

Design and *In vitro* Evaluation of a Novel Sustained Release Double Layered Tablets of Lornoxicam by using semi synthetic polymers

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ABSTRACT

The objective of the present study was to develop double layered tablets of lornoxicam, a highly potent non-steroidal anti-inflammatory drug. Double layered tablets comprised of fast release layer and a sustained release layer, anticipating the rapid drug release that starts in the stomach rapidly alleviate the symptoms and continuous in the intestine to maintain the prolonged analgesic effect. Double layered tablets are characterized by initial drug release in the stomach and comply the requirements of sustained release portion of the dosage form. An inclusion complex of lornoxicam with β -cyclodextrin at 1:2 (drug: β -CD) molar ratio, was incorporated in the fast release layer to increase the release rate of lornoxicam in the stomach to produce rapid analgesic effect. Hydroxy propyl methyl cellulose (HPMC), a hydrophilic matrix forming agent, was integrated in the sustained release layer to provide the sustainment of drug release, F2 was selected as the best formulation as it fulfilled all the criteria. The drug release of F2 extended up to 12 h period. Based on the statistical analysis the drug release follows Anomalous diffusion mechanism. Two months of short term stability study were carried out at $30 \pm 2^\circ\text{C} / 65 \pm 5\% \text{RH}$ and $40 \pm 2^\circ\text{C} / 75 \pm 5\% \text{RH}$ for the best selected formulation. The results showed that there were no significant changes in all the parameters evaluated for the best formulation.

Key words: β -cyclodextrin, Double layered tablets, Lornoxicam, NSAID's, Sustained release.

INTRODUCTION

Lornoxicam is also known as chlortenoxicam, and belongs to oxamic group of non-steroidal anti-inflammatory drugs (NSAIDs).¹ Lornoxicam is highly potent anti-inflammatory and analgesic properties. It is widely used for the inflammation in patients with rheumatoid arthritis, osteoarthritis and symptomatic treatment of pain.² Moreover, lornoxicam shows efficacy in clinical management of preoperative and postoperative pain associated with gynecological, dental and orthopedic surgeries.³ However its usage is limited mainly because of its shorter half-life (4 h). Lornoxicam exhibits pH dependent solubility, it shows very poor solubility in acidic conditions (in stomach) and gets in contact with the stomach mucosa for a longer period of time and causes irritation and leads to ulceration. So to reduce the contact with stomach mucosa

lornoxicam was complexed with cyclodextrin and also it increases the solubility of lornoxicam.⁴

The layered tablet concept has been utilized to develop controlled-release formulations.⁵ Such a tablet is considered as a biphasic delivery system that is designed to release the drug at two different rates and is usually composed of a fast-release layer combined with single or double sustained-release layers.⁶ Generally, conventional controlled-release dosage forms delay the release of drugs and do not provide a rapid onset of action after oral administration. Hence, the layered tablets offer a pharmacokinetic advantage over conventional controlled-release dosage forms as the drug is quickly released from the fast-release layer leading to rapid rise of drug plasma concentration followed by continuation of drug release

Submission Date :15-03-2013

Revision Date :22-09-2014

Accepted Date :02-04-2015

DOI: 10.5530/ijper.49.4.5

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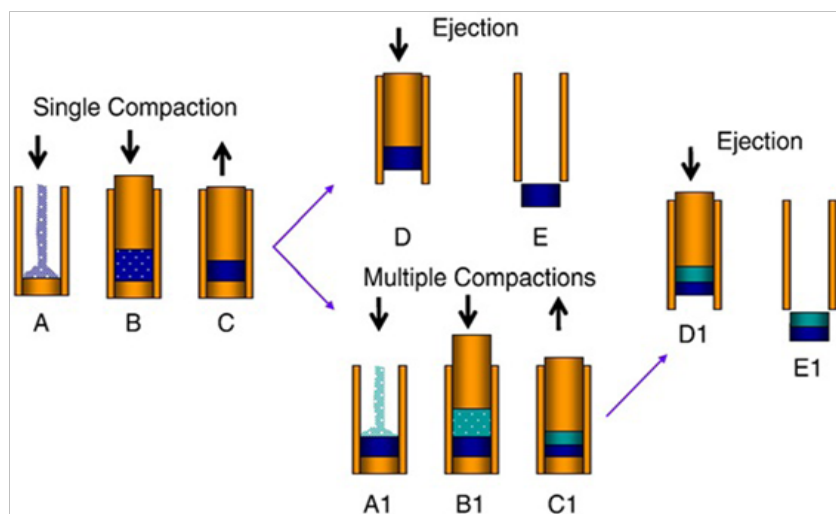
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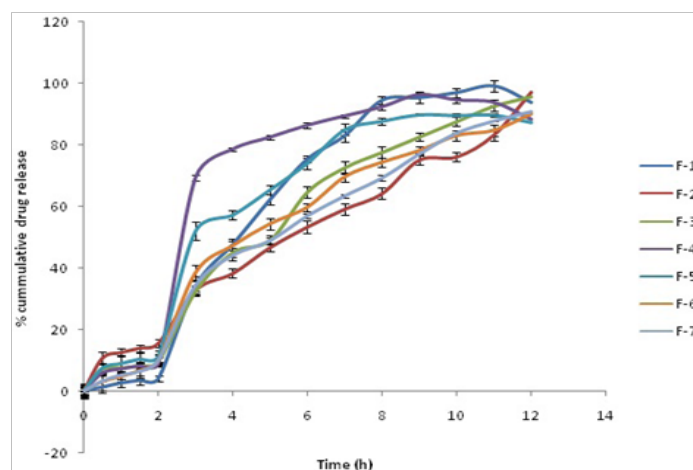
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Double layered tablets comprised of fast release layer and a sustained release layer, anticipating the rapid drug release that starts in the stomach rapidly alleviate the symptoms and continuous in the intestine to maintain the prolonged analgesic effect.



The drug release of F2 extended up to 12 h period. Based on the statistical analysis the drug release follows Anomalous diffusion mechanism.

Graphical Abstract

from the sustained release layer. This release pattern is required for successful treatment in many therapies, primarily when maximum relief needs to be achieved as soon as possible, and is followed by a sustained-release phase to avoid repeated drug administration. It is reported that the NSAIDs are suitable candidate drugs for this type of administration.⁷

Accordingly, the current study was undertaken to modify the release pattern of lornoxicam through its incorporation in an oral dosage form that is able to promptly release lornoxicam in a soluble form in the stomach with the aim to reaching high serum concentration in a short period of time, ensuring rapid palliative effect for the symptoms. This action is then followed by an extended release of lornoxicam for more than 12 h to avoid its repetitive administration.

Cyclodextrins (CDs) are a group of cyclic oligosaccharides, which have been investigated to improve the solubility and dissolution rate of various poorly soluble drugs. Moreover, CDs have been successfully employed to modify the release pattern of drugs in several modified release formulations. In addition, it has been reported that the local gastric irritation/ulceration associated with the oral use of NSAIDs is extensively reduced by averting their direct contact with the stomach wall through their entrapment and inclusion in the hydrophobic cavity of CDs.⁸ According to the aforementioned reasons, natural parent β -cyclodextrin (β -CD), were investigated for their suitability to be included in the fast-release layer of the DLTs. Hydroxy Propyl Methyl Cellulose (HPMC) was chosen as the candidate matrix-forming material to obtain suitable slow release of the drug from the sustained-release layer present in the prepared DLTs

Table 1: Formulation of the immediate release layer	
INGREDIENTS	QUANTITY TAKEN PER TABLET
Lornoxicam inclusion complex	13.33 mg \approx 4 mg of lornoxicam
Croscarmellose sodium	5 mg
Sodium carboxy methyl cellulose	5 mg
Magnesium stearate	2 mg
Lactose	qs to 100 mg

due to its biocompatibility, inertness,⁹ as well as its wide application as a sustained-release excipient.¹⁰

In order to reach the goal of this study, solid systems of lornoxicam with β -CD were prepared using different techniques, aiming to improve lornoxicam dissolution properties in acidic medium, as a primary step in development of DLTs.¹¹ The interaction between lornoxicam and the CD was investigated in solution state using phase solubility and in solid state using differential scanning calorimetry (DSC), and Fourier transform infrared spectroscopy (FTIR). Preliminary *in vitro* drug dissolution studies for the prepared solid systems were carried out in 0.1 N HCl to choose the solid system with superior dissolution characteristics to be incorporated into the fast-release layer present in the proposed DLTs. Matrix tablets containing different concentration grades of HPMC were initially prepared by wet granulation method.¹² Subsequently, their *in vitro* release behavior was investigated to select suitable concentrations of HPMC, which are capable of sustaining lornoxicam release, to be employed in the sustained-release layer of the designed DLTs. Finally, DLTs composed of different ratios of sustained-release layer to fast release layer were prepared by wet granulation method. and their physical properties and *in vitro* release behavior in simulated gastric and intestinal fluids used in sequence were evaluated.¹³

MATERIALS AND METHODS

Lornoxicam was received as a gift sample from FD&C Ltd; Roha R&D. HPMC (K4M, K15M, and K100M) was obtained as gift samples from colorcon, India. β -cyclodextrin, croscarmellose sodium was purchased from yarrow chem. Products, Mumbai. All other materials used were of the best possible laboratory reagents (LR) grade.

Preparation of inclusion complexation of lornoxicam with β -cyclodextrin

To improve the solubility and dissolution behavior of lornoxicam in gastric conditions, lornoxicam was com-

plexed with β -cyclodextrin in different stoichiometric ratios. Inclusion complex were prepared by using kneading method.

Kneading method

The stoichiometric amounts of lornoxicam and CD were accurately weighed, transferred into a glass mortar, and triturated with a small volume of water/ethanol. The obtained slurry was kneaded for 30 min and then dried under room temperature. Water/ethanol was used as wetting agent to attain better interaction of drug and CD during kneading process.

Physicochemical characterization of lornoxicam – CD complex

Differential Scanning Calorimetry

DSC was performed by using X. the apparatus was calibrated with pure indium (99.9%). Samples (4-5 mg) were placed in an aluminium pan and heated at a constant rate of 10°C/min in presence of nitrogen atmosphere in a temperature range of 20-400°C.

Solubility studies

The different stoichiometric ratios were subjected for solubility studies for 72 h by using Higuchi Corron's method. And the ratio which is showing the maximum solubility is selected as the best inclusion complex (2:8) is used for further research was given in (Table 1), (Figure 1).

Different stoichiometric ratios of inclusion complexes were prepared by kneading method and their dissolution studies were compared with the pure drug sample (Figure 2). The stoichiometric ratio of 2:8 inclusion complex shows better increased dissolution profile when compared with all the inclusion complexes and pure drug. Based on this data 2:8 inclusion complex was selected and it was used in fast release part of all the formulations of double layered tablet.

Formulation of double layered tablets of lornoxicam

Double layered tablets is considered as a biphasic drug delivery systems that is formulated in such a way that the drug is released at two different rates and is usually composed of conventional fast release layer and a sustained release layer.

Preparation of fast release layer

Lornoxicam- β -CD inclusion complex (2:8) was incorporated in the fast release layer. Along with this croscarmellose sodium is used as a super disintegrant, SCMC as binder, lactose as diluents, FDC No: 6 (sunset yellow) was used as coloring agent and magnesium stearate as lubricant. All the above mentioned ingredients was

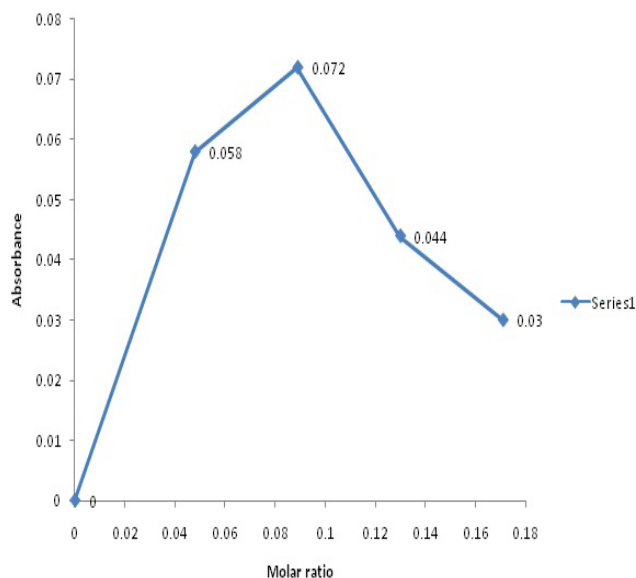


Figure 1: Solubility studies of different complexes

weighed accurately and mixed well for about 30 min (Table 1).

Preparation of sustained release layer

In the sustained release layer lornoxicam as such is used as active ingredient, along with this three different grades of HPMC (K4M, K15M, K100M) was used as a hydrophilic polymer and SCMC is used as a binder, lactose as diluent and magnesium stearate as lubricant. All the above mentioned ingredients were mixed and the granules were prepared by using SCMC as binder to form a damp mass. The damp mass was then passed through sieve # 12, the granules are dried at 50°C for 30 min. the dried granules were passed through sieve # 22 to obtain the uniform size of the granules. The dried granules are mixed with magnesium stearate for about 15 min (Table 2).

Characterization of granules

Prior to compression, the prepared granules were evaluated for their characteristic parameters, such as bulk density, tapped density, carr's index, angle of repose, hausner's ratio. Carr's compress ability index was calculated from the bulk and tapped densities using a digital tapped density apparatus (Electrolab Ltd, India) (Table 3, 4).

Compression of double layered tablets

Double layered tablets were prepared by using single head rotary tablet compression machine (Rimek, Karnataka). The sustained release granules were placed on the 9 mm die cavity and was pre-compressed and was then the die cavity was turned to the position, the immediate release granules were placed above the pre-compressed

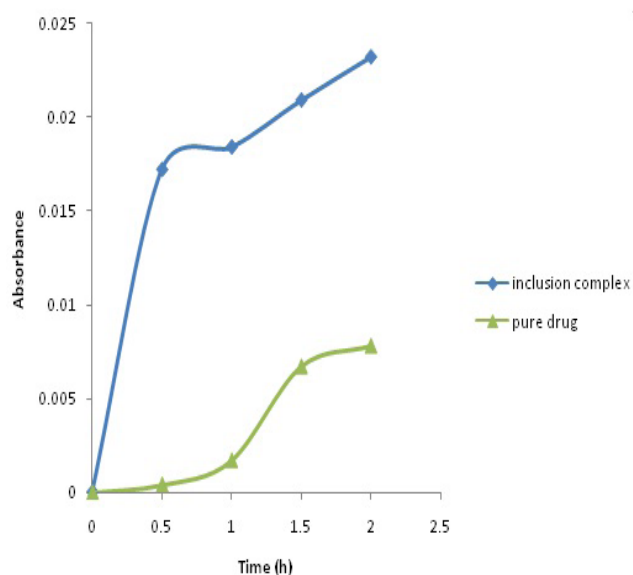


Figure 2: *In vitro* dissolution comparison of pure drug with inclusion complex

bed of sustained release granules and were subjected for full compression to obtain an intact double layered tablet. The hardness of the double layered tablet was adjusted to 4.5-6.76 kg/cm² (Figure 3).

Physical tests for double layered tablets

Standard physical tests for the double layered tablets were performed and average values were calculated along with their standard deviation. Weight variation was determined by weighing 20 tablets individually, the average weight was calculated and the percent variation of each tablet was calculated. Hardness was determined by taking 6 tablets from each formulation using a Monsanto hardness tester (Electro lab Ltd, India) and the average pressure (kg cm⁻²) applied for crushing the tablet was determined. Friability was determined by first weighing 10 tablets after dusting and placing them in the Roche's friability tester (Electro lab Ltd, India), which was rotated for 4 min at 25 rpm. After dusting, the total remaining mass of the tablets was recorded and the percent friability was calculated (Table 5).

Drug content uniformity

Ten tablets were finely powdered and an amount equivalent to 12.3 mg of lornoxicam was accurately weighed and transferred into 25 ml volumetric flask, then 20 ml of 6.8 buffer was added. The flask was shaken and sonicated for 10 min. finally the volume was made with 6.8 buffer. The mixture was then filtered and 1 ml of the filtrate was suitably diluted to obtain a solution containing 10 mcg/ml of lornoxicam and analysed for lornoxicam content at 376 nm using a double beam UV/

Table 2: Formulation of the sustained release layer

INGREDIENTS	F-1	F-2	F-3	F-4	F-5	F-6	F-7
Lornoxicam	8.3	8.3	8.3	8.3	8.3	8.3	8.3
HPMC K4M	49.95	150	-	-	25.05	25.05	-
HPMC K15M	49.95	-	150	-	25.05	-	25.05
HPMC K100M	49.95	-	-	150	-	25.05	25.05
Sodium carboxy methyl cellulose	6	6	6	6	6	6	6
Magnesium stearate	4	4	4	4	4	4	4
Lactose (qs)	200	200	200	200	200	200	200

Table 3: Micromeritic properties of immediate release granules

Formulation code	Angle of repose (°) ± SD	Bulk density(gm/ml) ± SD	Tapped density(gm/ml) ± SD	Carr's index (%) ± SD	Hausner's ratio ± SD
F-1	35.39 ± 3.2	0.39 ± 0.02	0.45 ± 0.06	13.07 ± 2.6	1.15 ± 0.07
F-2	24.42 ± 2.2	0.38 ± 0.03	0.45 ± 0.08	14.98 ± 0.4	1.17 ± 0.03
F-3	24.09 ± 1.8	0.38 ± 0.02	0.43 ± 0.04	14.11 ± 1.4	1.13 ± 0.03
F-4	26.32 ± 0.8	0.37 ± 0.04	0.41 ± 0.05	9.82 ± 1.3	1.11 ± 0.01
F-5	25.88 ± 0.9	0.41 ± 0.01	0.45 ± 0.04	8.89 ± 1.0	1.09 ± 0.02
F-6	26.91 ± 1.2	0.41 ± 0.03	0.45 ± 0.04	9.98 ± 2.1	1.10 ± 0.02
F-7	12.04 ± 0.4	0.37 ± 0.04	0.42 ± 0.04	11.28 ± 2.7	1.13 ± 0.01

Table 4: Micromeritic properties of sustained release granules

Formulation code	Angle of repose(°) ± SD	Bulk density(gm/ml) ± SD	Tapped density(gm/ml) ± SD	Carr's index(%) ± SD	Hausner's ratio ± SD
F-1	24.75 ± 0.16	0.39 ± 0.01	0.45 ± 0.03	15.31 ± 1.14	1.15 ± 0.02
F-2	26.82 ± 1.15	0.49 ± 0.03	0.55 ± 0.05	10.62 ± 0.89	1.11 ± 0.30
F-3	21.30 ± 0.51	0.42 ± 0.03	0.44 ± 0.02	14.86 ± 1.35	1.05 ± 0.03
F-4	27.10 ± 0.44	0.39 ± 0.09	0.43 ± 0.04	18.61 ± 1.78	1.14 ± 0.01
F-5	30.27 ± 0.50	0.41 ± 0.10	0.43 ± 0.12	15.28 ± 1.39	1.06 ± 0.02
F-6	26.25 ± 0.62	0.44 ± 0.02	0.46 ± 0.18	15.03 ± 2.75	1.05 ± 0.03
F-7	24.77 ± 0.76	0.38 ± 0.04	0.45 ± 0.09	14.48 ± 1.14	1.17 ± 0.07

Visible spectrophotometer (Shimadzu-1700, Japan) and 6.8 buffer as blank solution.

In vitro dissolution

Release of lornoxicam was performed by using a USP II six stage dissolution apparatus (Labindia Instruments Pvt Ltd, India) at 50 rpm. The dissolution was studied using 200 ml of simulated gastric fluid (pH 1.2 buffer without enzymes) for first 2 h and followed by addition of 400 ml of 0.2 M trisodium phosphate phosphate solution to raise the pH to 6.8 for the remaining hours. The temperature was maintained at $37 \pm 2^\circ\text{C}$. the sample 1 ml was withdrawn at different time intervals, i.e 30, 60,90,120,180,240, 300, 360, 420, 480, 540, 600, 660, 720 min respectively, and equal volume was replaced with

dissolution medium. Samples were suitably diluted and analysed for lornoxicam content at 376 nm (Table 6).

RESULTS AND DISCUSSION

Drug polymer compatibility study

The drug polymer compatibility studs and analytical investigation of drug by using FTIR and DSC studies showed that there is no interaction between drug and polymer. So, the drug and polymer are compatible (Figure 4, 5).

Preformulation studies

Estimation of lornoxicam was carried out by SHIMADZU-1700 UV spectrophotometer at λ_{max} 376 nm 0.1N NaOH solution. The linear coefficients of each

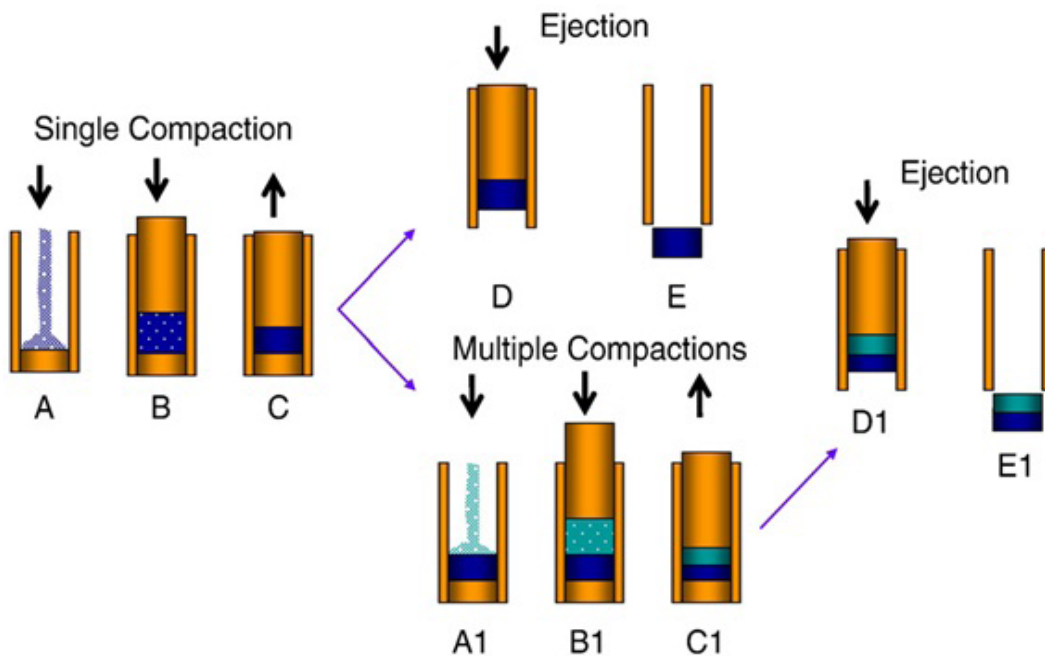


Figure 3: Pictorial representation to prepare double layered tablets

Table 5: physicochemical properties of double layered tablets

Formulation code	Thickness (mm) ± SD	Hardness (kg/mm ²) ± SD	Friability (% loss)	Weight variation (mg) ± SD	Separation of two layers (min)	Drug content (%)
F1	4.18 ± 0.1	7.16 ± 0.42	0.32 ± 0.05	296.20 ± 1.66	21	97.56 ± 1.03
F2	4.20 ± 0.15	6.56 ± 0.11	0.37 ± 0.11	298.68 ± 0.82	17	99.18 ± 0.89
F3	4.18 ± 0.15	7.60 ± 0.34	0.25 ± 0.05	296.95 ± 1.06	17.6	100.16 ± 0.68
F4	4.20 ± 0.20	5.70 ± 0.30	0.49 ± 0.08	299.2 ± 0.74	4.30	103.57 ± 2.19
F5	4.14 ± 0.25	5.86 ± 0.14	0.32 ± 0.10	294.3 ± 1.32	3.11	99.19 ± 0.89
F6	3.72 ± 0.05	6.16 ± 0.56	0.21 ± 0.13	295.24 ± 1.21	5.47	97.56 ± 1.86
F7	4.56 ± 0.11	4.56 ± 0.04	0.22 ± 0.05	299.33 ± 0.69	3.37	102.4 ± 1.17

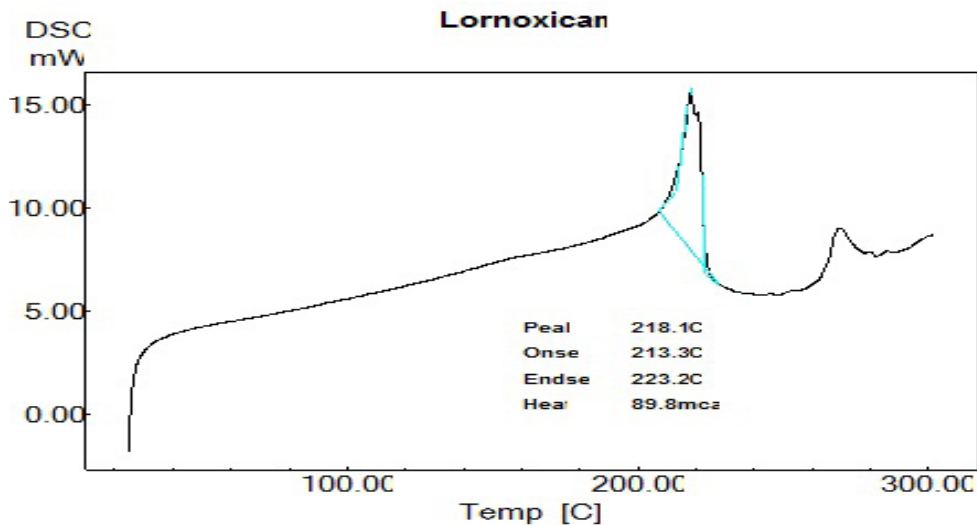


Figure 4: DSC graph of pure drug

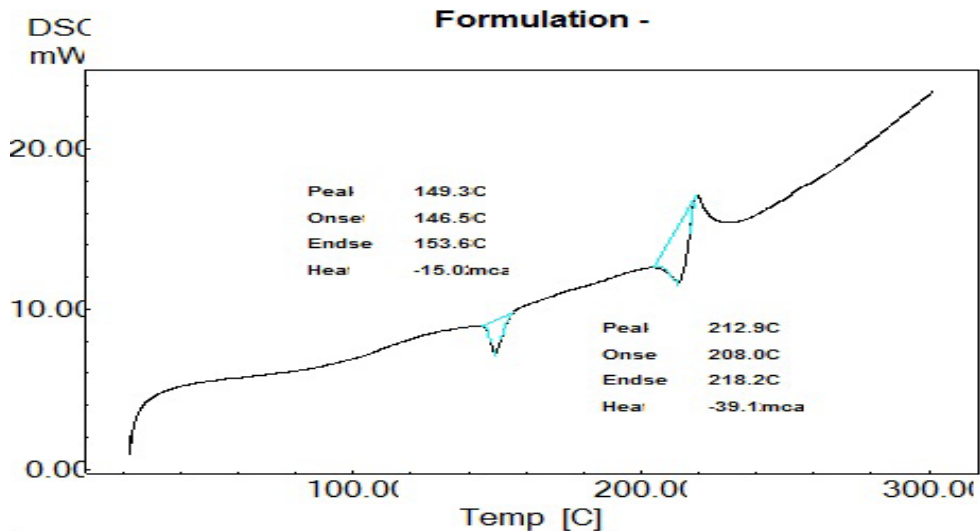


Figure 5: DSC graph of optimized formulation

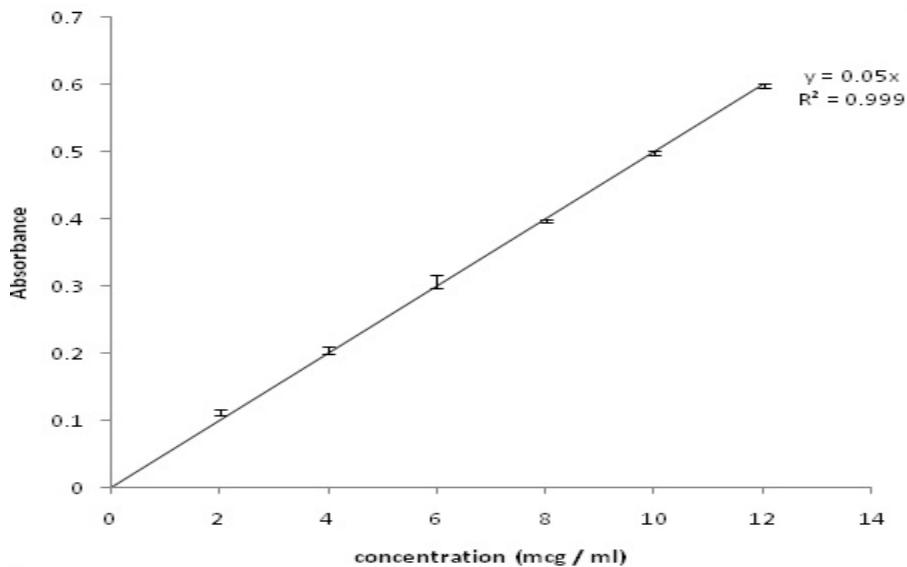


Figure 6: Calibration curve of lornoxicam

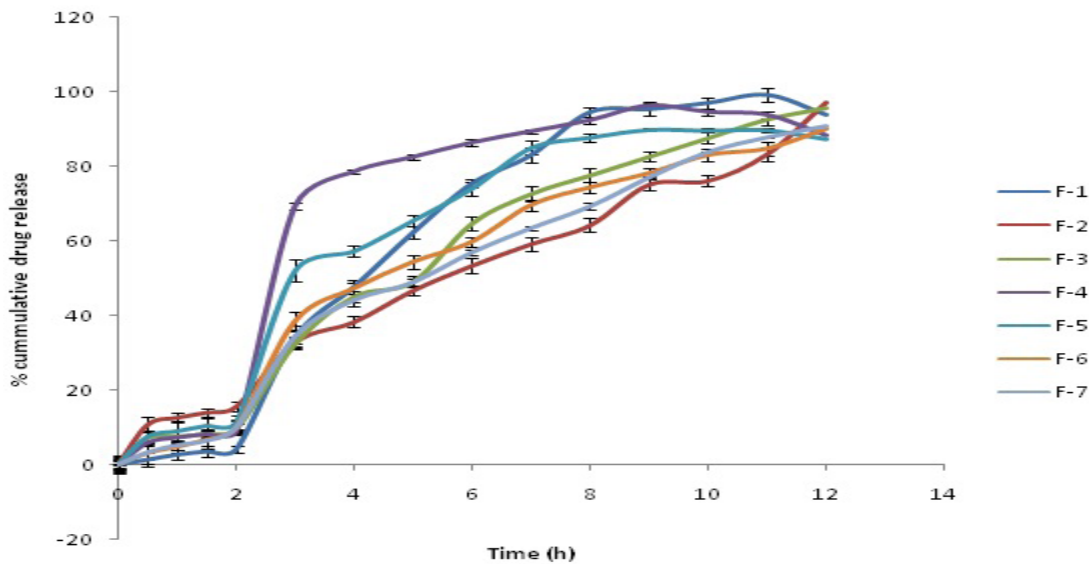


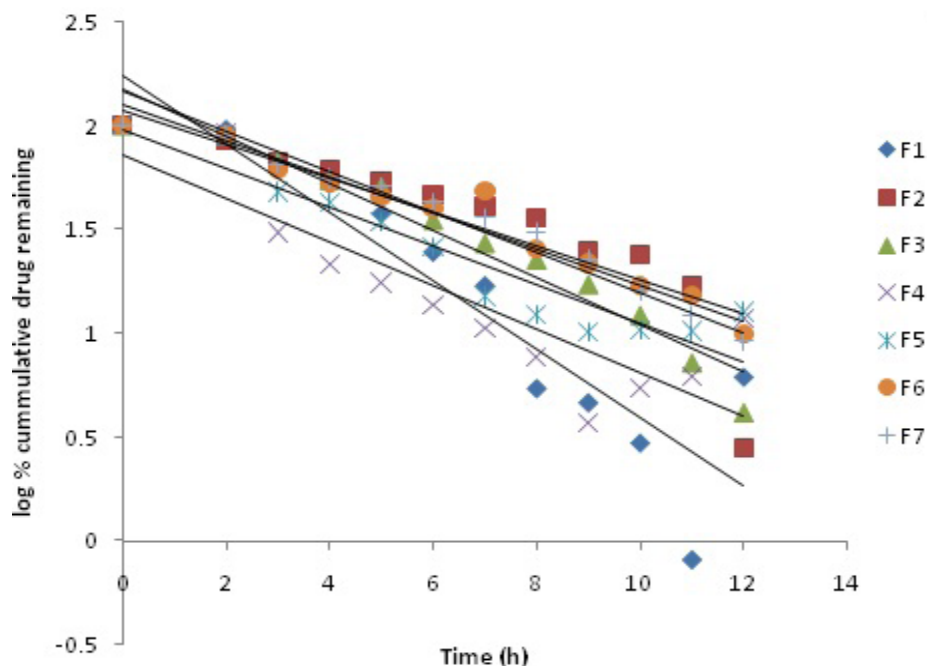
Figure 7: Graph of *in vitro* release studies

Table 6: *in vitro* release studies

Time (h)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	F7 (%)
0	0	0	0	0	0	0	0
0.5	1.34 ± 1.54	10.71 ± 1.23	7.18 ± 0.48	5.9 ± 0.17	7.52 ± 1.88	3.12 ± 1.11	3.29 ± 2.38
1	2.68 ± 1.89	12.57 ± 1.98	7.54 ± 0.87	7.28 ± 0.29	8.96 ± 1.65	4.81 ± 2.89	5.22 ± 1.86
1.5	3.54 ± 1.39	13.95 ± 1.39	8.23 ± 0.35	8.27 ± 0.76	10.41 ± 2.89	6.74 ± 1.09	6.42 ± 2.09
2	4.06 ± 1.32	15.51 ± 1.01	9.57 ± 0.89	8.94 ± 0.75	11.25 ± 2.11	9.89 ± 2.79	9.96 ± 1.98
3	34.11 ± 1.09	32.77 ± 1.22	32.36 ± 0.12	69.34 ± 0.36	51.98 ± 2.01	38.48 ± 1.79	34.36 ± 2.05
4	47.69 ± 1.78	38.25 ± 1.39	45.09 ± 0.01	78.57 ± 0.76	57.24 ± 2.99	47.26 ± 2.30	44.06 ± 2.78
5	62.29 ± 1.76	46.68 ± 1.49	49.07 ± 0.79	82.48 ± 0.66	65.45 ± 1.56	54.35 ± 1.35	48.90 ± 1.78
6	75.42 ± 1.59	53.36 ± 1.37	64.76 ± 1.87	86.35 ± 0.87	74.06 ± 1.45	59.75 ± 1.89	56.90 ± 0.98
7	83.05 ± 1.26	59.16 ± 1.93	72.67 ± 1.40	89.36 ± 0.78	84.93 ± 1.87	69.57 ± 1.27	63.38 ± 0.60
8	94.59 ± 1.89	64.18 ± 1.87	77.67 ± 1.58	92.34 ± 0.54	87.71 ± 1.88	74.29 ± 1.39	69.21 ± 0.68
9	95.37 ± 1.27	75.13 ± 1.89	82.68 ± 1.20	96.27 ± 0.79	89.81 ± 0.97	78.12 ± 1.49	76.96 ± 0.98
10	97.03 ± 1.76	76.13 ± 1.43	87.69 ± 1.62	94.54 ± 0.65	89.57 ± 0.33	82.95 ± 1.57	83.77 ± 0.18
11	99.19 ± 1.52	83.26 ± 1.56	92.71 ± 1.98	93.75 ± 0.78	89.71 ± 0.54	84.69 ± 1.76	87.72 ± 0.03
12	93.85 ± 1.78	97.19 ± 1.88	95.79 ± 1.73	88.24 ± 0.99	87.33 ± 0.38	89.94 ± 2.02	90.73 ± 0.11

Table 7: Kinetic modeling data

Formulation code	Zero order (r ²)	First order (r ²)	Higuchi (r ²)	Peppas	
				(r ²)	(n)
F1	0.847	0.911	0.935	0.907	0.755
F2	0.949	0.987	0.999	0.999	0.762
F3	0.764	0.963	0.962	0.975	0.778
F4	0.763	0.746	0.868	0.805	0.196
F5	0.900	0.860	0.957	0.908	0.431
F6	0.950	0.939	0.947	0.991	0.611
F7	0.966	0.967	0.974	0.996	0.705

**Figure 8: Graph of first order kinetics**

were found closer to 1. By using the regression coefficient equation the assay and % CDR were calculated (Figure 6).

UV spectrum analysis of lornoxicam

At the outset, method for the estimation for the drug was developed. Lornoxicam showed maximum absorption at wavelength 376 nm in 0.1N NaOH solution. Standard calibration curve obeyed Beer's law at given concentration range of 2 µg/ml to 12 µg/ml and when subjected to regression analysis, the value of regression coefficient was found to be 0.999, which showed linear relationship between concentration and absorbance.

Micrometric properties of granules

Angle of repose

The results of angle of repose were ranged between $21.30^\circ \pm 0.51$ to $30.27^\circ \pm 0.50$ which indicates good flow properties of powder.

Compressibility index

The results of angle of repose were ranged between $21.30^\circ \pm 0.51$ to $30.27^\circ \pm 0.50$ which indicates good flow properties of powder.

EVALUATION OF PHYSICO-CHEMICAL PARAMETERS

Tablet Hardness

Hardness of the developed formulations F1 to F7 varied from 4.56 ± 0.04 to 7.6 ± 0.34 kg/cm² in all the formulation indicating good mechanical strength with an ability to withstand physical and mechanical stress condition while handling.

Tablet Thickness

Thickness of the developed formulations F1 to F7 varied from 3.72 ± 0.05 mm to 4.56 ± 0.11 mm in all the formulation and the average thickness is within the range of $\pm 5\%$. Each sample was analyzed in triplicate.

Friability

The loss in total weight of the tablets due to friability was in the range of $0.21 \pm 0.13\%$ to $0.49 \pm 0.08\%$ in all the formulation and the friability value is less than 1% which ensures that formulated tablets were mechanically stable.

Weight variation

The maximum % deviation was found to be $\pm 2.19\%$ from all the formulations. As none of the formulation showed a deviation of more than $\pm 5\%$ (I.P. limit) for any of the tablets tested, the prepared formulations comply with the weight variation test, thus it fulfills the I.P. requirements.

Uniformity of drug content

The drug content in different tablet formulations was highly uniform and in the range of $97.56 \pm 1.86\%$ to $103.57 \pm 2.19\%$. The maximum % drug content for all the formulation was found to be $103.57 \pm 2.19\%$. The minimum % drug content for all the formulation was found to be $97.56 \pm 1.86\%$. It is in the limits specified by IP (i.e. $\pm 10\%$).

In vitro drug release studies

The release of lornoxicam from double layered tablets varied according to the types and proportion of matrix forming polymers.

Ideally, a double layered tablet should release the required quantity of drug in order to maintain an effective drug plasma concentration. From *in vitro* drug dissolution profile of lornoxicam double layered tablet, it was found that $15.51 \pm 1.01\%$ of the drug was released till 2 h from F2 formulation. During 2 to 8 h the marked percentage release was found to be 65%. After 8 h the release rate decreased slightly and a sustained release pattern was observed for 12 h. The hydrophilic matrix of HPMC controlled the lornoxicam release effectively for 12 h. It was observed that formulation (F2) showed high drug release rates in the range of $97.19 \pm 1.88\%$. (Figure 7), (Table 6).

KINETIC MODELING OF DRUG DISSOLUTION PROFILES

The *in vitro* release data obtained were fitted into various kinetic models. Correlation coefficients of formulation F2 batch showed higher correlation with First order plots than zero order plots, Higuchi and Peppas were also calculated and the 'n' value was found to be 0.762. So, predominant drug release mechanism is Anomalous diffusion (Table 7), (Figure 8, 9,10).

Stability data

Stability studies were carried out of the most satisfactory formulation F2, at $30 \pm 2^\circ\text{C} / 65 \pm 5\%$ RH and $40 \pm 2^\circ\text{C} / 75 \pm 5\%$ RH for two months to assess their short term stability as per ICH guidelines.

CONCLUSION

Various formulations were developed by using release rate controlling and gel forming polymers like HPMC (K4M, K15M, K100M) by wet granulation method. Different proportion of HPMC was associated with decrease in the overall cumulative drug release rate. The higher viscosity polymer had been seen to inhibit the initial burst release of lornoxicam. Thus, we conclude that from among all the developed formulations, F2 for-

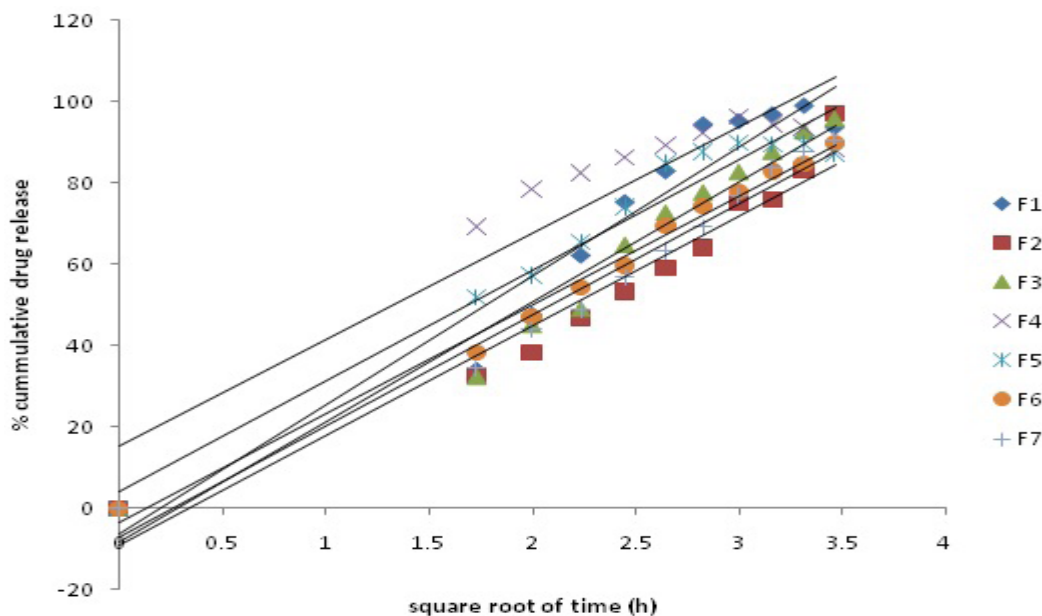


Figure 9: Graph of Higuchi plot

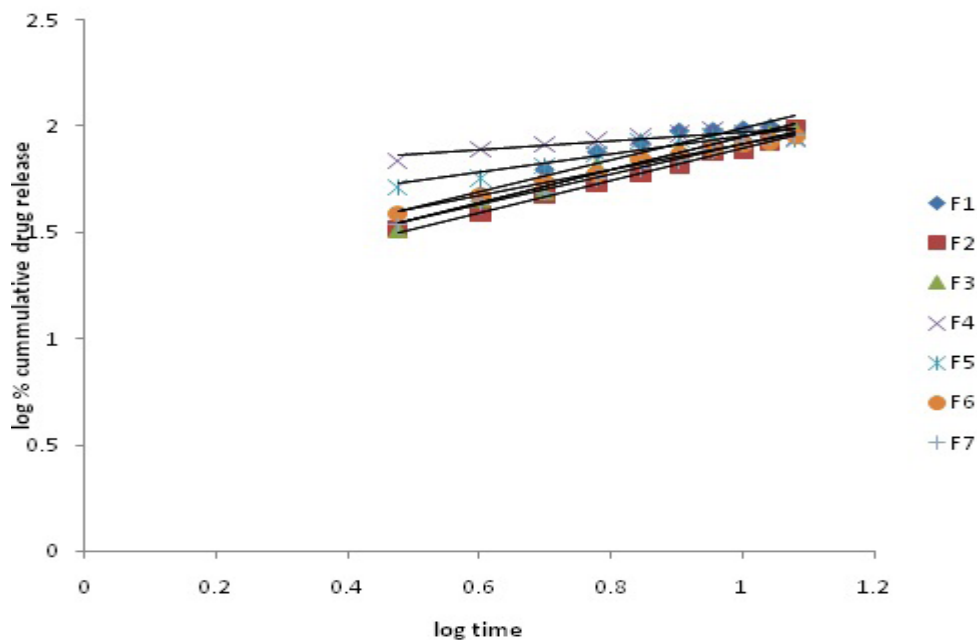


Figure 10: Graph of Peppas plot

mulation sustained the drug release for longer period of time over 12 h when compare to other formulations. So, F2 was selected as the best formulation which has HPMC K4M as a polymer.

ACKNOWLEDGEMENT

The authors wish to thank Acharya & BM Reddy College of Pharmacy for providing necessary facilities to carry out the research work. The authors are also thank-

ful to Vision Group of Science & Technology, Ministry of IT, BT & ST, Govt. of Karnataka for their support.

Highlights of Paper

- The layered tablet concept has been designed to release the drug at two different rates and is usually composed of a fast-release layer combined with single or double sustained-release layers.
- Various formulations were developed by using release rate controlling and gel forming polymers like HPMC (K4M, K15M, K100M) by wet granulation method.
- The higher viscosity polymer had been seen to inhibit the initial burst release of lornoxicam.
- The release of lornoxicam from double layered tablets varied according to the types and proportion of matrix forming polymers.

Author Profile

- **Dr Shivanand Kalyanappa:** Presently working as Associate Professor in Department of Pharmaceutics, Acharya & BM Reddy College of Pharmacy Bangalore. He has 16 Nos of Research Paper, Presented 6 No of Poster presentation in national conferences; successfully conducted AICTE Sponsored Staff Development Programme, also having two projects from AICTE MODROF and VGST K-Fist L1.
- **Dr Divakar Goli:** Presently Working as Principal Acharya & BM Reddy College of Pharmacy Bangalore. He has published more than 100 research papers, presented papers in national and international conferences, received best principal award from APTI in 2013, also received IPA Fellowship award in 2012 from Indian Pharmaceutical Association. He also having number of projects from AICTE.
- **Muppa RamKrishna:** Completed M. Pharmacy from Acharya & BM Reddy College of Pharmacy Bangalore. Worked in Geltec pvt ltd Bangalore duration 6 months and Microlabs ltd GOA duration 2 years. Presently working in Optimus generics Hyderabad.

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