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FORMULATION AND EVALUATION OF pH DEPENDENT COLON SPECIFIC PULSATILE DRUG DELIVERY SYSTEM OF LORNOXICAM

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ABSTRACT

Chronotherapeutics is the purposeful delivery of medications in unequal amounts over time during 24 hours. Rheumatoid arthritis (RA) is an autoimmune disease that follow rhythmic pattern. In the present study attempt has been made to design an oral site-specific, pulsatile drug delivery system containing Lornoxicam. The core tablet containing Lornoxicam(4mg) was prepared by direct compression method using 2 different polymers HPMC E15, HPMC E50 and other excepients. The core tablets were then coated with pH sensitive polymer Eudragit L100 and subjected to *in vitro* drug release studies and lag time. From the *in vitro* release it was observed that with all formulations, there was absolutely no drug release in simulated gastric fluid (0.1 N Hcl) for 2 hours and complete drug release was observed after lag time. The optimized formulation (F12) comprising 20mg of HPMC E50 showed a desired lag time of 5.5 hrs, which mimics the fluctuating symptoms of rheumatoid arthritis, followed by rapid release of lornoxicam.

Key words: Chronotherapeutics, Rheumatoid arthritis, Autoimmune disease, Lag time, invitro drug release.

INTRODUCTION

CHRONOBIOLOGY: Time is a component of a measuring system used to sequence events, to compare the duration of events and the interval between them, and to quantify the motion of objects. Every event in life depends on time. It is not possible to imagine the life we are leading without the invention of the concept of time. Time brings regulation in our life and unless we regulate ourselves we are no able to do anything [1].

BIOLOGICAL RHYTHMS: The study of biological rhythms and their mechanisms is known as chronobiology. They are regulated by sunlight. There are three types of mechanical rhythms in our body [2,3].

1. Ultradian
2. Infradian
3. Circadian

1. Ultradian rhythms: They are the rhythms that have a period of shorter than 24 hours.

2. Infradian rhythms: They are the rhythms which have a frequency ranging from 28 hours to 6 days.

3. Circadian rhythms: The term "circadian", coined by Franz Halberd, comes from the Latin circa, "around", and diem of dies, "day", meaning literally "approximately one day".

Our body appears to be genetically programmed to function on roughly a 24-hour cycle. These rhythms allow organisms to anticipate and prepare for precise and regular environmental changes. They are important in determining the sleeping and feeding patterns of animals including human beings. There are clear patterns of core body temperature, brain wave activity, hormone production, and other biological activities linked to this cycle. Some people function best in the morning while others have their peak in the noon or evening. If our normal rhythm is disrupted we tend to become anxious. E.g. many people have difficulty in adjusting to swing-shift work schedules. e.g. in sleep wake cycle an animal will settle into a 24 hour cycle activity and sleep even if deprived of light. Diurnal

blood pressure fluctuations are super imposed by a 24-hour rhythm with lower levels during the night and higher in the day[4-6].

CHRONOTHERAPEUTICS: It is the purposeful delivery of medications in unequal amounts over time during 24 hours Chronotherapeutics takes into account rhythm determinants in disease pathophysiology, chronopharmacology of medications, dose and administration time to optimise desired/ minimise adverse effects[7,8].

Chronotherapeutics does not involve only new medicines but also the improved applications of established once in a different and more biologically efficient manner. In certain instances, chronotherapeutics may be achieved by unequal morning and evening dosing schedules of sustained release 12 hours medication systems, better timing of conventional once a day medication/delivery systems, or application of special tablet and capsule formulations dosed at designated times to proportion medications over 24 hours in synchrony with rhythm determined requirements. The current first generation, drug delivery systems used in chronotherapeutics demands strict adherence by patients to recommended dosing time to achieve desired outcome[9].

"*The goal of chronotherapeutics is the management or reversal of existing acute or chronic medical conditions" & "Delivery of drugs to the body to the right site, at the right time, at optimal dose".*

Introduction to oral colon-specific drug delivery system: Dosage forms that deliver drugs into the colon rather than upper GIT offers number of advantages. Oral delivery of drugs to the colon is valuable in the treatment of diseases of colon (ulcerative colitis, Crohn's disease, carcinomas and infections) whereby high local concentration can be achieved while minimizing side effects that occur because of release of drugs in the upper GIT or unnecessary systemic absorption. The colon is attracting interest as a site where poorly absorbed drug molecule may have an improved bioavailability. This region of the colon is recognized as having a somewhat less hostile environment with less diversity and intensity of activity than the stomach and small intestine. Additionally, the colon has a longer retention time and appears highly responsive to agents that enhance the absorption of poorly absorbed drugs. Apart from retarding or targeting dosage forms, reliable colonic drug delivery could also be an important starting position for the colonic absorption of perorally applied, undigested, unchanged and fully active peptide drugs. The simplest method for targeting of drugs to the colon is to obtain slower release rates or longer release periods by the application of thicker layers of conventional enteric coatings or extremely slow releasing matrices[10-12].

Rheumatoid arthritis (**RA**) is an autoimmune disease that results in a chronic, systemic inflammatory disorder. It may affect many tissues and organs, but principally attacks flexible (synovial) joints. It can be a disabling and painful condition, which can lead to substantial loss of functioning and mobility if not adequately treated[13].

Treatment:

- ✓ NSAIDs reduce both pain and stiffness in those with RA.
- ✓ COX-2 inhibitors, such as celecoxib and NSAIDs are equally effective.
- ✓ Glucocorticoids can be used in the short term for flare-ups, while waiting for slow-onset drugs to take effect.
- ✓ **Surgery**: In early phases of the disease, an arthroscopic or open synovectomy may be performed. Severely affected joints may require joint replacement surgery, such as knee replacement [14].

Postoperatively, physiotherapy is always necessary.

MATERIALS AND METHODS:

Lornoxicam was collected as a gift sample from Inventia Health care Pvt. Ltd., Eudragit L-100 from Evonik India Pvt. Ltd. Mumbai, Mannitol. From SS Pharmaceuticals Pvt.Ltd and All other chemicals and solvents used were of analytical graded.

Preformulation Studies:

Identification of pure drug: Identification of Lornoxicam was carried out by FT-IR spectroscopy.

Melting point determination: Melting point of Lornoxicam was determined by Open capillary Method.

Drug - Excipient Compatibility Studies:

Compatibility of Lornoxicam with the respective polymers that is Eudragit L100 and HPMC E15, HPMC E50 and physical mixture of main formulation was established by Infrared Absorption Spectral Analysis (FTIR). Any changes in the chemical composition after combining with the excipients were investigated with IR spectra.

Analytical Method: Standard Calibration curve of Lornoxicam: Calibration curve of Lornoxicam was taken in 0.1 N NaOH.

Preparation of Standard Stock Solutions: Standard stock solution was prepared by dissolving 100 mg of drug in 100 mL of 0.1 N NaOH to get concentration of 1000 µg mL. The standard solution (1000 µg mL-1) was further diluted with 0.1N NaOH to obtain concentration range 5, 10, 15, 20, 25 and 30 µg mL respectively. All samples were analyzed by UV spectrophotometer by measuring the absorbance at 375 nm.

Preparation of core tablet: Tablets of Lornoxicam were made by direct compression method. All ingredients were weighed accurately and blended homogeneously for 15 minutes by trituration using glass mortar and pestle. Microcrystalline cellulose was used as direct compressing agent. Mannitol was used as diluents.starch was used as disintegrating agents Magnesium stearate and Talc were used as lubricants. Tablets were compressed in Minipress Tablet Compression Machine using 6mm punches.(Riddhi's minipress). The composition of core tablets is given in Table No.1.

EVALUATION OF CORE TABLETS:

Precompressional Studies:

Angle of repose:

The angle of repose of blend was determined by the funnel method. The accurately weight blendwas taken in the funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the blend. The blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose wascalculated using the following equation[15].

$$\tan Ø = h/r$$

Where, h and r are the height and radius of the powder cone

Bulk density and Tapped density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. A quantity of 2 gm of blend from each formula previously shaken to break any agglomerates formed was introduced in to 10 ml measuring cylinder. After that the initial volume was noted and the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted[16].

Compressibility Index: The Compressibility Index of the blend was determined by Carr's compressibility index. It is a simple test to evaluate the LBD and TBD of a powder and the rate at which it packed down[9].The formula for Carr's Index is as below:

Carr's Index (%) = [(TBD-LBD) x100]/TBD

Hausner's Ratio:

Hausner's Ratio was determined by Following Equation:

Hausner's Ratio = Tapped Density / Bulk Density

Post-Compressional Studies:

Shape and appearance: Tablets were examined under a lens for the shape of the tablet, and color wasobserved by keeping the tablets in light.

Uniformity of thickness: Thickness and diameter of both core tablets and coated tablets were measured using a calibrated dial calipers. Three tablets of each formulation were picked randomly and dimensions determined.

Weight variation test: Twenty tablets were selected randomly from each batch and weighed individually to check for weight variation.

Hardness test: Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. Hardness of core tablets was determined using a validated dial type hardness tester.It is expressed in kg/cm2. Three tablets were randomly picked from each batch and analyzed for hardness.

Friability test: For each pulse dose tablet formulation, the friability of 6 tablets was determined using the Roche friabilator[17-20].

***In vitro* Disintegration test for tablet:** Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 6.8 SIF (simulated intestinal fluid) and pH 7.4 SCF (simulated colonic fluid) maintained at 37 0C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 maintained at 37 0C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded. The experiment was carried out in triplicate.

Drug content: Ten tablets were weighed and average weight is calculated. All tablets were crushed and powder equivalent to 4 mg drug was dissolved in 4 ml of 0.1N NaOH. The volume was then made upto 100 ml with pH 6.8 phosphate buffer. The solution was shaken for 1 h and kept for 24 hrs. From the stock solution, 1 ml solution was taken in 10ml volumetric flask and the volume was made up with pH 6.8 phosphate buffer. Solution was then filtered and absorbance was measured spectrophotometrically at 375 nm against pH 6.8 phosphate buffer as a

blank. The amount of drug present in each tablet was then calculated

PREPARATION OF ENTERIC COATED TABLET:

Preparation of Coating Solution: Coating solution was made using PH sensitive polymer like Eudragit L100. Polymeric content in the coating solution was kept constant as 6.25%w/v. required quantity of polymer was dissolved in half of the quantity of mixture of solvents (acetone & isopropyl alcohol) and stirred on magnetic stirrer to get homogeneous coating solution. Added talc (3%) as anti-caking agent and Tri ethyl citrate (1%) as plasticizer to the remaining solvent mixture. Stirred for 10 min with high shear mixer and poured the excepient suspension slowly in to the Eudragit solution with stirring. After getting homogeneous coating solution, coating was done on tablets.
The process conditions were presented in table 2.

Lag time of coated tablets: Coated tablets were evaluated for lag time in pH 6.8 buffer respectively. Coated tablets were placed in 900 ml of above mentioned buffers, agitated at 50 rpm and maintained at 37±0.50C. The time taken for outer coating to rupture was monitored and reported as lag time.

Dissolution Studies of the Coated Tablets: Drug release studies of coated tablets were carried out using USP XXIII dissolution test apparatus. Initially tablets were placed in 900 ml of 0.1 N HCl for 2 hours maintained at 37±0.50C, 50 rpm followed by pH 6.8 phosphate buffer 12 hours. Aliquots of predetermined quantity were collected manually at definite time intervals replacing with fresh buffer to maintain sink condition and analysed for drug content using a UV-visible spectrophotometer at λ max of 375 nm.

Kinetic Analysis of Dissolution Data:
There are several linear and non-linear kinetic models to describe release mechanisms

- **Zero order kinetics**
- **First order kinetics**
- **Korsmeyer-Peppas model**
- **Higuchi model**

RESULTS AND DISCUSSION

PREFORMULATION STUDIES OF PURE DRUG:

Identification of Drug: The IR spectrum obtained of pure drug shows characteristic absorption peaks as given below depicted in table No.3.

Melting point determination: Melting point of Lornoxicam was found to be in the range of 220°C to 230°C with decomposition as reported in the pharmacopoeia, thus indicating purity of the drug sample.

Drug - excipient Compatibility Studies: Compatibility studies of pure drug Lornoxicam with and with polymers were carried out prior to the preparation of tablets. I.R spectra of pure drug Lornoxicam, and polymers were obtained, which are depicted in Figure No.1. All the characteristic peaks of Lornoxicam were present in spectra at respective wavelengths thus indicating compatibility between drug and polymers. It shows that there was no significant change in the chemical integrity of the drug.

Analytical Method: Lornoxicam standard is made as a solution 5 – 20 µg/ml (Beers range) of drug in pH 6.8 phosphate buffer at the maximum wavelength of 375nm. Figure No.2 shows the standard calibration curve for Lornoxicam with slope, intercept, and regression coefficient.

EVALUATION OF CORE TABLETS:

Precompressional parameters: Blend of formulation was subjected for precompressional evaluations such as angle of repose, bulk and tapped density, compressibility index and Hausner's Ratio. Results of the pre-compression parameters performed on the blend for batch F1 to F12 are tabulated in Table No.4. The results of angle of repose (<30) indicate good flow properties of the powder. This was further supported by lower compressibility index values.

Post-compressional parameters: The formulated tablets were subjected for evaluation according to official specifications for shape, thickness, hardness, friability, weight variation, drug content and *in vitro* disintegration time.

Physical appearance: Tablets were yellow in color, having concave surface with cylindrical shape.

Drug Content: The formulated tablets were assayed in triplicate. The average value and standard deviations were calculated. The results were within the limit (90% to 110%) as specified in pharmacopoeia. The cumulative percentage drug released from each tablet in the *in vitro* release studies was based on the average drug content present in the tablet (Table No.5).

***In vitro* Disintegration time:** *In vitro* disintegration time in different tablet formulations F1 to F12 was found to be in the range of 125 min to 184 min as tabulated in Table No.5. Batch F1 was considered as optimum formulation as it showed least disintegration time.

EVALUATION OF PULSATILE RELEASE TABLETS:

Lag time of coated tablets: From the preliminary study it was found that the polymers which are being selected in present study produced tablets with pulsatile release profile. The lag time of the tablets varied according to the grade of HPMC used and the concentration of HPMC used (Table No.6 and Fig.No.4)

***In vitro* drug release studies:** The release profile of Lornoxicam tablets varied according to the grade of HPMC used and the concentration of HPMC. Ideally, a pulsatile release tablet should release the required quantity of drug after the lag time in order to maintain an effective drug plasma concentration. From the *in vitro* drug dissolution profile of Lornoxicam tablet, it was found that the thickness of the swelling layer was the critical parameter which influenced the rupture of outer coating. The lag time of the tablet decreased with increasing concentration of HPMC. This is because higher amount of swelling layer absorbs water more rapidly thus creating pressure on outer Eudragit layer to get ruptured.It was observed that the formulations having least concentrations of HPMCE15(F7) and HPMC E50 (F12) had a lag time of 4.5 hrs and 5.5 hrs respectively and the formulations (F7-F12)where HPMC E 50 was used showed higher lag times than HPMC E15 formultions (F1-F6) as evident from Table No.7.

CONCLUSION

A satisfactory attempt was made to develop pH dependent colon specific, pulsatile drug delivery system of Lornoxicam to treat Rheumatoid Arthritis. Pulsatile release tablets were prepared using different polymers (HPMC E15, HPMC E50) and evaluated for *In vitro* characterization.

From the results obtained in the present study, it can be concluded that-

- From IR and physical observation it was observed that there was no significant Drug-Excipient interaction
- To achieve colonic delivery, core tablets were formulated with two different polymers (HPMC E15& E50) and coated using pH sensitive polymer (Eudragit L100) and evaluated for lag time and *in vitro* drug release.
- The lag time and *in vitro* drug release profile for all formulations at variable drug and polymer ratio indicated that lag time is indirectly proportional to the polymer level used
- The release profiles of drug from all formulations followed first order kinetics.
- Between two grades of polymers HPMC E50 provided the most appropriate polymer for pulsatile drug delivery.
- From this study it was concluded that a pH dependent pulsatile drug delivery of Lornoxicam has a lag time of 5.5 hours. Tablet is taken at bed time and expected to release the drug in early morning hours, when the symptoms of Rheumatoid arthritis are more prevalent.

Table No.1: Composition of Lornoxicam Core Tablet

Formulations	Drug (mg)	Mannitol (mg)	MCC (mg)	Starch (mg)	Mg Stearate(mg)	Talc (mg)	HPMC E15	HPMC E50
F1	4	160	120	81	5	10	120	-
F2	4	167	130	84	5	10	100	-
F3	4	167	150	84		10	80	-
F4	4	167	174	84	5	10	60	-
F5	4	180	177	80	5	10	40	-
F6	4	267	114	81	5	10	20	-
F7	4	160	120	81	5	10	-	120
F8	4	167	130	84	5	10	-	100
F9	4	167	150	84	5	10	-	80
F10	4	167	174	84	5	10	-	60
F11	4	180	177	80	5	10	-	40
F12	4	267	114	81	5	10	-	20

Table No.2: Process Conditions for Coating

PARAMETER	VALUE
Inlet temperature	40-45 0C
Exhaust temperature	30-35 0C
Spray rate	3-5 ml /min
Spray nozzle diameter	1 mm
Distance(Tablet bed-spray gun)	10 – 15 cm
Pan speed(RPM)	20

Table No.3: Characteristic Absorption peaks of Lornoxicam.

Groups	Peaks (cm^{-1})
-NH Stretching	3067 cm^{-1}
C=O Group	1646 cm^{-1}
1N-H Group	1597 cm^{-1}, 1559 cm^{-1}
O=S=O Group	1157 cm^{-1},1146 cm^{-1} ,1173 cm^{-1}
CH Stretching	829 cm^{-1}
C-Cl bending vibration	765 cm^{-1}

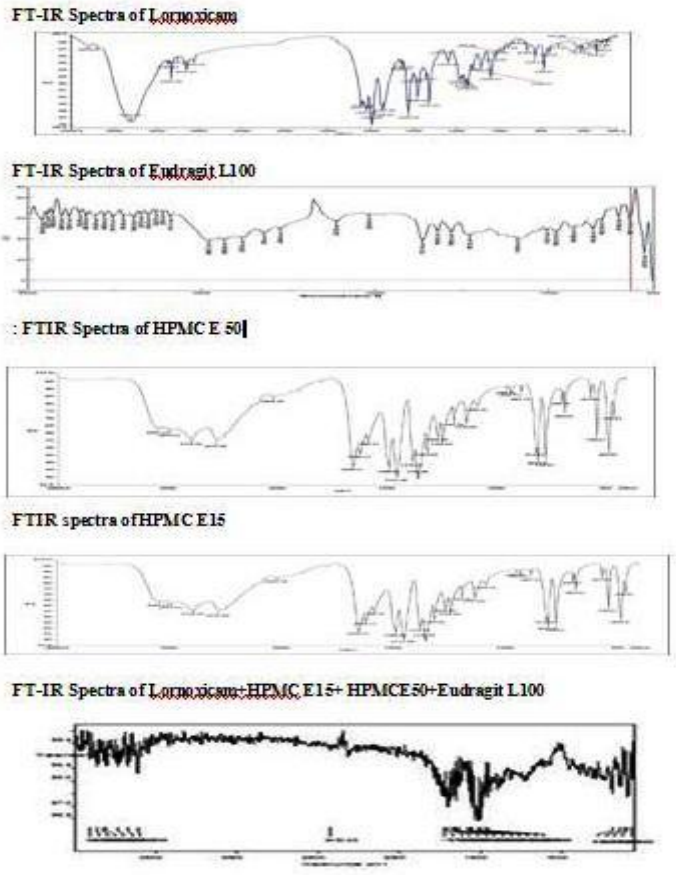

Fig.No.1: FTIR Spectra of Drug and excipients.

Table No.4: Pre-compression evaluation of the blend

Formulations	Bulkdensity(gm/cc) ±SD	Tapped density(gm/cc) ±SD	Angle of repose(±SD)	% carr's index(±SD)	Hausner's ratio
Lornoxicam	0.378±0.02	0.512±0.06	32.56±0.16	26±1.32	1.88±0.05
F1	0.658±0.04	0.734±0.04	26.96±1.39	10.34±1.16	1.45±0.15
F2	0.656±0.02	0.722±0.08	25.87±1.39	9.14±1.11	1.33±0.15
F2	0.699±0.04	0.776±0.05	21.83±1.13	22.2±1.78	1.65±0.19
F4	0.624±0.06	0.723±0.07	32.56±1.15	9.14±1.14	1.17±0.12
F5	0.614±0.02	0.789±0.08	26.96±0.18	22.2±1.78	1.15±0.16
F6	0.656±0.04	0.732±0.06	25.87±1.15	13.69±1.32	1.35±0.12
F7	0.719±0.22	0.722±0.05	21.97±1.16	22.21.78	1.65±0.19
F8	0.658±0.15	0.854±0.04	25.86±1.15	10.34±1.33	1.45±0.12
F9	0.621±0.06	0.744±0.06	21.43±0.39	12.78±1.15	1.83v0.11
F10	0.621±0.15	0.726±0.08	25.86±1.13	22.2±1.78	1.51±0.15
F11	0.668±0.01	0.723±0.06	21.43±1.39	14.36±1.45	1.88v0.05
F12	0.677±0.05	0.778±0.03	26.96±1.15	16.12±62	1.45±0.15
F13	0.624±0.06	0.689±0.06	32.86±1.13	18.23±1.34	1.33±0.15
F14	0.614±0.22	0.714±0.07	28.76±0.39	22.2±1.87	1.65±0.19
F15	0.719±0.03	0.739±0.03	26.76±0.16	10.67±1.45	1.17±0.12
F16	0.658±0.06	0.776±0.02	21.97±1.13	19.76±1.89	1.65±0.15

Table No.5: Post compression evaluation of prepared tablets

Formulations	Weight variation(mg) ±SD	Drug content(%)±SD	Hardness (kg/cm2) ±SD	Friability (%)±SD	Disintegration time (min) ±SD
F1	504.0±0.87	85.55±1.16	5.9±0.11	0.41±0.08	125±0.74
F2	506.8±1.03	79.83±2.23	5.7±0.45	0.53±0.11	130±0.12
F3	505.8±0.92	81.23±2.11	5.8±0.06	0.46±0.09	128±0.32
F4	505.8±1.55	80.79±2.16	5.6±0.12	0.53±0.05	151±0.12
F5	507.1±0.82	83.76±1.01	5.8±0.11	0.32±0.05	150±0.23
F6	507.0±0.87	84.63±1.11	6.0±0.06	0.44±0.08	180±0.23
F7	506.0±0.82	86.32±1.13	6.1±0.12	0.68±0.09	181±0.34
F8	509.1±155	82.72±1.12	5.8±0.67	0.34±0.05	161±0.43
F9	504.1±1.10	86.10±0.56	5.9±0.34	0.76±0.05	152±0.34
F10	505.1±0.74	84.70±0.88	6.2±0.13	0.60±0.05	184±0.46
F11	507.2±0.43	83.12±1.13	5.7±0.12	0.63±0.08	170±0.43
F12	505.6±0.67	86.22±0.76	6.1±0.23	0.78±0.03	168±0.12
F13	505.7±0.87	84.65±1.18	5.9±0.15	0.44±0.09	180±0.56
F14	505.0±0.82	85.98±1.14	6.2±0.45	0.32±0.05	171±0.45
F15	506.8±1.55	84.12±0.65	5.8±0.11	0.56±0.11	178±0.54
F16	506.8±1.03	83.43±1.16	6.0±0.06	0.56±0.06	180±0.23

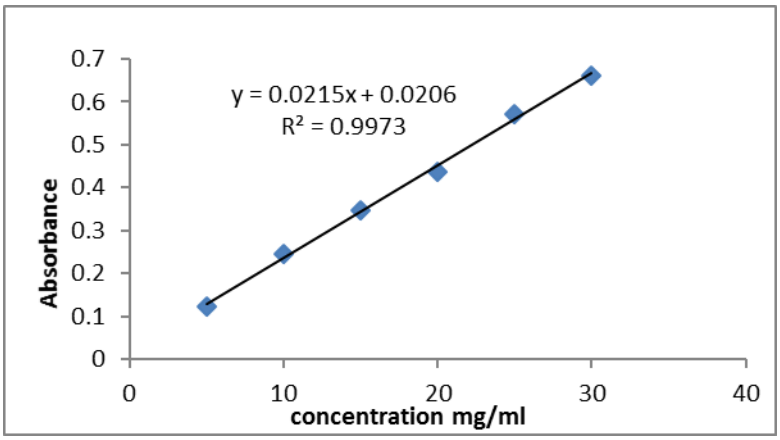

Figure No.2: Standard calibration curve of Lornoxicam in 0.1 N NaOH

Table No.6: Lag Time of all Formulations

FORMULATIONS	LAG TIME (HOURS)
F1	2.0
F2	2.5
F3	2.5
F4	2.5
F5	3
F6	4.5
F7	2.0
F8	2.5
F9	2.5
F10	3.0
F11	4.0
F12	5.5

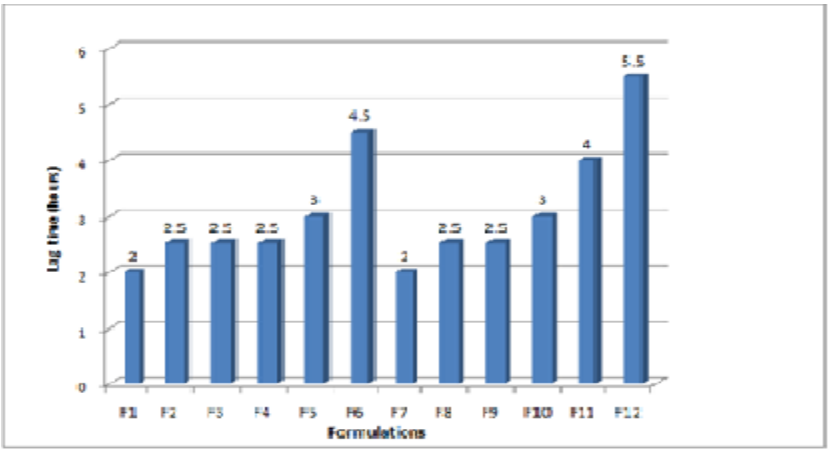

Figure No.4: Lag time of all Formulations

Table No.7: *In-vitro* drug release study of coated tablets (F1-F6)

Dissolution Medium	Time in (hours)	% Drug release					
		F1	F2	F3	F4	F5	F6
0.1 N HCl	0	0	0	0	0	0	0
	1	0	0	0	0	0	0
	2	0	0	0	0	0	0
6.8 pH Buffer	3	20.20	19.01	18.40	18.56	0	0
	4	24.56	28.30	28.56	27.41	16.60	0
	5	31.82	31.39	33.40	31.20	20.91	13.25
	6	35.26	36.78	38.42	37.43	26.27	23.65
	7	39.87	39.80	51.86	43.42	29.48	37.45
	8	42.48	42.78	54.20	48.48	31.56	44.23
	9	46.42	46.20	60.89	52.92	38.67	53.36
	10	59.84	57.58	63.23	57.20	40.82	66.51
	11	78.49	73.02	81.86	66.52	74.48	89.20
	12	98.20	84.21	95.02	81.05	96.90	94.80

Table No.8: *In-vitro drug* release study of coated tablets (F7-F12)

Dissolution Medium	Time in (hours)	% Drug release					
		F7	F8	F9	F10	F11	F12
0.1 N Hcl	0	0	0	0	0	0	0
	1	0	0	0	0	0	0
	2	0	0	0	0	0	0
6.8 pH buffer	3	23.29	22.34	16.23	0	0	0
	4	29.86	30.89	22.56	14.36	0	0
	5	32.95	40.23	26.98	21.67	21.23	0
	6	41.47	54.68	33.67	26.32	24.46	24.46
	7	46.79	60.12	41.37	32.45	30.36	40.91
	8	53.97	69.54	44.78	42.89	32.64	58.24
	9	59.86	74.65	52.65	54.78	37.85	64.86
	10	71.24	79.20	63.89	66.43	51.67	76.90
	11	78.67	84.34	70.56	72.34	62.56	87.45
	12	95.86	95.58	84.89	84.56	83.67	96.20

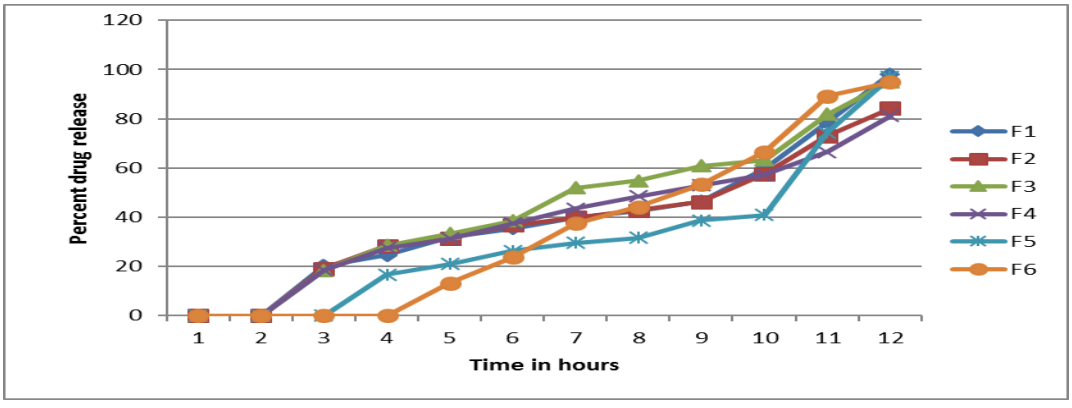

Figure No.5: Dissolution profile of pulsatile tablets of Lornoxicam usingHPMC E15

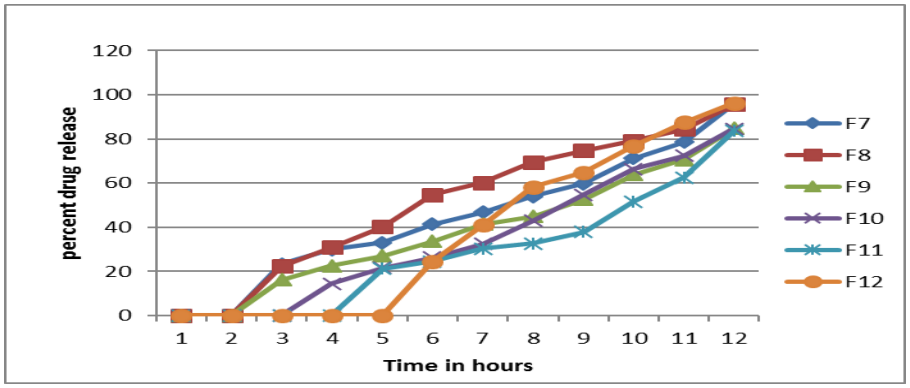

Figure No.6: Dissolution profile of pulsatile tablets of Lornoxicam using HPMC E50

Table No.9: Model fitting of release profile of formulated tablets using different models

Formulation code	Mathematical models	
	Zero order	First order
	Regression Coefficient (R Values)	Regression Coefficient (R Values)
F1	0.938	0.794
F2	0.942	0.743
F3	0.963	0.760
F4	0.966	0.772
F5	0.937	0.808
F6	0.886	0.863
F7	0.967	0.834
F8	0.971	0.711
F9	0.976	0.795
F10	0.933	0.942
F11	0.896	0.823
F12	0.829	0.805

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