International Journal of Biomedical and Advance Research
ISSN: 2229-3809 (Online); 2455-0558 (Print)
Journal DOI: 10.7439/ijbar
CODEN: IJBABN

Original Research Article

Design and Characterization of Controlled Release Lornoxicam Nanofibers by Electrospinning Technique

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Abstract

The objective of the present study was to prepare nanofibers of Lornoxicam by Electro spinning technique and to increase the drug bioavailability using different polymers such as PMMA, Ethyl Cellulose, Polyethylene oxide, Gelatin. Totally 15 different formulations of Lornoxicam were prepared by Electro spinning technique and prepared nanofibers are evaluated for various characteristics like drug content, in-vitro release studies, DSC, XRD and SEM studies. The dissolution profile of optimized formulation was compared with that of the API and the marketed product (Lofecam) and the Optimized formulation (F15) exhibited similar dissolution profiles as that of innovator brand. The drug release from the optimized formulation (F15) was slow and extended over a period of 8hrs and these nanofibers were found to be suitable for the oral controlled release formulation. The Optimized formulation (F15) followed First-order release kinetics as it showed highest linearity (r^2=0.952).

Keywords: SEM, FT-IR, Lornoxicam, Electro spinning, Nanofibers, Polymethylmethacrylate (PMMA), Ethyl Cellulose, Polyethylene oxide, Gelatin, In-vitro dissolution studies, In-vivo studies.

1. Introduction

The term extended release implies a system that provides continuous delivery of the drug for a predetermined period with predictable and reproducible kinetics and a known mechanism of release. The oral route of administration for extended release systems has received greater attention because of more flexibility in dosage form design. A dosage form that allows at least a two-fold reduction in dosage frequency as compared to that drug presented as an immediate-release (conventional) dosage form. Examples of extended-release dosage forms include controlled-release, sustained-release and long-acting drug products. The term modified-release drug product is used to describe products that alter the timing and/or the rate of release of the drug substance [1]. Recently, nano-scaled materials have been investigated with amazing increased interest due to their advantages, such as large surface area and many active surface sites. Among different nano-scaled materials, nanofibers have been widely applied in industry due to the ease in production processes compared to other nano-materials. Nanofibers are defined as ultrafine fibers with diameters less than 100nm.When the diameter of polymer fiber materials are shrunk from micrometer to submicron or nano meter there appear several amazing characteristics such as very large surface area to volume ratio, flexibility in surface functionalities and superior mechanical performance compared to other known form of material. Recently nanofibers are used in the healthcare systems, as a tool for drug delivery system in various diseases [2]. The use of nanofibers proves the importance and convenience of them as drug carriers. There smaller size plays an important role in delivering the drug to the appropriate site in the body. Electro spinning is a very simple and versatile

process by which polymer nanofibers with diameters ranging from few nano meters to several micrometers (usually between 50-500nm) can be produced using an electrically driven jet of polymer solution or polymer melt. Electro spinning is a straight-forward, cost-effective to produce novel fibers with diameters in the range of from less than 3nm to over 1 µm. The polymer is usually dissolved in suitable solvent and spun from solution. Nanofibers in the range of 10-to 2000 nm diameter can be achieved by choosing the appropriate polymer solvent [3,4].

2. Materials and Methods

2.1. Materials used: Lomoxicam, Polymethyl Methacrylate (PMMA), Gelatin, Polyethyle oxide, Ethylcellulose,N, N, Dimethyl formamide,Sodium Carboxy methyl cellulose, Carrageenan, Sodium Chloride, Ethylcellulose.

2.2. Methods Used: All the formulations were prepared by Electro spinning method using E-SPIN NANO apparatus. The compositions of the different formulations are given in Table. The nanofibers were prepared as per the procedure given below and the aim was to prolong the release of the drug.

2.2.1. Preparation of Lornoxicam: Gelatin nanofibers: ESPIN – NANO was used for the preparation of the Nanofibers. The solution was prepared with drug: polymer at the ratio of 1:4, 1:6, (W/W) (Lornoxicam: Gelatin), 1:6:1, 1:6:0.75, 1:6:0.5, 1:6:0.25(W/W) (Lornoxicam: Gelatin: Ethyl cellulose). The polymer was taken and dissolved in 5ml of 70% Acetic acid, stirred for 1 hr in magnetic stirrer to obtain a clear solution. Then the drug was added to the polymer solution and kept for stirring for 30min.

2.2.2. Preparation of Lornoxicam: PEO nanofibers: ESPIN – NANO was used for the preparation of the Nanofibers. The solution was prepared with drug: polymer at the ratio of 1:4, 1:8, (W/W) (Lornoxicam: Polyethylene oxide). The polymer was dissolved in 5ml of Dimethyl formamide (DMF), stirred for 1 hr in magnetic stirrer to obtain a clear solution. Then the drug was added to the polymer solution and kept for stirring for 30min.

2.2.3. Preparation of Lornoxicam: PMMA nanofibers: ESPIN – NANO was used for the preparation of the Nanofibers. The solution was prepared with drug: polymer at the ratio of 1:1, 1:0.75, 1:0.5, 1:0.25 (W/W) (Lornoxicam: PMMA). The polymer was taken and dissolved in 10ml of DMF, stirred overnight in magnetic stirrer to obtain a clear solution. Then the drug was added to the polymer solution and kept for stirring for 30min.

3. Evaluation of lornoxicam nanofibers

3.1. Assay of Lornoxicam Nanofibers: Weighed nanofibers equivalent to 100mg of the drug was transferred into a 100ml volumetric flask, the fibers was solubilized in few ml of 0.1 M NaOH and finally the volume was made up to the mark with 7.4 Phosphate buffer. From the obtained stock, dilutions were made such that we finally obtain 10µg/ml solution. The obtained solution was assayed for drug content using the UV spectrophotometer at366nm.The drug content is calculated from the absorbance obtained with the help of the calibration curve [4,5]. The results are given Table.

3.2. *In Vitro* drug release studies of Nanofibers: Dissolution rate of Lornoxicam from the Nanofibers were performed using the dissolution testing apparatus with a paddle. The dissolution fluid was 900ml of pH 7.4 Phosphate buffer, a speed of 50rpm and a temperature of 37±0.5°C, was used in each test. Samples of dissolution medium (5ml) were withdrawn at different time intervals (0.5, 1, 2, 3, 4, 5, 6, 7and 8hrs), suitably diluted and assayed for Lornoxicam by measuring the absorbance at 366nm [6,7]. The dissolution experiments were conducted in triplicate and the results are tabulated in Tables.

***3.3. In Vitro* Drug Release Kinetics:** The analysis of the drug release mechanism from a pharmaceutical dosage form is an important but complicated process. As a model-dependent approach, the dissolution data was fitted to four popular release models such as zero-order, first-order, diffusion and the Korsemeyer-Peppas equations, which have been described in the literature. The order of drug release was described by using the zero order kinetics or the first orders kinetics. The mechanism of drug release was studied by using the Higuchi equation and the Korsemeyer - Peppas equation [7,8].

3.3.1. Zero Order Release Kinetics: It defines a linear relationship between the fractions of drug released versus time. $\mathbf{Q = k_o t}$

Where, Q is the fraction of drug released at time t and k_o is the zero order release rate constant.

3.3.2. First Order Release Kinetics: Wagner assuming that the exposed surface area of a tablet decreased exponentially with time during dissolution process suggested that drug release from most of the slow release tablets could be described adequately by apparent first-order kinetics[9]. The equation that describes first order kinetics was $\mathbf{\ln (1-Q) = - K_1 t}$

3.3.3. Higuchi equation: It defines a linear dependence of the active fraction released per unit of surface (Q) and the square root of time [10].

$$\mathbf{Q = K_2 t^{1/2}}$$

Where, K_2 is the release rate constant.

3.3.4. Power Law: In order to define a model, which would represent a better fit for the formulation,

dissolution data was further analyzed by Peppa's and Korsemeyer equation [11] (Power Law).

$$M_t/M_\alpha = K.t^n$$

4. Characterisation of Nanofibers

4.1. FTIR Spectroscopy studies: FTIR spectra of the Lornoxicam- PMMA Nanofibers were studied to confirm the compatibility of the API with the excipients. FTIR spectra was obtained by the FTIR spectrophotometer (Bruker) using potassium bromide pellets and the scanning range used was 4400 to 400 cm-1 at a scan period of 1min.Spectra of theoptimized batches are shown in Figures.

4.2. DSC studies:

4.3. Studies: The phenomenon of X-Ray diffraction by crystals results from a scattering process in which X-rays are scattered by the electrons of the atom without change in wavelength. The crystallinity of the sample is reflected by a characteristic finger print region in the diffraction pattern. The physical state of Lornoxicam in different samples was evaluated with the powder X – ray diffraction [12]. The samples included pure drug (API) and the Optimized Formulation and the results are shown in Figures.

4.4. SEM studies: The external surface morphology and the diameter of the nanofibers were studied by the scanning electron microscopy. The nanofibers were observed under a scanning electron microscope[13,14]. They were mounted directly on to the SEM sample stub using double sided sticking tape and coated with gold film (thickness 200nm) under reduced pressure (0.0001 mm of Hg) and the results are shown in Figures.

4.5. *In vivo* studies:

4.6. Stability Studies: Stabilty studies are conducted as per the ICH guidelines[15,16,17].

DSC thermo gram of the optimized nanofiber and the pure

5. Results

Table no-1: Spectrophotometric data for the estimation of Lornoxicam at 366 nm

S.No	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.059
3	4	0.137
4	8	0.293
5	16	0.559
6	20	0.687
7	24	0.815

Fig no- 1: Standard curve of Lornoxicam in pH 7.4 phosphate buffer in 366nm

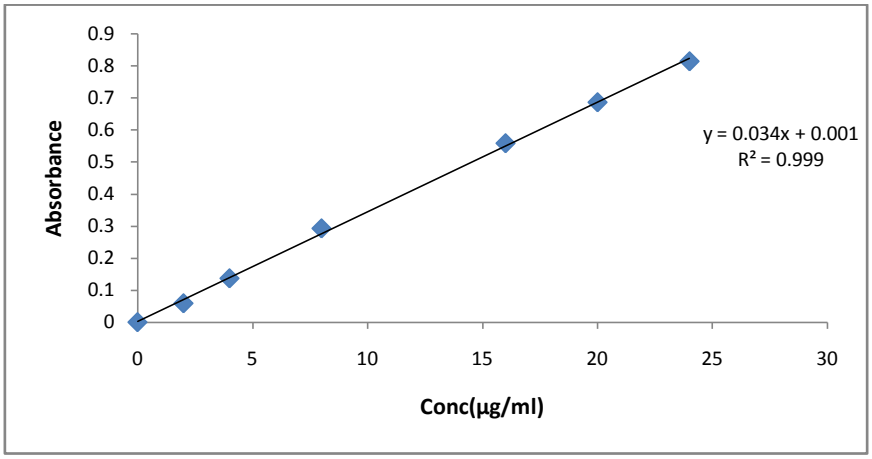

Table no- 2: Composition of Electro spinning samples

S.no.	Formulation	Composition	Solvents used	Ratio
1	F1	Drug: Gelatin	70%Acetic acid	1:4
2	F2	Drug: Gelatin	70%Acetic acid	1:6
3	F3	Drug: Gelatin: Ethyl cellulose	70%Acetic acid	1:6:1
4	F4	Drug: Gelatin: Ethyl cellulose	70%Acetic acid	1:6:0.75
5	F5	Drug: Gelatin: Ethyl cellulose	70%Acetic acid	1:6:0.5
6	F6	Drug: Gelatin: Ethyl cellulose	70%Acetic acid	1:6:0.25
7	F7	Drug: Poly ethylene oxide	DMF	1:4
8	F8	Drug: Poly ethylene oxide	DMF	1:8
9	F9	Drug: Poly methylmethacrylate	DMF	1:1
10	F10	Drug: Poly methylmethacrylate	DMF	1:0.75
11	F11	Drug: Poly methylmethacrylate	DMF	1:0.5
12	F12	Drug: Poly methylmethacrylate	DMF	1:0.1
13	F13	Drug: Poly methylmethacrylate	DMF	1:1
14	F14	Drug: Poly methylmethacrylate physical mixture	DMF	1:0.25
15	F15	Drug: Poly methylmethacrylate	DMF	1:0.25
16	BRAND	Branded Lornoxicam Extended release tablet		16mg
17	Pure drug	Pure drug		16mg

Table no- 3: Assay values of different formulations

Drug Content%	Batch code
98.6±0.84	F1
96.9±0.56	F2
100.08±0.41	3
82.44±0.544	F4
86.56±1.079	F5
100.09±0.81	F6
95.8±0.95	F7
101±0.84	F8
89.5±0.74	F9
100±0.84	F10
95.8±0.84	F11
98.5±0.54	F12
100±1.56	F13
99.5±1.75	F14
98.5±0.35	**F15**
99.8±0.84	Brand

Table no -4: Dissolution Profiles of Lornoxicam nanofibers in pH7.4Phosphate Buffer

Time(hrs)	Cumulative % drug dissolved ± SD (n=3)			
	F1	F2	F3	F4
0	0	0	0	0
0.5	78.8±1.62	61.6±2.2	6.7±0.59	15.1±1.30
1	83.5±1.25	69.4±0.97	8.7±.1.08	17.6±0.63
2	87.3±1.16	76.2±1.26	9.9±0.95	19.8±1.73
3	93.55±1.2	81.33±0.86	12.2±0.83	22.3±1.24
4	-	86.4±0.39	13.8±1.17	25.5±1.62
5	-	95±4.04	17.1±1.36	28.4±1.26
6	-	-	19.98±1.64	31.3±0.5
7	-	-	22.1±1.8	33.4±0.5
8	-	-	23.73±1.57	36.7±0.75

Fig no- 2: Dissolution profiles of nanofibers of Lornoxicam (F1, F2, F3, F4 formulations)

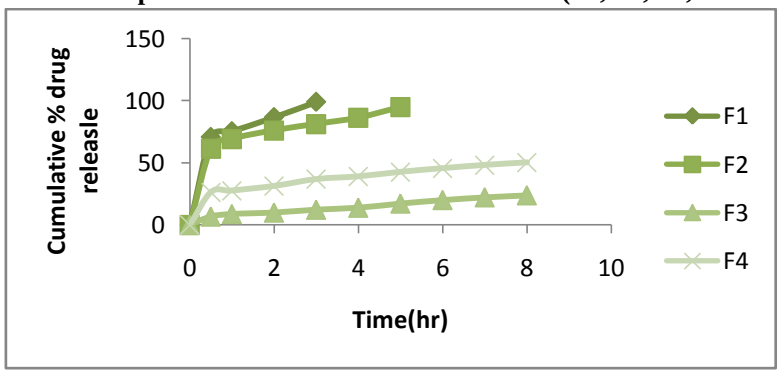

Table no- 5: Dissolution Profiles of Lornoxicam nanofibers in pH7.4Phosphate Buffer

Time(hrs)	Cumulative % drug dissolved ± SD (n=3)			
	F5	F6	F7	F8
0	0	0	0	0
0.5	26.4±1.64	33.4±1.5	78.8±1.62	69.4±2.13
1	27.6±1.75	35.9±0.64	83.5±2.25	71.9±1.23
2	31.3±1.32	43.8±1.4	87.3±1.16	72.8±3.98
3	36.8±1.26	49.5±1.3	93.55±1.2	82.7±1.57
4	39±1.32	55.2±1.86	-	93.6±0.26
5	42.63±1.56	62.3±3.4	-	96.9±1.16
6	45.58±1.24	68.3±2.9	-	-
7	48.2±1.34	72.3±1.79	-	-
8	50.24±1.25	77.6±1.2	-	-

Fig no -3: Dissolution profiles of nanofibers of Lornoxicam (F5, F6, F7, and F8) formulations

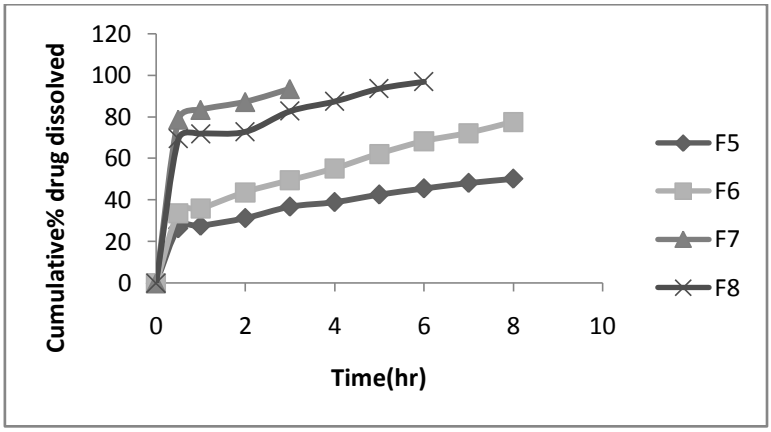

Table no- 6: Dissolution Profiles of Lornoxicam nanofibers in pH7.4Phosphate Buffer

Time (hrs)	Cumulative % drug dissolved ± SD (n=3)		
	F9	F10	F11
0	0	0	0
0.5	2.7±0.63	8.59±0.8	9.06±1.45
1	3.93±1.37	10.6±1.56	15.2±1.26
2	7.1±1.6	14.4±1.35	25.9±1.98
3	8.61±1.1	18.3±1.64	27.6±1.45
4	9.53±1.6	21.4±1.75	31.3±1.25
5	11.03±1.58	23.1±1.36	38.5±1.86
6	12.9±1.94	27.7±1.5	43.03±1.1
7	14.4±3.4	29.6±0.92	49.5±1.68
8	15.7±1.76	30.8±0.79	55.4±1.46

Fig no -4: Dissolution profiles of nanofibers of Lornoxicam (F9, F10 and F11) formulations

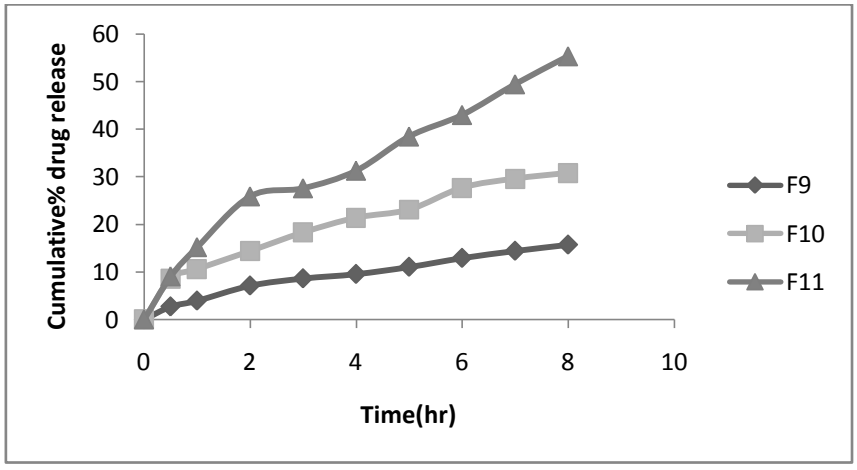

Table no -7: Dissolution Profiles of Lornoxicam nanofibers in pH 7.4Phosphate Buffer

Time (hrs)	Cumulative % drug dissolved ± SD (n=3)		
	F12	F13	F14
0	0	0	0
0.5	17.9±1.32	7.16±1.28	12.1±1.45
1	20.3±1.94	18.08±1.76	15.4±1.76
2	24±1.36	23.06±1.26	40.3±0.36
3	34.3±1.76	28.5±1.35	71.54±0.48
4	40.3±1.64	37.7±1.72	-
5	48±0.15	43.8±1.04	-
6	53.6±0.45	50.7±1.36	-
7	69.3±0.4	61.73±1.83	-
8	75.4±1.64	69±1.49	-

Fig no- 5: Dissolution profiles of nanofibers of Lornoxicam (F12, F13 and F14) formulations

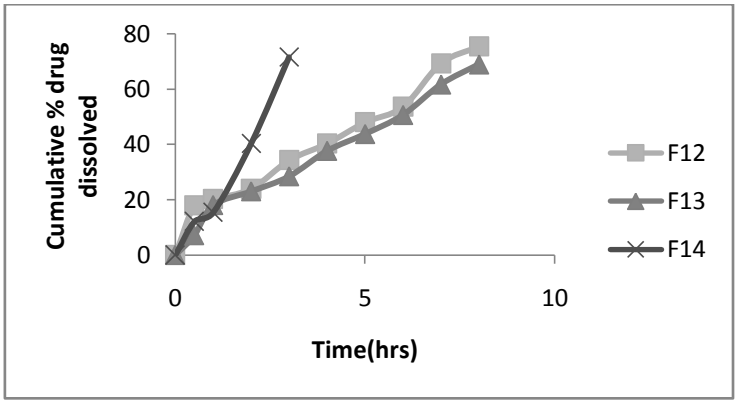

Table no -8: Dissolution Profiles of Lornoxicam nanofibers in pH 7.4Phosphate Buffer

Time (hrs)	Cumulative % drug dissolved ± SD (n=3)		
	F15	BRAND	Pure Drug
0	0	0	0
0.5	36.5±0.5	37.4±1.45	40.6±1.2
1	42.3±1.74	45.3±1.48	77.5±1.68
2	52±1.8	55.6±1.64	90.13±1.46
3	62.4±1.72	66.6±1.84	96.8±0.46
4	69.3±0.26	71.5±1.2	-
5	71.5±1.45	73.7±1.36	-
6	74.2±0.46	76.3±1.25	-
7	80.1±1.34	80.9±0.46	-
8	84.6±1.68	86.8±0.5	-

Fig no-6: Dissolution profiles of nanofibers of Lornoxicam (F15, Brand and Pure drug) formulations.

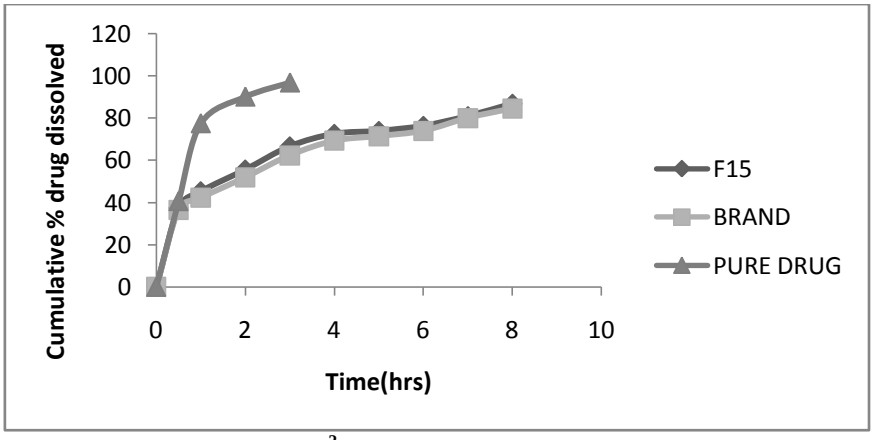

Table no -9: Coefficient of Correlation (r^2) Values of Different Batches of Electrospun Nanofibers of Lornoxicam

Formulation	Zero order	First order	Higuchi's	Peppa's
F1	0.612	0.895	0.845	0.792
F2	0.646	0.913	0.886	0.847
F3	0.950	0.960	0.972	0.973
F4	0.859	0.895	0.966	0.973
F5	0.764	0.843	0.927	0.978
F6	0.853	0.958	0.968	0.905
F7	0.500	0.781	0.782	0.832
F8	0.567	0.908	0.792	0.740
F9	0.965	0.977	0.986	0.994
F10	0.938	0.952	0.993	0.994
F11	0.963	0.976	0.977	0.917
F12	0.971	0.942	0.975	0.851
F13	0.905	0.925	0.962	0.923
F14	0.976	0.921	0.835	0.713
F15	**0.797**	**0.958**	**0.958**	**0.860**
Brand	0.928	0.899	0.968	0.928

Table no-10: Dissolution parameters of Lornoxicam nanofibers

Formulation	Dissolution Parameters					
	n	K_0(µg/hr)	K_1(hr^{-1})	T_{50}(hrs)	T_{75}(hrs)	T_{90}(hrs)
F1	0.882	25.7	1.323	0.23	0.49	2.95
F2	0.091	13.21	0.472	0.38	1.86	4.69
F3	0.527	2.5884	0.030	5.9	8.9	9.4
F4	0.371	3.451	0.045	-	-	-
F5	0.267	4.596	0.068	7.96	-	-
F6	0.237	7.574	0.157	3.5	7.9	-
F7	0.043	22.76	0.75	0.25	0.46	2.59
F8	0.795	24.41	0.462	0.26	2.58	4.32
F9	0.679	1.814	0.020	-	-	-
F10	0.481	3.462	0.044	-	-	-
F11	0.458	6.214	0.087	7.86	-	-
F12	0.378	8.34	0.155	5.82	7.85	-
F13	0.446	9.298	0.112	5.96	-	-
F14	0.382	23.36	0.40	2.68	-	-
F15	**0.208**	**8.248**	**0.201**	**3.96**	**6.96**	-
BRAND	0.178	0.325	8.16	1.26	5.67	-

Fig no -7: Zero Order Kinetics of the Brand Formulation

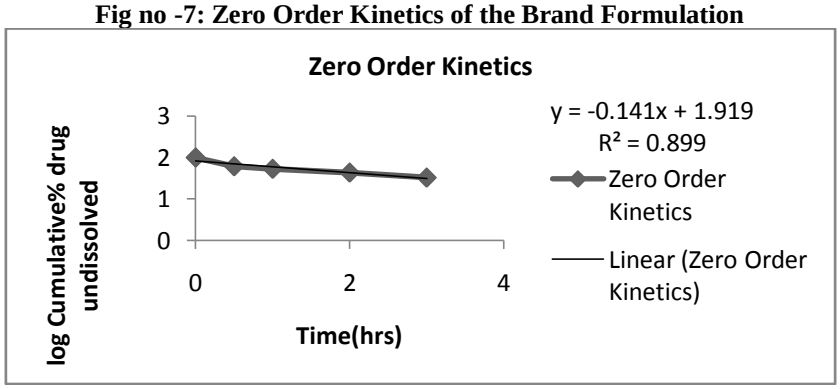

Fig no- 8: First Order Kinetics of the Brand Formulation

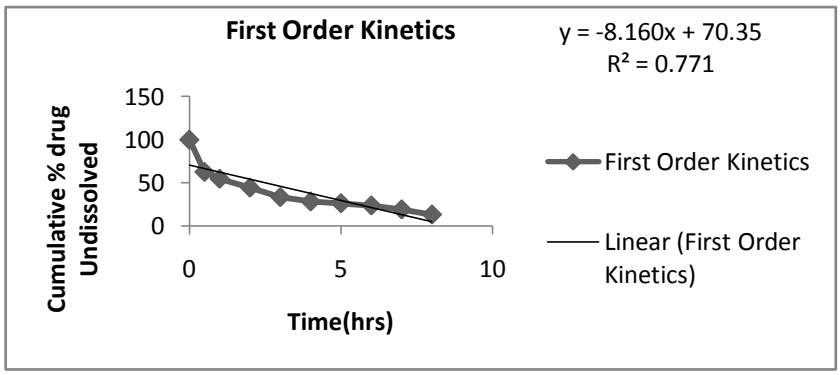

Fig no -9: Higuchi Kinetics of the Brand formulation

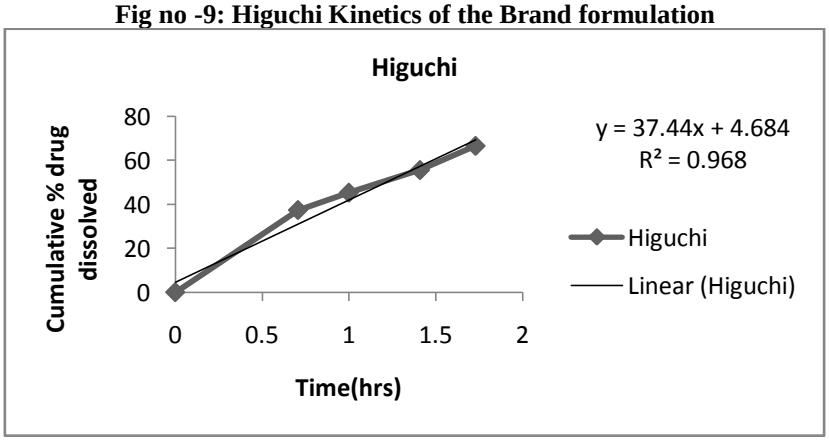

Fig no- 10: Korsemeyer Peppas of the Brand product

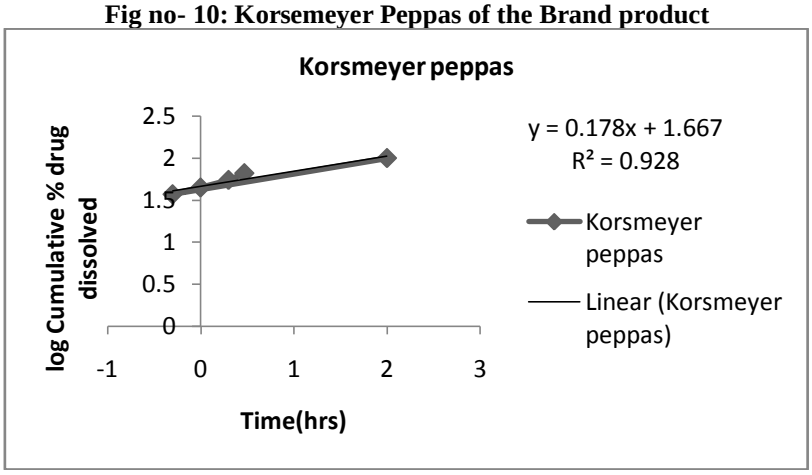

Fig no -11: Zero Order Kinetics of the Optimized formulation (F15)

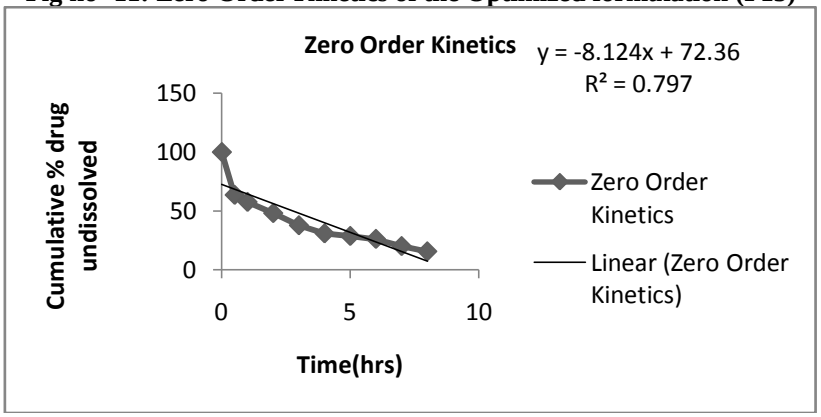

Fig no -12: First Order Kinetics of the Optimized formulation (F15)

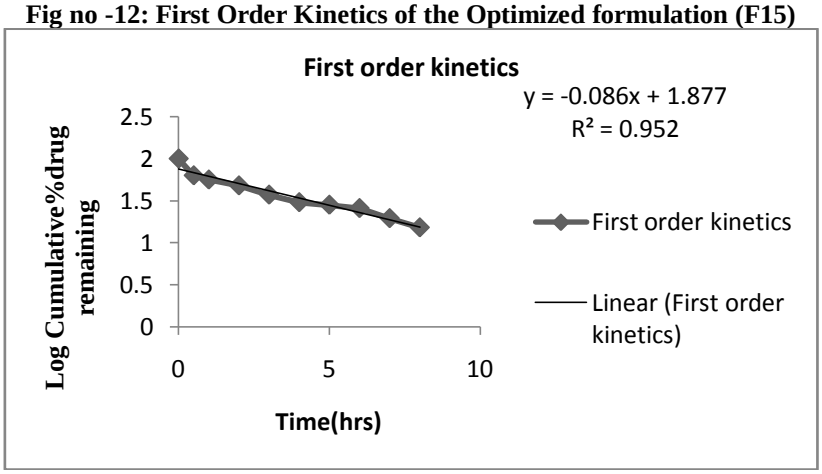

Fig no- 13: Higuchi kinetics of the Optimized formulation (F15)

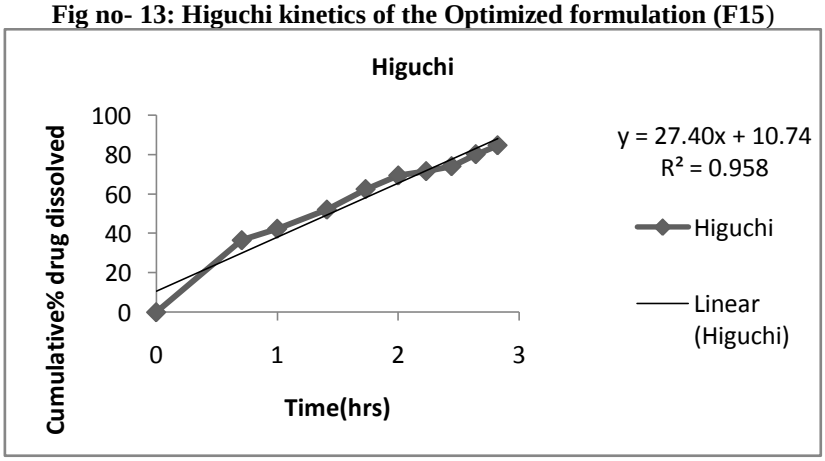

Fig no -14: Korsemeyer Peppas of the Optimized formulation (F15)

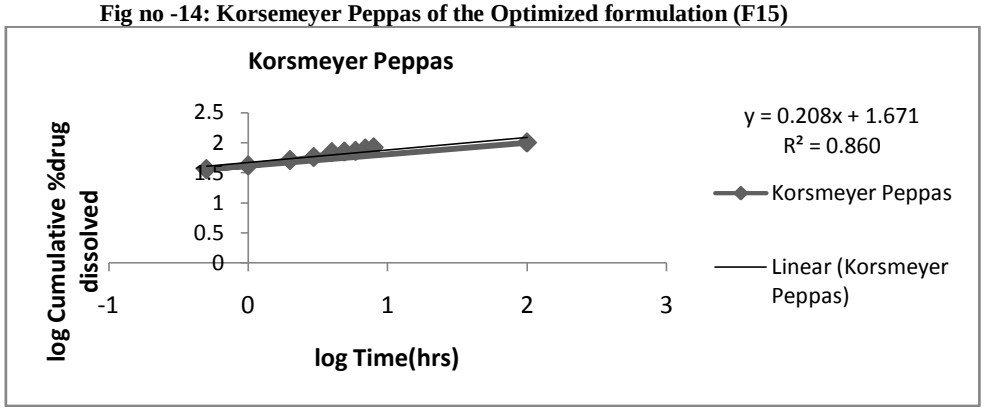

Fig no- 15: FTIR spectrum of Pure drug (Lornoxicam)

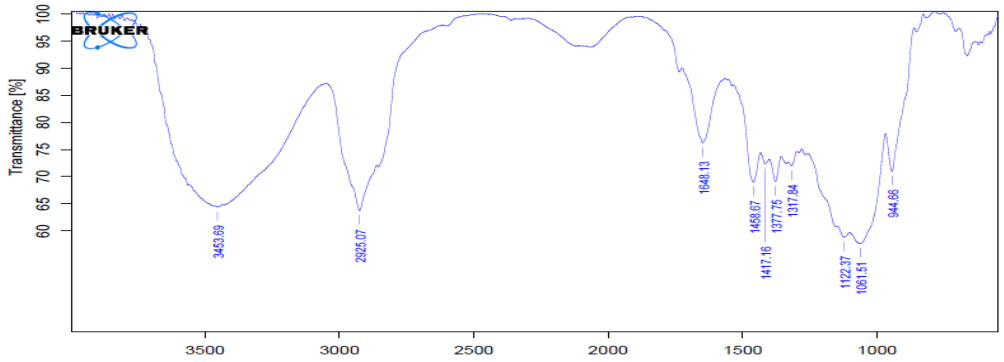

Fig no -16: FTIR spectrum of PMMA

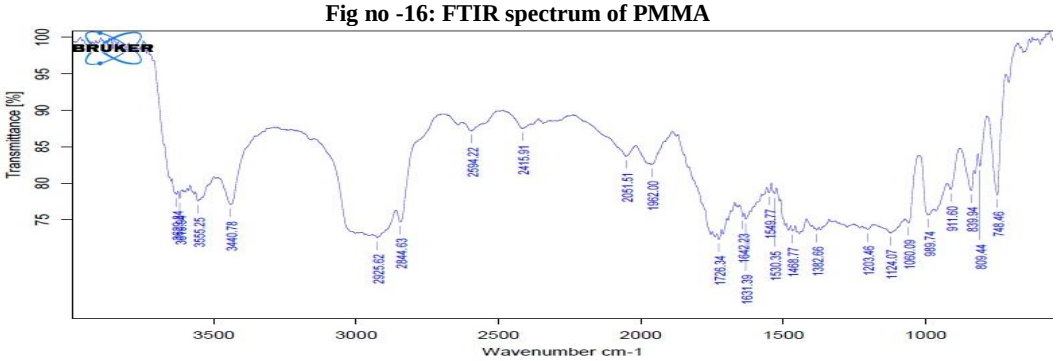

Fig no- 17: FTIR spectrum of Physical mixture

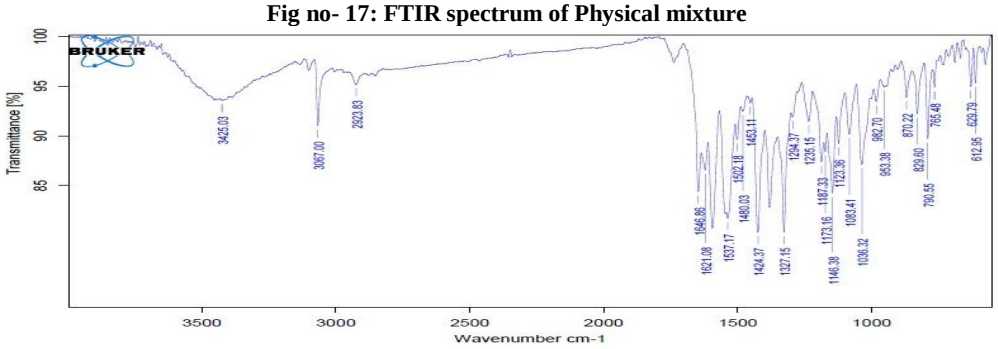

Fig no- 18: FTIR spectrum of Optimized formulation (F15)

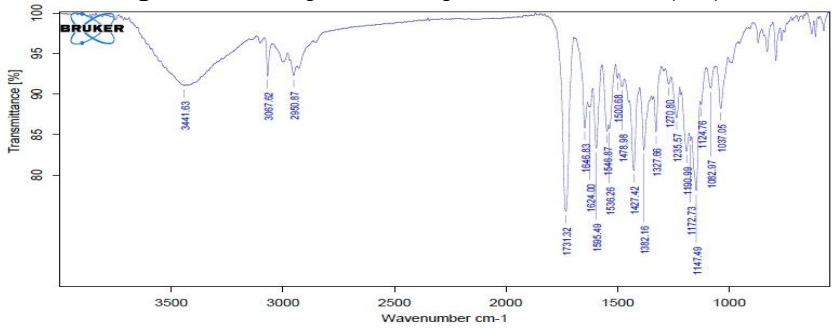

Fig no -19:DSC thermogram of Pure drug

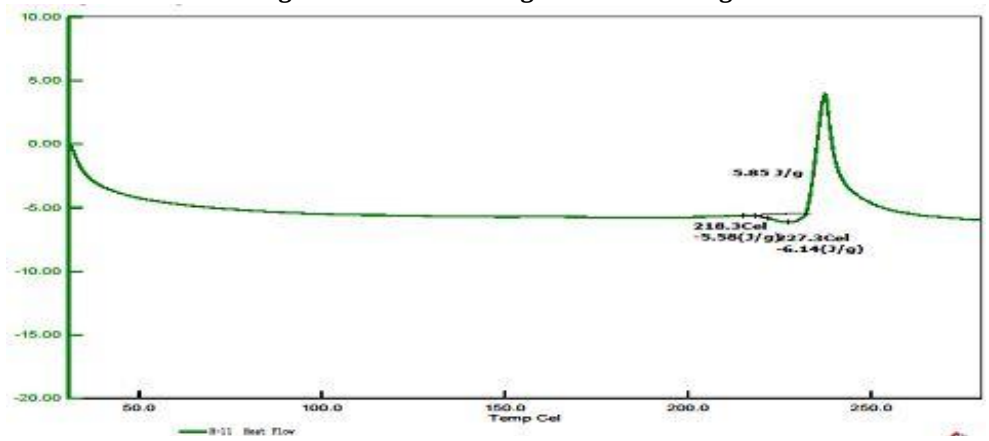

Fig no- 20:DSC thermogram of the Optimized formulation(F15)

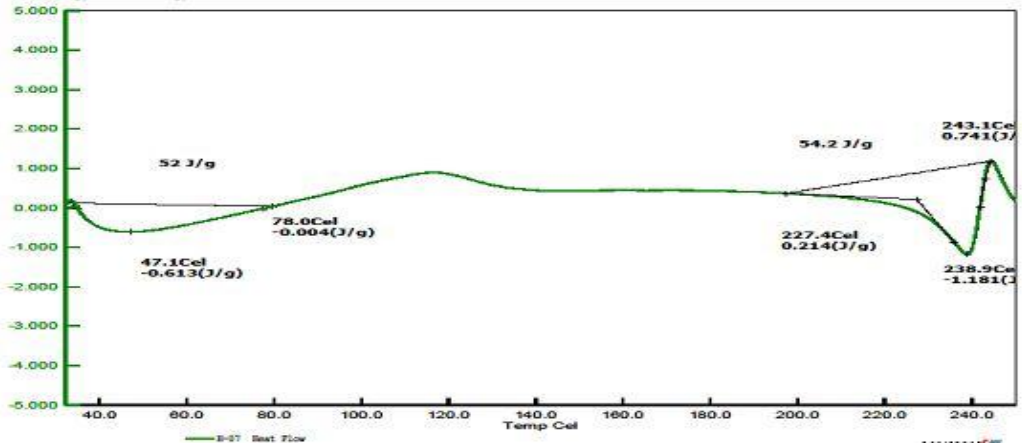

Fig no- 21: XRD studies of the Pure drug

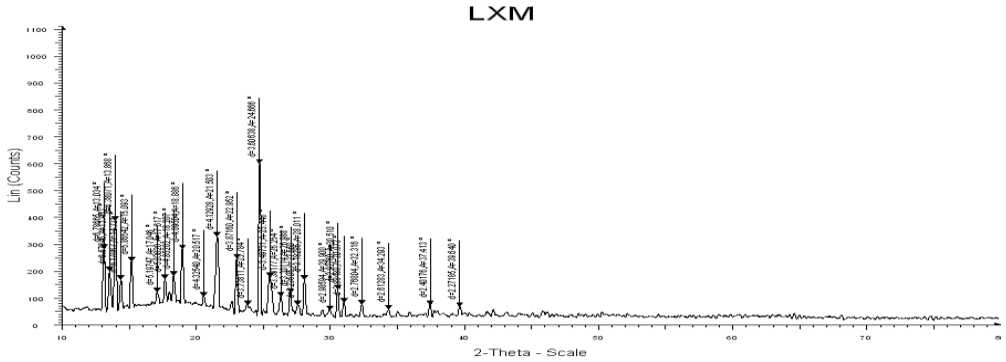

Fig no -22: XRD studies of the Optimized formulation(F15)

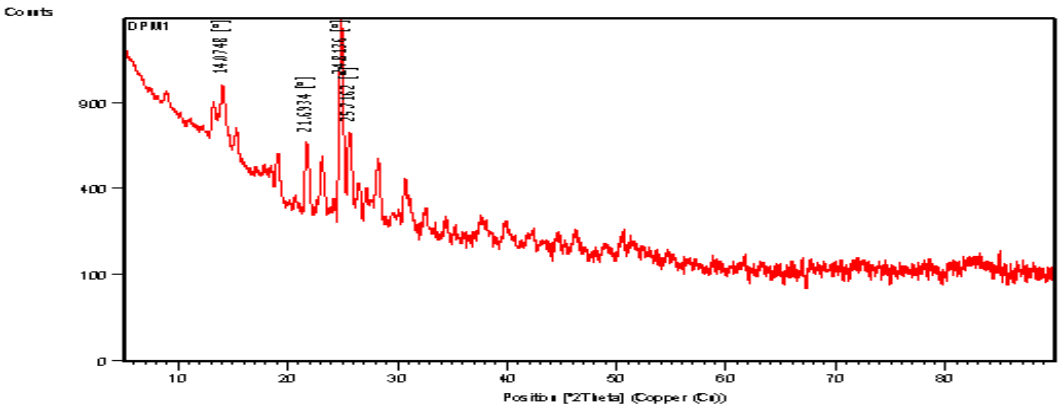

Fig no -23: SEM images of the pure drug with increased magnification

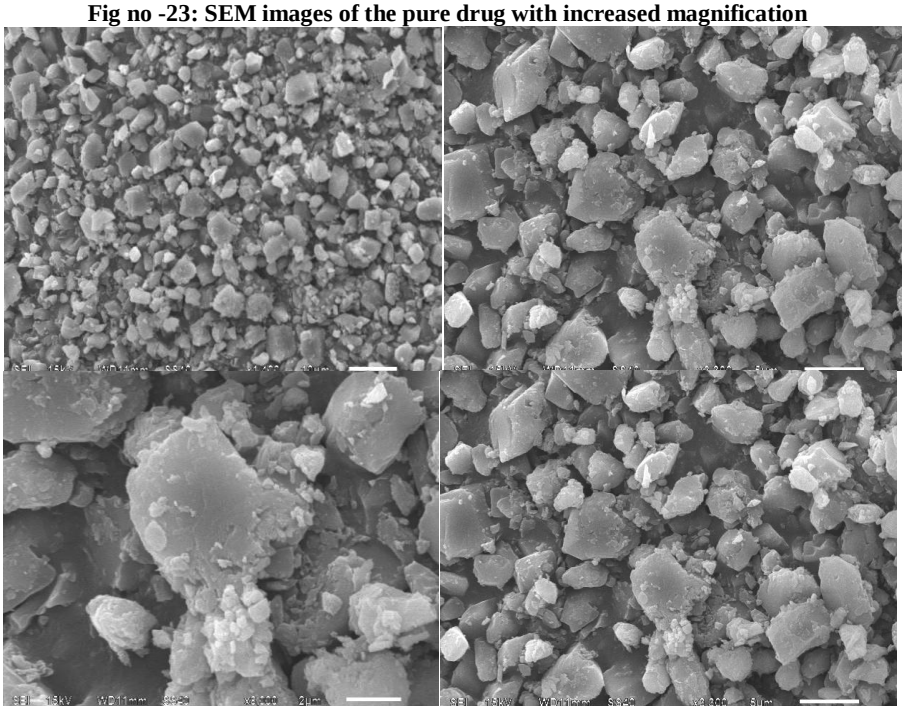

Fig no- 24: SEM images of Optimized formulation(F15)

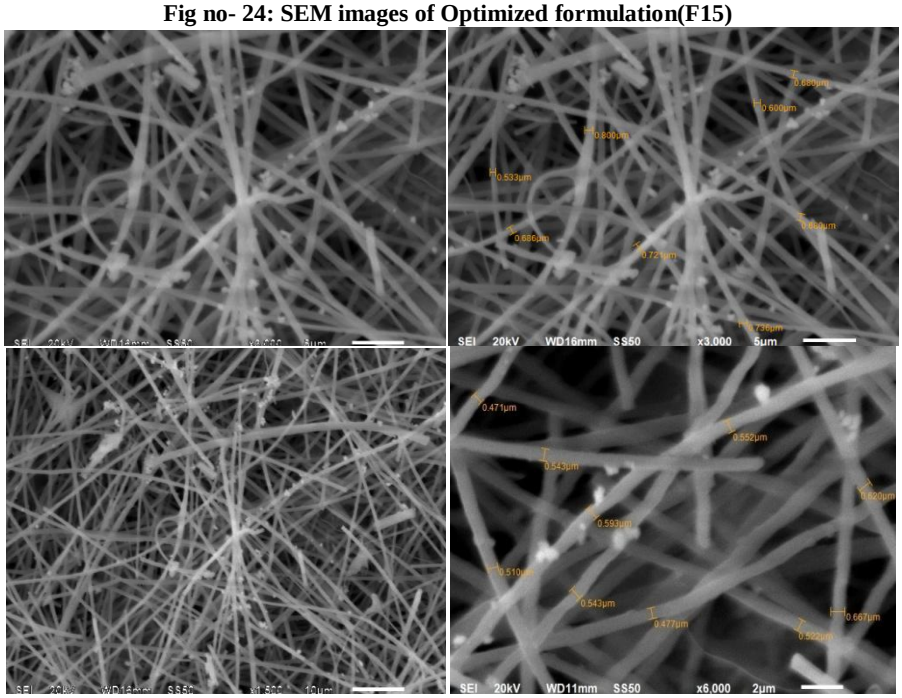

Fig no-25: Graphs showing diameter of Paw edema in Control, Reference and Optimized formulation (F15) at 1st hr, 4thhr & 8thhr.

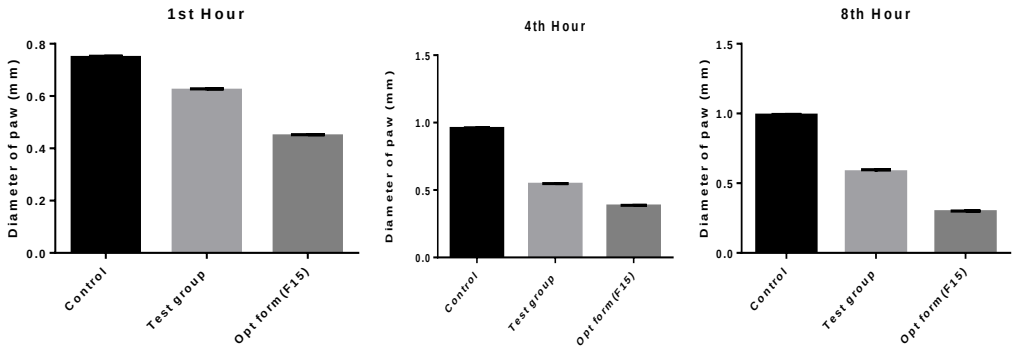

Table no-11: *In Vivo* evaluation of Anti-inflammatory Activity(Mean reduction in Paw edema)

Group	Treatment Hour	Control Mean±SEM (mm)	Reference Mean±SEM(mm)	%inhibition	TestMean±SEM (mm)	%inhibition
1	1	0.75±0.01	0.62±0.001	17.3%	0.45±0.001	40%
2	4	0.96±0.002	0.54±0.002	44%	0.38±0.002	60%
6	8	0.98±0.004	0.45±0.009**	66%	0.3±0.001**	72%

Table no-12: Stability studies of the Optimized formulation(F15)

Time (hrs)	Cumulative % drug dissolved ± SD (n=3)					
	At 25°C / 60% RH			At 40°C / 75% RH		
	1 month	2months	3months	1month	2months	3months
0	0	0	0	0	0	0
0.5	36±0.48	35.8±0.48	35.5±0.45	35.6±1.06	35±0.6	34.9±0.47
1	42.1±1.35	42±1.35	41±0.4	41.5±0.18	41±1.05	39.5±1.20
2	51.5±1.32	51±1.16	49.5±0.45	49±0.17	48.6±1.43	48±1.44
3	62±0.86	61.5±2.11	61±0.56	61.8±0.52	59.5±1.01	59±1.26
4	69.2±1.72	67.8±0.45	66.5±1.55	68±1.50	65.5±1.26	64.5±1.42
5	71.3±1.64	69.5±0.64	68±1.45	69±1.28	68.5±0.32	58.1±0.74
6	73.9±1.32	71.8±0.58	66.6±2.54	66.9±1.32	68.4±0.46	67.4±1.72
7	79.8±1.59	76.3±1.24	74.6±1.56	78.9±0.54	75.3±0.996	73.2±1.29
8	84.4±1.04	84.2±0.96	83.9±0.36	84±0.36	84±0.49	82.9±0.92

6. Discussion

The nanofibers were prepared by Electro spinning method using different polymers such as PMMA, Ethyl Cellulose, Polyethylene oxide, Gelatin. Totally 15 different formulations of Lornoxicam were prepared by Electro spinning technique. Finally the nanofibers are evaluated for various characteristics like drug content, in-vitro release studies. The API and the Optimized formulations were evaluated for solid state characterization by DSC, XRD and SEM studies. The optimized formulation showed fairly acceptable values for all the parameters evaluated.

The DSC thermogram of the pure drug exhibited a single endothermic peak at 227.3°C corresponding to the Melting point of the drug and the sharp peak indicated its crystallinity. The DSC curve of Optimized nanofiber Formulation (F15) exhibited two broad peaks from 47.1°to78°C indicating evaporation of water from the formulation, and 243.1°C corresponding to the Melting Point of the formulation, but the drug's peak was no longer observed. It could be attributed to the destruction of crystal lattice, because of progressive amorphization or dissolution into the polymers, or complete entrapment of the drug in the polymer. Solid state studies did not indicate chemical decomposition of the components (drug and excipients), showing compatibility and formation of homogenous systems.

The X-ray diffraction patterns of the pure dug exhibited its characteristic diffraction peaks at various diffraction angles indicating the crystallinity. But in the nanofiber formulation reduction and absence of major drug diffraction peaks indicated the presence of drug mostly in amorphous form or completely entrapped within the polymer. Diffraction patterns of the API and the Optimized nanofiber formulation (F15) were represented in the Figures. The SEM studies indicated the diameter of the Optimized formulation (F15) having diameter 400-800 nm.

The Compatibility studies were performed using FTIR spectrophotometer. The IR spectrum of the pure drug, the physical mixture of drug and the excipients, Optimized formulation were studied. From the FTIR spectra it was clearly evident that the drug-polymer interactions were absent. FTIR Spectra of the pure drug showed characteristic peaks at 3453.69cm^{-1}, 2925.07cm^{-1} and 1648.13cm^{-1}.The FTIR Spectra of Drug and the polymer mixture exhibited peaks at 3440.78cm^{-1}, 2952.62 cm^{-1} and 1642.23cm^{-1}. This confirms the undisturbed structure of the drug in the formulation. This proves the fact that there was no potential incompatibility of the drug with the polymers used in the formulation. Hence, the formula for preparing Lornoxicam nanofibers can be reproduced in the industrial scale without any apprehension of possible drug-polymer interaction.

The prepared formulations were evaluated for the dissolution profile, and the optimized formulation was screened by comparing with that of the API and the marketed product (Lofecam). The Optimized nanofiber formulation (F15) exhibited similar dissolution profiles compared to the innovator brand. Lornoxicam release from the nanofibers was studied in phosphate buffer (pH 7.4) for 8 hrs. Drug release from the nanofibers is slow and dependent on

the polymer composition. The drug release from the Optimized formulation (F15) followed First-order kinetics as it showed highest linearity (r^2=0.952).

The drug release from the optimized formulation (F15) was slow and extended over a period of 8 hrs and these nanofibers were found to be suitable for the oral controlled release formulation. Higuchi plot showed an r^2 value of 0.958 suggesting that the diffusion plays an important role in the release of the drug. The data was fitted to the Korsemeyer peppas equation and the value of diffusional exponent 'n' (0.208), in which is less than 0.45 this indicated that the drug release shows Fickian diffusion. The Optimized formulation (F15) exhibited increased inhibitory effect (72%) of inflammation compared to that of the pure drug (66%) against Carrageenan induced paw-edema in rats.

Stabilty studies were conducted at 25°C /60% RH and 45°C/75% RH and the Cumulative % drug release values of the Optimised formulation revealved that there is no significant difference in In-vitro dissolution studies after 3months of stability studies. This indicates that the Optimized formulation is stable for 3months.

7. Conclusion

The Optimized nanofiber formulation (F15) exhibited similar dissolution profiles compared to the brand formulation and the Optimized formulation (F15) was quite stable at 25^0C/60% RH and 40^0C / 75% RH for three months with regard to dissolution rate and the formulation is considered to be stable.The Optimized formulation (F15) exhibited increased inhibitory effect of inflammation compared to that of pure drug against Carrageenan induced paw-edema in rats. The drug release from the optimized formulation (F15) was slow and extended over a period of 8 hrs and these nanofibers were found to be suitable for the oral controlled release formulation.

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