release vs. time)

CONCLUSION

Sustained release tablet formulated by using HPMC as release retardant, two grades of HPMC that are HPMC K4M and HPMC K100M selected, PVP-K30 Selected As Binder. Batch F1 and F2 Increases the binder concentration to increase hardness and pass the friability test. Various trial batches are taken to get sustained release profile for 24 hr by addition of HPMC K4M and HPMC K100M extragranular to intragranular ratio. Batch F7 give maximum release 97.0% in 24 hr is selected as batch in formulation of sustained release tablet. Batch F8 formulate as sustained release tablet which shows 24.10 % of drug release in 1 hr and 98. % drug release in 24 hr is selected as optimized batch of sustained release tablet formulation.

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Conflict of interest

The authors of this study declare that there is no conflict of interest in present research work.

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