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Development and Evaluation of Fast Disintegrating Tablets Containing Lornoxicam Solid Dispersions

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ABSTRACT

Lornoxicam is a non steroidal anti-inflammatory drug (NSAID) of the oxicam class. It belongs to BCS class II substance with low solubility and high permeability. The aim of current research is to formulate solid dispersion incorporated Fast disintegrating tablets of Lornoxicam to enhance the dissolution rate and aqueous solubility and to enable faster onset of action. Solid dispersions are prepared with polymers like Kolliwax GMS, Soluplus and HPMC in three different ratios 1:1:1, 1:2:1 and 1:3:1. Formulations were characterized for drug content studies, drug release studies and drug-polymer interactions using Fourier transform infrared spectroscopy (FTIR) spectrum. The solid dispersions can be evaluated by in-vitro dissolution studies. The optimized solid dispersion SD9 was further used to prepare fast disintegrating tablet by direct compression method using 3^3 Response surface method (3 variables and 3 levels of superdisintegrants) by using Design of experiment software with superdisintegrants like locust bean gum, gum karaya, Plant ago ovata. The values of pre-compression parameters evaluated were within prescribed limits that indicated good free flowing properties. The data obtained of post-compression parameters such as weight variation, hardness, friability, content uniformity, disintegration time (33 sec) and percentage drug release was maximum in LF24(99.21±1.87%) and was found to superior over conventional formulation. It can be concluded that fast disintegrating tablets using Lornoxicam solid dispersion could be used to improve better patient compliance in the effective management of pain and inflammation.

Keywords: Lornoxicam, NSAID's, Solid dispersion, fast disintegrating tablets, Response surface methodology.

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INTRODUCTION

According to BCS class II the drugs have low solubility and high permeability, therefore in most of the current research as well as in pharmaceutical industry the strategies are ongoing to improve the solubility of poorly soluble drugs [1]. The purpose of this work is to increase the dissolution rate of drug by formation of solid dispersion with different water-soluble carriers [2]. Solid dispersion (SD) is defined as the dispersion of one or more active ingredients in inert carriers at solid state prepared by fusion, solvent or solvent fusion methods [3] Solid dispersion technique has been used for a wide variety of poorly aqueous soluble drugs such as Nimsulide, Ketoprofen, Tenoxicam, Lornoxicam, Nifedipine, Aceclofenac, Valdecoxib using various hydrophilic carriers like polyethylene glycol, polyvinyl pyrrolidone, hydroxypropyl methyl cellulose, sugar, mannitol, urea etc. [4]. Most commonly used carriers for the preparation of SDs are different grade of polyethylene glycols (PEGs) and polyvinyl pyrrolidone (PVPs), Gelucire 44/14, Labrasol, HPMC grades, sugars, and urea [5]. Tablet is the most popular among all dosage forms existing today because of its convenience of self-administration, compactness and easy manufacturing; however hand tremors, dysphagia in case of geriatric patients, the underdeveloped muscular and nervous systems in young individuals and in case of uncooperative patients, the problem of swallowing is common phenomenon which leads to poor patient compliance. To overcome these drawbacks, FDTs has emerged as an alternative oral dosage form. The basic approach used in development of FDTs is the use of superdisintegrants which provide instantaneous disintegration of tablet after placing on tongue, thereby releasing the drug in saliva [6]. Lornoxicam, (2-[2-[2-(2,6dichlorophenyl) aminophenyl] acetyl] oxy tactic acid), a non steroidal anti-inflammatory, analgesic and antipyretic drug used in rheumatoid arthritis, post-traumatic pain, masculo-skeletal and joint disorders, with lower indications of gastro-intestinal adverse effects and thus, resulted in a greater compliance with treatment. Lornoxicam is practically insoluble. For poorly soluble and oral administered drugs, the rate of absorption is usually controlled by the rate of dissolution, which is the rate limiting step for absorption [7]. The dissolution of a drug can also be influenced by disintegration time of the tablets [8]. The aim of present study is to formulate Fast disintegrating tablets of lornoxicam with all possible properties of it by using solid dispersions and also to mask the bitter taste of the drug.

MATERIALS AND METHOD

Materials

Lornoxicam pure drug was generous gift from Aurobindo Pharma Ltd, Hyderabad, India. Kolliwax GMS II, Labrosol, Kolliphor EL and Aerosil 200 were obtained from Signet Chemical Corp. Pvt.

Ltd., Mumbai. Solu plus was gifted by BASF, Germany. HPMC and PVP K-25 were gifted by Dow Chemicals, USA. Locust Bean Gum, Gum Karaya and Plantago Ovata were obtained from Yarrow chemicals, Mumbai, Mannitol, Avicel PH 101, Aspartame, Magnesium Stearate and Talc were obtained from SD fine chemicals. All other chemicals used were of analytical grade.

Preliminary solubility studies of Lornoxicam

Solubility measurements of Lornoxicam were performed according to a published method given by Higuchi and Connors in 1965 [9]. An excess amount of Lornoxicam was added to 25ml of aqueous solution of water-soluble carriers like PEG 4000, Labrosol, Soluplus, Kolliphor EL, Kolliwax GMS II, HPMC, Colloidal Silicone dioxide (Aerosil 200), and PVPK-25 in screw capped bottles. Samples were shaken for the 24 hours at room temperature. Subsequently, the suspensions were filtered through a Whatman filter paper no. 1. Filtered solution was diluted with methanol and analyzed for the Lornoxicam at UV 370 nm. (Table 1)

Table 1: Preliminary solubility studies of Lornoxicam in different polymers

Physical Mixture (1:1)	Solubility(µg/ml) *
Lornoxicam Pure drug	0.0085±0.09
Drug + Kolliwax GMS II	0.2004±0.01
Drug + Labrosol	0.179±0.19
Drug + Aerosil 200	0.133±0.41
Drug + PEG 4000	0.169±0.66
Drug + PVP K25	0.144±0.023
Drug +Soluplus	0.2125±0.13
Drug + HPMC	0.194±0.19
Drug + Kolliphor EL	0.171±0.21

Preparation of Lornoxicam solid dispersion by the solvent evaporation method

The calculated amount of Lornoxicam and the employed polymers of Soluplus, Kolliwax GMS II, HPMC and SLS in different drug, polymer and surfactant ratios of 1:1:1, 1:2:1 and 1:3:1(Table 2) are weighed and mixed together in a porcelain dish. Nine different formulae were prepared by the solvent evaporation method. The mixture was dissolved in small amount of methanol. Then the solvent was evaporated in oven at temperature 50ºC until complete evaporation. The solid dispersions prepared were pulverized in a mortar and sieved. The fraction of the powder that passed through 45 µm was stored in a desiccator and utilized for further study.

Table 2: Composition of Lornoxicam solid dispersions

Ingredients (mg)	SD1 (1:1:1)	SD2 (1:2:1)	SD3 (1:3:1)	SD4 (1:1:1)	SD5 (1:2:1)	SD6 (1:3:1)	SD7 (1:1:1)	SD8 (1:2:1)	SD9 (1:3:1)
Lornoxicam(mg)	8	8	8	8	8	8	8	8	8
Kolliwax GMS II	8	16	24	-	-	-	-	-	-
HPMC (mg)	-	-	-	8	16	24	-	-	-
Soluplus (mg)	-	-	-	-	-	-	8	16	24
SLS (mg)	8	8	8	8	8	8	8	8	8
Ethanol (ml)	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs

Evaluation of Lornoxicam solid dispersions

Solid dispersions obtained by solvent evaporation method were tested for their percentage practical yield, drug content, FTIR, SEM, XRD, *in-vitro* release and stability studies.

Percentage Practical Yield

Percentage practical yield was calculated to know about percent yield or efficiency of any method and help in selection of appropriate method of production [10].

Drug content

Solid dispersions equivalent to 8 mg of Lornoxicam was weighed accurately and dissolved in 100 ml of methanol. The solution was filtered, diluted suitable and drug content was analysed at λ_{max} 370 nm against blank by UV spectrophotometer [11].

***In vitro* Dissolution study of solid dispersion**

The USP dissolution test type II apparatus (Electro lab TDT- 06 N, India) was used. Amount of samples equivalent to 8 mg of drug were dispersed into the dissolution vessel containing 900 mL of with pH 6.8 phosphate buffer at 37°C and stirred at 50 rpm. Samples were withdrawn periodically, filtered and replaced with a fresh dissolution medium. After filtration through 0.45 µm micro filter, concentration of Lornoxicam was determined spectrophotometrically at λ_{max} 370nm [12].

Characterization

FTIR studies

The instrument used for FTIR study was Shimadzu FTIR-8700 spectrophotometer [13].

Powder X-ray diffraction (XRD)

X-ray powder diffraction patterns were recorded on an X-ray powder diffraction system (Shimadzu, Japan) using copper target, a voltage of 40 Kv and a current of 30 mA. The scanning was done over 2 range of 5ºC to 60ºC [14].

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) studies were carried out using DSC 60, having TA60 software, Shimadzu, Japan. Samples were accurately weighed and heated in sealed aluminum pans

at a rate of 10°C/min between 40°C and 350°C temperature rang under nitrogen atmosphere. Empty aluminum pan was used as a reference [15].

SEM (Scanning Electron microscope) studies

The surface morphology of the layered sample was examined by SEM (Hitachi, Japan). A small amount of powder was manually dispersed onto a carbon tab (double adhesive carbon coated tape) adhered to aluminum stubs. These sample stubs were coated with a thin layer (30Å) of gold by employing POLARON-E 3000 sputter coater. The samples were examined by SEM and photographed under various magnifications with direct data capture of the images onto a computer [16].

Stability studies

The optimized solid dispersions were placed inside sealed 40cc HDPE container with child resistant cap under controlled temperature environment inside stability chamber (Thermo Lab, India) with relative humidity of 75%±5%RH and temperature of 40^0C±2^0C for stability studies. Samples were removed after 1, 2 and 3 months and evaluated for percent drug content and *in vitro* dissolution studies [17].

Preparation of Lornoxicam of fast disintegrating tablets

Twenty-seven formulations (LF1-LF27) for active layer were prepared by direct compression method using 3^3 Response surface method (3 variables and 3 levels of superdisintegrants) by using Design of experiment software with superdisintegrants like locust bean gum, gum karaya, Plant

Table 5: Formulation trials of Lornoxicam fast disintegrating tablets

F.NO	Lornoxicam	Locust Bean gum	Gum Karaya	Plantago Ovata	Aspartame	Mannitol	MCC	TOTAL
F1	40	8	15	32	7	30	62	200
F2	40	14	15	32	7	30	59	200
F3	40	8	23	32	7	30	54	200
F4	40	32	23	30	7	30	32	200
F5	40	8	15	40	7	30	54	200
F6	40	16	15	40	7	30	46	200
F7	40	8	23	40	7	30	46	200
F8	40	32	23	40	7	30	22	200
F9	40	8	23	40	7	30	46	200
F10	40	16	19	36	7	30	46	200
F11	40	12	15	36	7	30	54	200
F12	40	12	23	36	7	30	46	200
F13	40	12	19	32	7	30	76	200
F14	40	12	19	40	7	30	46	200
F15	40	12	19	36	7	30	50	200

F16	40	12	15	40	7	30	50	200
F17	40	12	15	32	7	30	58	200
F18	40	12	23	36	7	30	46	200
F19	40	16	15	36	7	30	50	200
F20	40	12	23	32	7	30	50	200
F21	40	16	19	32	7	30	50	200
F22	40	16	19	36	7	30	46	200
F23	40	18	18	36	7	30	45	200
F24	40	8	20	36	7	30	53	200
F25	40	16	19	40	7	30	42	200
F26	40	8	19	32	7	30	58	200
F27	40	12	19	32	7	30	54	200

ago ovata. All the formulations were varied in concentration of superdisintegrants, magnesium stearate constituted in all the formulations. These materials were screened through #60 and mixed together in motor by using pestle. Final mixtures were compressed by using 8 mm diameter flat punches on an eight-station rotary tablet press. Formulations were depicted in Table 5. The prepared tablets were subjected to different evaluation parameters [18].

Note: Magnesium stearate and Talc were added in 3mg each

Response surface methodology

Study type: Response surface

Design type: central composite

Design mode: quadratic

Design Summary

Study Type	Response Surface	Runs	27
Initial Design	3 Level Factorial	Blocks	No Blocks
Design Model	Quadratic		

Factor	Name	Units	Type	Low Actual	High Actual	Low Coded	High Coded	Mean	Std. Dev.
A	LOCUST BEAN (	mg	Numeric	4.00	8.00	-1.000	1.000	6.000	1.500
B	GUM KARAYA	mg	Numeric	10.00	14.00	-1.000	1.000	12.000	1.500
C	PLANTAGO OV/	mg	Numeric	16.00	20.00	-1.000	1.000	18.000	1.500

Response	Name	Units	Obs	Analysis	Minimum	Maximum	Mean	Std. Dev.	Ratio
Y1	%CDR	%	0	Polynomial	No Data	No Data	No Data	No Data	N/A
Y2	DT	%	0	Polynomial	No Data	No Data	No Data	No Data	N/A

Twenty-seven formulations (F1-LF27) were prepared by direct compression method using 3^3 Response surface method where 3^3 indicates 3 variables and 3 levels of superdisintegrants like locust bean gum, gum karaya, Plant ago ovate mucilage (low, middle and high concentrations) by using

Design of experiment software[19].

Drug-excipients compatibility study by FTIR

The spectrum analysis of pure drug and physical-mixture of drug and different excipients which are used for preparation of tablets was studied by FTIR. FTIR spectra were recorded by preparing potassium bromide (KBr) Disks using a Shimadzu Corporation (Japan) facility (model-8400S). Potassium bromide (KBr) disks were prepared by mixing few mg of sample with potassium bromide by compacting in a hydrostatic press under vacuum at 6-8 tons pressure. There sultant disc was mounted in a suitable holder in IR spectrophotometer and the IR spectrum was recorded from 4000cm^{-1} to 400cm^{-1} in a scan time of 12 minutes[20].

Pre-compression parameters

Preformulation studies: Prior to compression, solid dispersions were evaluated for their characteristic pre-compression parameters, such as bulk density, tapped density, Hausner ratio, Car's compressibility index and angle of repose [21].

Post compression parameters

Post compression parameters like Weight Variation, Thicknesses, Hardness, Friability, Content Uniformity and *in vitro* disintegration time studies were performed [22].

***In Vitro* Drug Dissolution Study**

The dissolution of prepared Fast Disintegrating tablet formulations was carried out by using USP Dissolution Apparatus Type II and Phosphate buffer pH 6.8 of media volume 900 ml by maintaining the temperature of 37±0.2°C and the withdrawn samples are estimated at 370 nm.

Stability studies

The stability study of the formulated drug layered pellets was carried out under different conditions according to ICH guidelines. The drug layered pellets were stored in a stability chamber for stability studies (REMI make). Accelerated Stability studies were carried out at 40^0C/75% RH for the best formulations for 6 months. The drug layered pellets were characterized for the drug content and cumulative % drug released during the stability study period.

RESULTS AND DISCUSSION

Preliminary solubility studies of Lornoxicam

Initially preliminary solubility analysis was carried out to select the appropriate water-soluble carriers for the preparation of solid dispersion in which Lornoxicam pure drug solubility was found to be 0.0085±0.09 µg/ml [23]**.** From this study, drug and Soluplus in the ratio of 1:1 exhibits highest drug solubility of 0.2125±0.13 µg/ml, almost 25-foldincrease compared to that of pure drug. Among

all the water-soluble carriers used, Labrosol, PEG 4000, PVP K 25, Kolliphor EL and Aerosil 200 showed low solubility and therefore are not included in the preparation of Lornoxicam solid dispersions.

Preparation of Lornoxicam solid dispersions

Solid dispersions of Lornoxicam were prepared by solvent evaporation method using different carriers like PEG 4000, Labrosol, Soluplus, Kolliphor EL, Kolliwax GMS II, HPMC, Colloidal Silicone dioxide (Aerosil 200), and PVPK-25 in three different drug: polymer: surfactant (SLS) ratios of 1:1:1, 1:2:1 and 1:3:1 (Table 2). Total 9 formulations were prepared; the mixture was dissolved in the least amount of methanol as a common solvent. Then the solvent was evaporated in oven at temperature 50ºC till complete evaporation. The resultant solid dispersion was scraped out with a spatula. Solid dispersions were pulverized in a mortar and pestle and passed through a 45µm sieve before packing in an airtight container, stored in a desiccator and used for further investigations. All the solid dispersions prepared were found to be fine and free flowing powers (Figure 1).

Figure 1: Lornoxicam optimized solid dispersions

Evaluation parameters

Solubility studies of Lornoxicam solid dispersions

Lornoxicam solid dispersions were prepared by solvent evaporation method with their respective carriers. After preparation of solid dispersion solubility analysis was carried out. The formulation (SD9) with Soluplus in the ratio of 1:3 and with SLS shown highest solubility i.e. 0.68±0.10µg/ml, almost 75-fold compared to that of the pure drug (Pure drug solubility is 0.0085±0.09µg/ml. The results are given graphical representation in Figure 2 and 3.

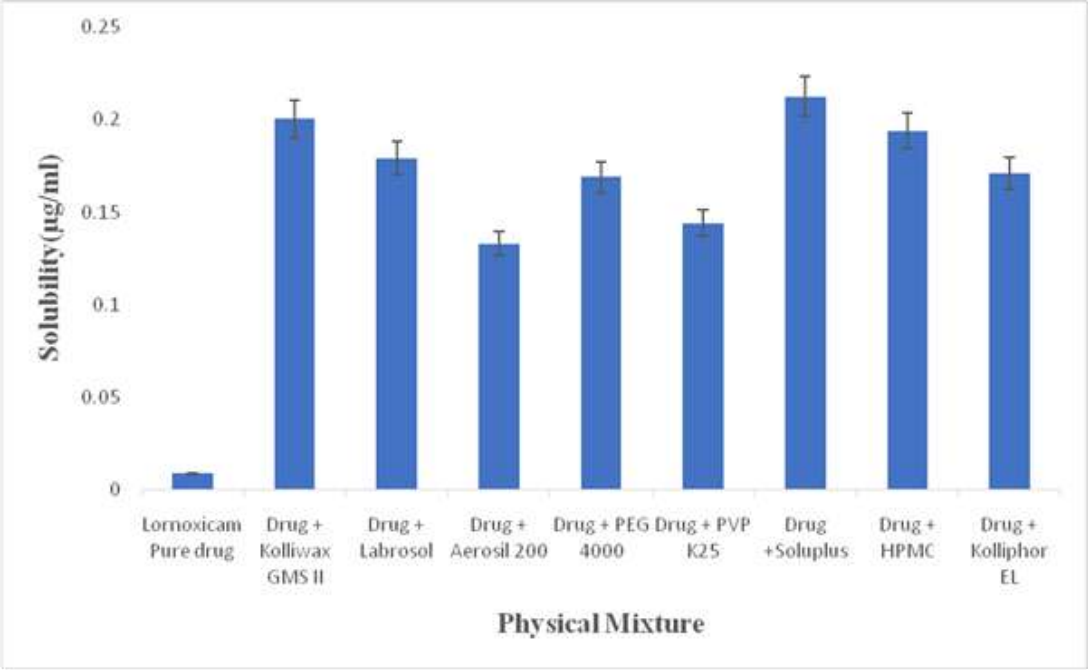

Figure 2: Solubility studies of Lornoxicam physical mixture

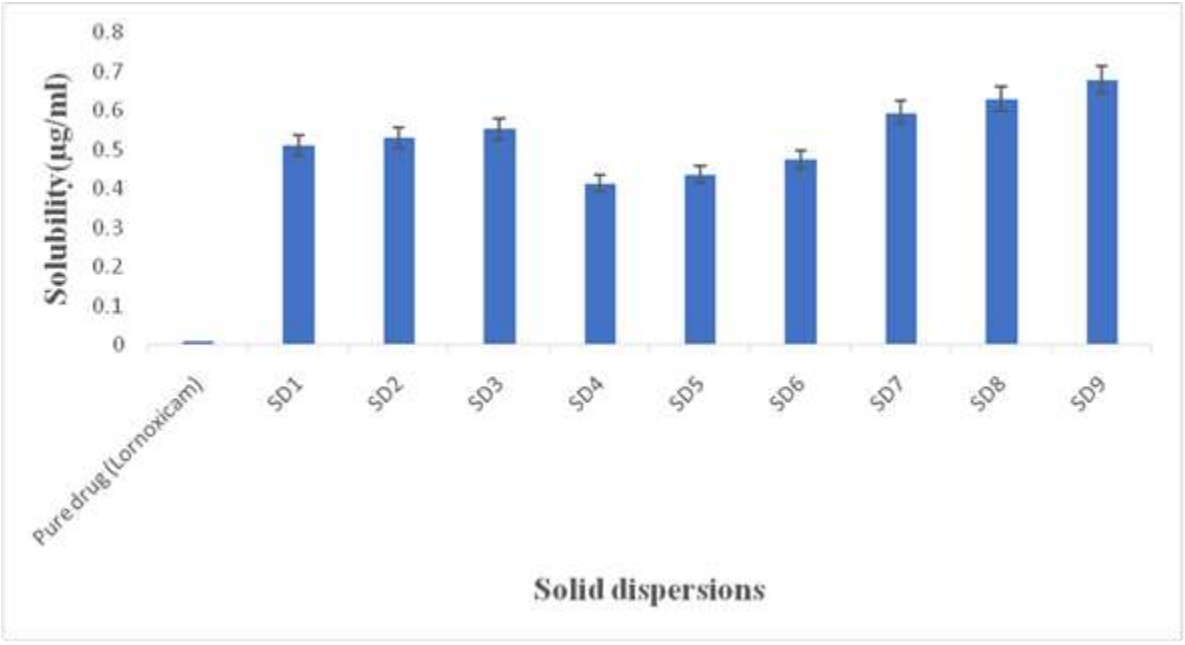

Figure 3: Solubility studies of Lornoxicam solid dispersion

Percent Practical yield and drug content

The formulation SD9 was found to have highest percent practical yield and percent drug content of 98.97% and 99.13% respectively when compared with other formulations. The results are given in Table 3.

Table 3: Percent Practical yield and drug content for Lornoxicam solid dispersions

S. No	Formulation code	% Practical Yield	% Drug content
1	SD1	95.11±0.12	90.47±0.01
2	SD2	94.46±0.01	92.49±0.15
3	SD3	93.68±0.23	94.73±0.11
4	SD4	96.11±0.20	96.16±0.27
5	SD5	95.06±0.12	95.34±0.07
6	SD6	96.68±0.08	94.26±0.19
7	SD7	96.44±0.04	95.50±0.10
8	SD8	97.32±0.12	96.52±0.03
9	SD9	98.97±0.49	99.13±0.24

***In vitro* dissolution studies**

The drug release data obtained for formulations SD1-SD9 which represent the cumulative percent drug released as a function of time for all formulations. *In vitro* studies reveal that there is marked increase in the dissolution rate of Lornoxicam from all the solid dispersions when compared to pure Lornoxicam itself. From the *in vitro* drug release profile, it can be seen that formulation SD9 containing Lornoxicam, Soluplus and SLS in 1:3:1 ratio shows higher dissolution rate of 98.99±5.29 compared with other formulations. The graphical representation of solid dispersions of SD1-SD9 with pure drug is shown in Figure 4.

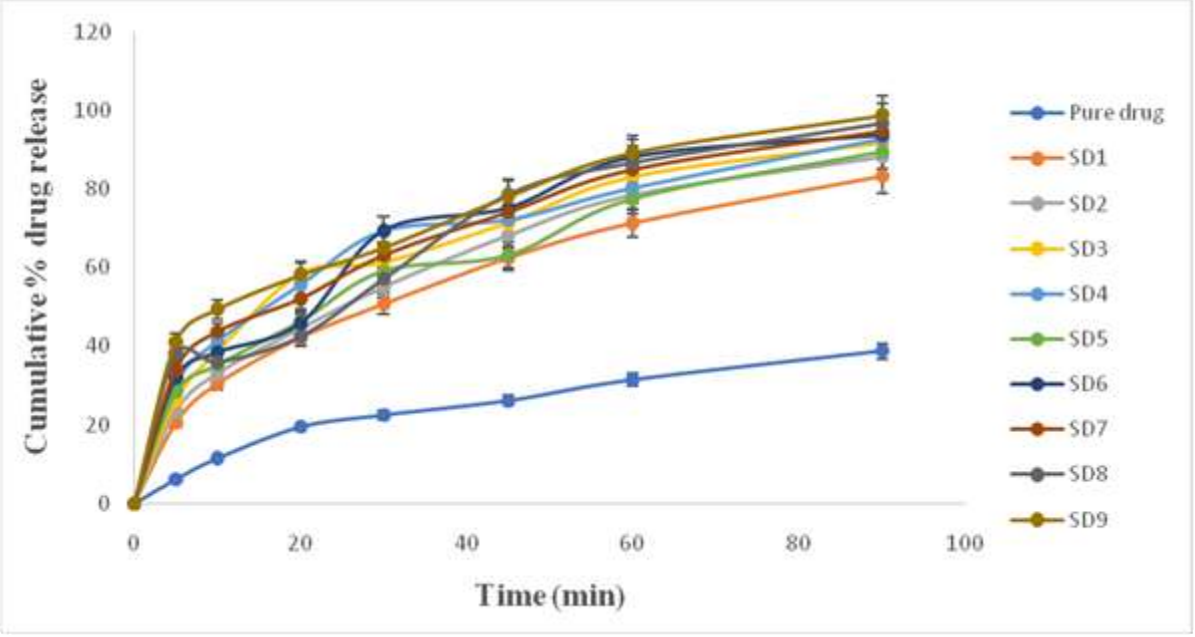

Figure 4: *In vitro* dissolution profile of pure drug and different formulations of Lornoxicam solid dispersions (SD1-SD9)

Characterization

FTIR Studies

The FTIR spectra of Lornoxicam and compare it with the formulation at 3,333 cm^{-1} (NH stretching), 1,690 cm^{-1}(C=O stretching), 1,529 cm^{-1} and 1,492 cm^{-1} (which were assigned to bending vibrations of the N-H group in the secondary amide), 1,190 cm^{-1}, 1,387 cm^{-1}, and 1,350 cm^{-1} (O=S=O group stretching), 829.42 cm^{-1} (-CH aromatic ring bending) and 744.55 cm^{-1} (C-Cl vibration bending). The characteristic IR absorption peaks of Lornoxicam were not altered in the optimized formulation, indicating no chemical interactions between the drug and used excipients. (Figure 5, 6 and 7).

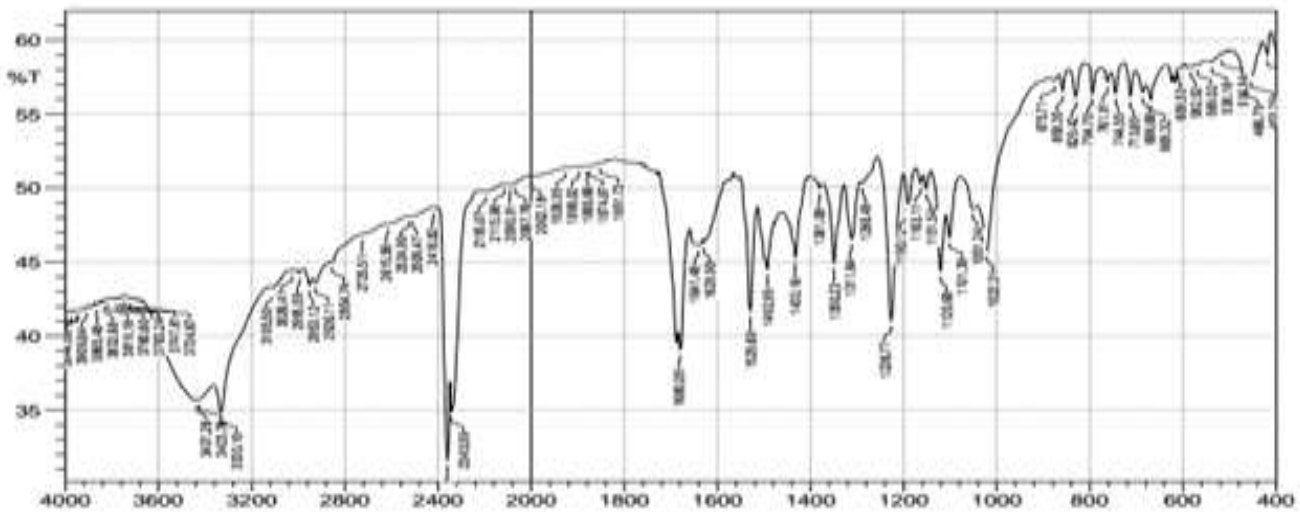

Figure 5: FTIR spectrum of Lornoxicam pure drug

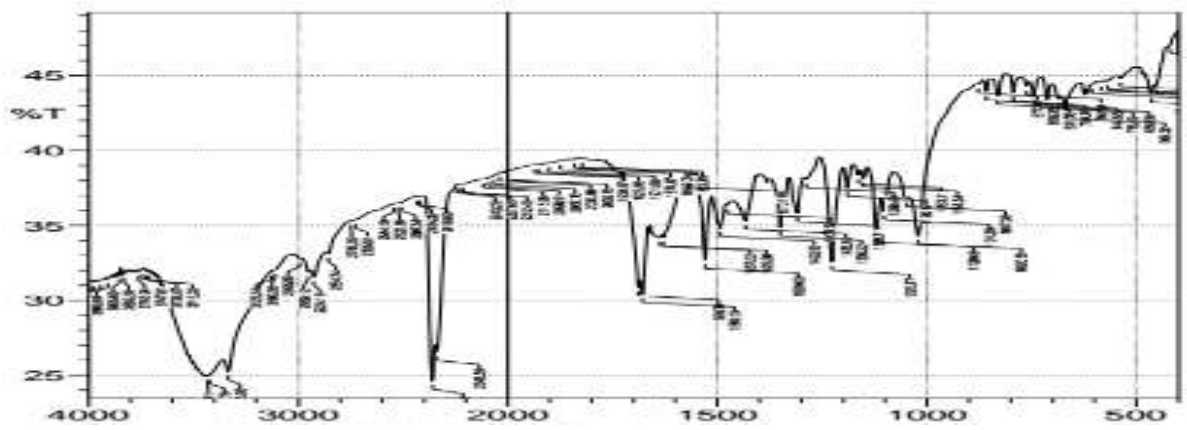

Figure 6: FTIR spectrum of physical mixture

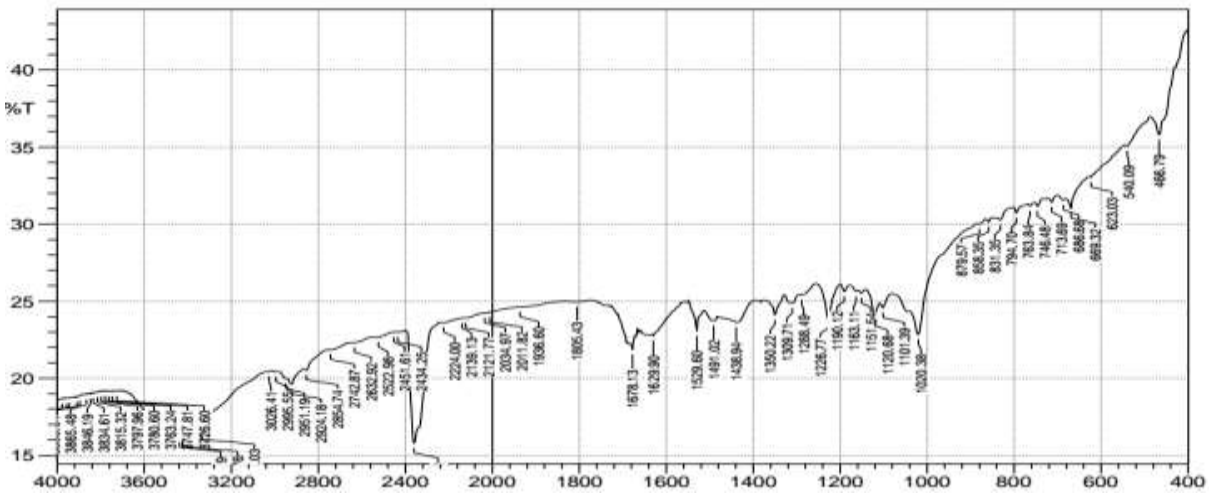

Figure 7: FTIR spectrum of optimized formulation of Lornoxicam

X-Ray Diffraction patterns

The Lornoxicam solid dispersions were studied for XRD to know whether the solid dispersions are crystalline or amorphous. The presence of numerous distinct peaks in the XRD spectrum of pure Lornoxicam indicates that Lornoxicam was present as a crystalline material (Figure 8).

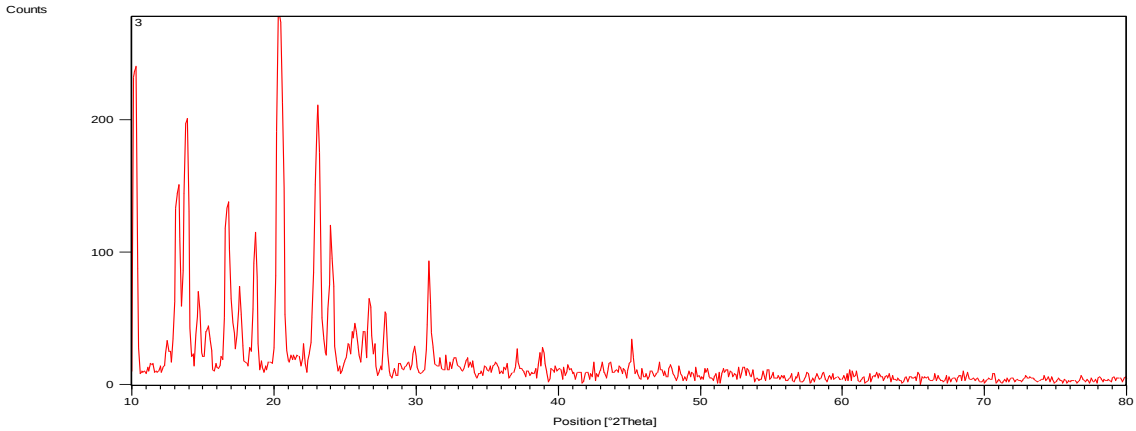

Figure 8: XRD of Lornoxicam pure drug

On the other hand, the spectrum of optimized formulation SD9 was characterized by the complete absence of any diffraction peak, which is characteristic of an amorphous compound (Figure 9).

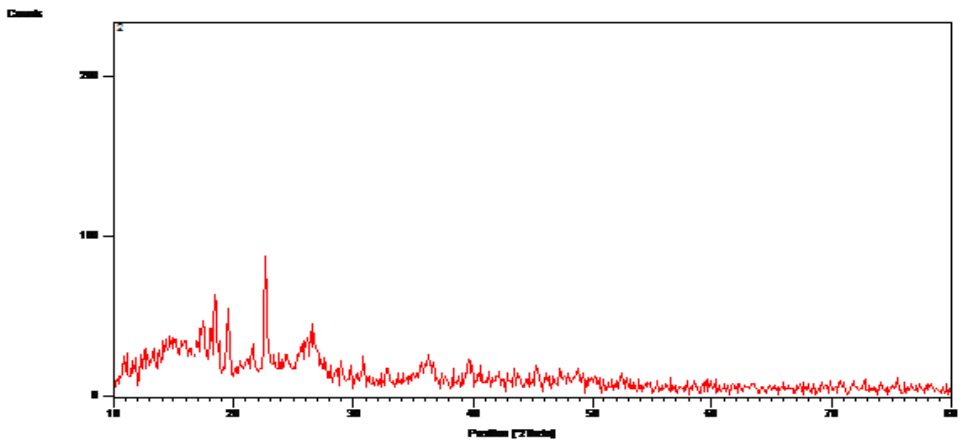

Figure 9: XRD of Lornoxicam optimized formulation

The enhancement in the dissolution rate of the drug from the drug-Soluplus-SLS solid dispersion is because of marked reduction in the crystallinity of the drug.

DSC studies

The DSC thermo grams of Pure Lornoxicam showed (Figure 10) sharp endothermic peak at melting point 229^{0}C, indicating that the drug is highly crystalline. The absence of drug peak in the solid dispersion formulation indicating the drug was converted into an amorphous form. As the intensity of the endotherm was markedly decreased in the drug – Soluplus with SLS solid dispersion, the faster dissolution rate of the drug from the solid dispersion is attributed to the reduction in the crystallinity of the drug. Crystallization inhibition is attributed to the entrapment of the drug molecules in the polymer matrix during solvent evaporation.

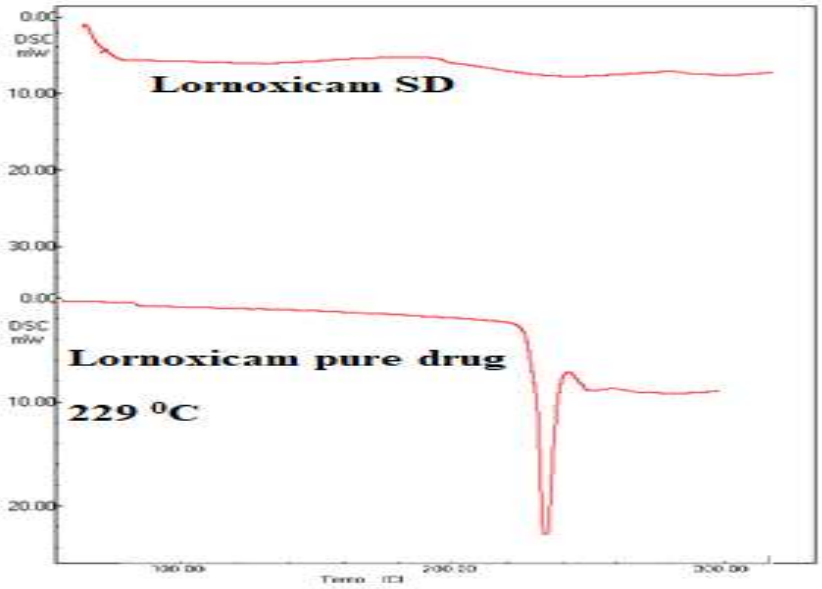

Figure 10: DSC thermograms of Lornoxicam pure drug and Optimized formulatin

SEM Studies

SEM photographs for Lornoxicam pure drug (a) and optimized formulation SE9 (b) are shown in Figure 11**.** The drug crystals seemed to be smooth-surfaced, irregular in shape and size. In case of Solid dispersions, it was difficult to distinguish the presence of drug crystals. The drug surface in solid dispersion seems to be more porous in nature. Solid dispersions appeared as uniform and homogeneously mixed mass with wrinkled surface. Drug crystals appeared to be incorporated into the particles of the polymers. The solid dispersion looked like a matrix particle. The results could be attributed to dispersion of the drug in the molten mass of the polymer.

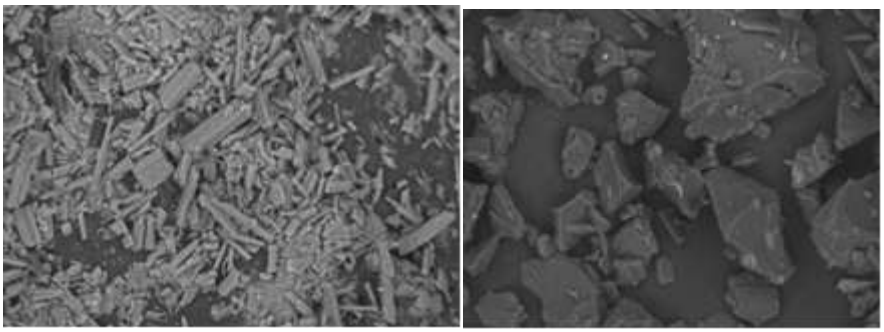

Figure 11: SEM photographs of Lornoxicam pure drug (a) and optimized formulation (b.)

Stability studies of Lornoxicam solid dispersions

Stability studies of SD9 formulation was performed for drug content and *in vitro* drug release studies for 3 months at accelerated stability conditions as per ICH guidelines. The optimized formulation was stable during 3 months period. From these results it was concluded that the formulation was stable and retained most of its properties with minor differences. The results are summarized in Table 4.

Table 4: Evaluation parameters of SD9 stored at 40 ±2^{0}C /75 ±5%RH

Retest time for optimized formulation SD9	% Drug content	*In-vitro* drug release (%)
0 days	99.13	98.74
30 days	98.09	98.01
60 days	97.15	97.09
90 days	96.11	96.04

Micromeretic properties of powder blends of fast disintegrating tablets

The micro meretic properties of powder blends are found to be within the IP limits and summarized in Table 6.

Table 6: Physical properties of prepared powder blends of fast disintegrating tablets

Formulation code	Bulk density(g/cc)	Tapped density(g/cc)	Angle of repose(Θ)	Carr's index(%)	Hausner ratio
LF1	0.56±0.02	0.54±0.01	24.34±0.4	09.23±0.8	1.13±0.02
LF2	0.58±0.12	0.58±0.04	21.67±0.3	08.23±1.0	1.11±0.07
LF3	0.59±0.04	0.64±0.05	26.54±0.1	10.12±0.7	1.13±0.09
LF4	0.50±0.04	0.68±0.04	23.89±0.2	11.34±0.6	1.14±0.03
LF5	0.65±0.02	0.59±0.02	22.56±0.1	11.23±0.8	1.11±0.05
LF6	0.50±0.21	0.66±0.12	23.30±0.1	10.23±0.5	1.12±0.06
LF7	0.52±0.06	0.64±0.03	25.56±0.2	10.34±1.0	1.14±0.06
LF8	0.53±0.01	0.68±0.03	24.67±0.3	09.11±0.8	1.12±0.03
LF9	0.57±0.01	0.61±0.01	25.56±0.3	09.45±0.7	1.13±0.02
LF10	0.58±0.13	0.67±0.06	21.66±0.2	11.45±0.5	1.15±0.01
LF11	0.53±0.09	0.68±0.12	25.34±0.2	10.23±0.5	1.13±0.01
LF12	0.57±0.06	0.64±0.21	22.99±0.5	11.34±0.5	1.12±0.01
LF13	0.54±0.01	0.67±0.04	25.14±0.3	09.67±0.4	1.11±0.02
LF14	0.51±0.04	0.66±0.07	24.09±0.2	10.23±0.4	1.14±0.03
LF15	0.53±0.01	0.63±0.04	22.78±0.4	10.45±0.3	1.10±0.02
LF16	0.54±0.02	0.61±0.07	22.45±0.4	09.68±0.2	1.13±0.02
LF17	0.59±0.21	0.68±0.03	25.09±0.3	11.47±0.8	1.12±0.02
LF18	0.58±0.03	0.67±0.08	23.05±0.2	11.99±0.3	1.14±0.02
LF19	0.56±0.02	0.61±0.12	25.06±0.2	11.45±0.6	1.13±0.01
LF20	0.59±0.06	0.64±0.1	24.78±0.1	10.12±0.5	1.15±0.01
LF21	0.59±0.07	0.63±0.03	25.34±0.4	11.09±0.4	1.16±0.02
LF22	0.56±0.15	0.63±0.04	23.42±0.3	09.34±0.2	1.10±0.03
LF23	0.58±0.13	0.66±0.13	24.45±0.3	10.67±0.4	1.14±0.02
LF24	0.56±0.12	0.68±0.05	21.12±0.2	09.68±0.6	1.14±0.05
LF25	0.56±0.13	0.62±0.06	23.67±0.5	11.24±0.5	1.11±0.05
LF26	0.53±0.12	0.65±0.02	24.12±0.3	09.39±0.5	1.13±0.05
LF27	0.55±0.09	0.66±0.12	25.56±0.2	11.05±0.7	1.14±0.02

Above parameters are communicated as Average ± Standard Deviation; (n=6)

Preparation of fast disintegrating tablets of Lornoxicam

Twenty-seven formulations (LF1-LF27) for active layer were prepared by direct compression method (Table 5) using 3^3 Response surface method with superdisintegrants like locust bean gum, gum karaya, Plantago ovata and the prepared tablets were shown in Figure 12.

Figure 12: Fast disintegrating tablets of Lornoxicam

Physico-chemical properties of fast disintegrating tablets of Lornoxicam

The prepared tablets were evaluated for different physicochemical properties and the results are found to be within the Pharmacopoeial limits, which depicted in Table 7.

Table 7: Physico-chemical parameters of Fast Disintegrating Tablets of Lornoxicam

F.NO	*Weight variation(mg)	#Thickness (mm)	#Hardness (Kg/Cm^2)	#Friability (%)	#Content uniformity(%)	DT (Sec)
LF1	201.65±1.2	4.0±0.12	3.0±0.12	0.52±0.01	95.23±0.63	49±1.23
LF2	198.69±0.8	4.1±0.06	3.1±0.06	0.55±0.02	97.04±0.06	71±1.51
LF3	198.04±0.5	4.1±0.06	3.1±0.06	0.63±0.03	95.56±0.14	65±1.40
LF4	201.05±0.0	4.2±0.12	3.2±0.12	0.72±0.01	98.11±1.01	55±1.19
LF5	201.54±0.4	4.0±0.00	3.0±0.00	0.62±0.02	94.23±0.8	65±1.25
LF6	200.78±0.4	4.3±0.10	3.1±0.06	0.66±0.01	95.45±0.31	48±1.87
LF7	200.65±0.3	4.1±0.10	3.1±0.10	0.58±0.02	94.11±0.49	57±1.63
LF8	199.57±0.2	4.3±0.25	3.3±0.40	0.69±0.01	97.23±0.51	68±1.37
LF9	200.76±0.35	4.3±0.06	3.3±0.06	0.58±0.00	96.13±0.56	56±1.19
LF10	200.49±0.2	4.2±0.20	3.2±0.42	0.79±0.02	95.23±0.24	58±1.24
LF11	201.53±0.4	4.2±0.06	3.3±0.06	0.76±0.01	97.97±0.21	63±1.19
LF12	202.58±0.3	4.3±0.00	3.4±0.06	0.73±0.02	97.45±0.76	56±1.40
LF13	201.34±0.2	4.3±0.26	3.8±0.35	0.72±0.02	97.45±0.48	52±1.73
LF14	198.67±0.3	4.1±0.21	3.4±0.21	0.74±0.03	96.98±0.23	55±1.87
LF15	199.65±0.2	4.4±0.06	3.8±0.23	0.75±0.02	96.45±0.36	68±1.35
LF16	200.65±0.3	4.2±0.25	3.4±0.23	0.78±0.01	96.45±0.69	54±1.81
LF17	201.79±0.4	4.5±0.15	3.8±0.32	0.79±0.01	96.34±0.35	53±1.56
LF18	201.87±0.1	4.5±0.25	3.7±0.35	0.82±0.01	97.56±0.23	52±1.12
LF19	199.67±0.3	4.0±0.12	3.±0.12	0.84±0.03	96.29±0.34	57±1.33
LF20	199.32±0.2	4.2±0.12	3.5±0.2	0.63±0.03	97.18±0.81	48±132
LF21	198.27±0.4	4.2±0.06	3.3±0.06	0.66±0.02	96.27±0.11	55±1.27
LF22	200.27±0.1	4.0±0.12	3.0±0.12	0.53±0.03	96.78±0.07	60±1.61
LF23	200.26±0.13	4.3±0.17	3.8±0.4	0.76±0.05	96.14±0.76	68±1.49
LF24	200.10±0.5	4.3±0.13	3.7±0.23	0.43±0.08	99.16±0.12	33±1.31
LF25	199.12±0.6	4.1±0.17	3.6±0.12	0.67±0.02	96.23±0.00	51±1.39
LF26	200.16±0.8	4.4±0.10	3.7±0.21	0.72±0.89	97.34±0.23	69±1.40
LF27	200.29±0.15	4.5±0.29	3.9±0.45	0.89±0.03	97.10±0.40	53±1.77

*Values are expressed in mean± SD :(n=20)

#Values are expressed in mean± SD :(n=3)

In vitro Drug Release Profile of Fast Disintegrating Tablets of Lornoxicam was shown in Figure 13, 14, 15 and 16.

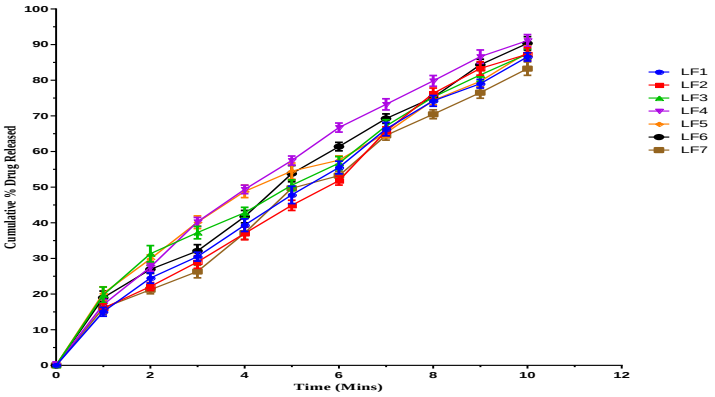

Figure 13: *In vitro* Drug Release Profile of Fast Disintegrating Tablets of Lornoxicam LF1-LF7

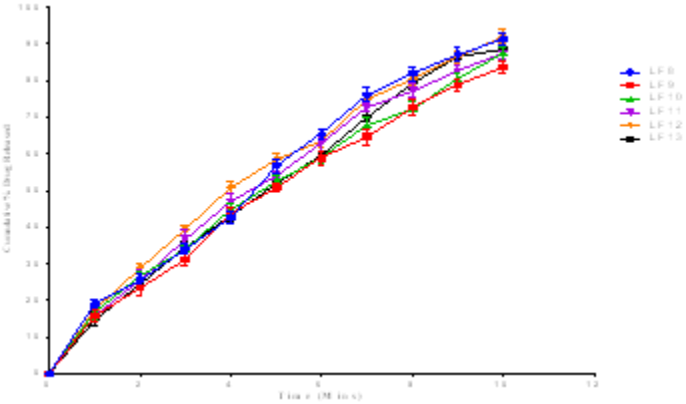

Figure 14: *In vitro* Drug Release Profile of Fast Disintegrating Tablets of Lornoxicam LF8-LF13

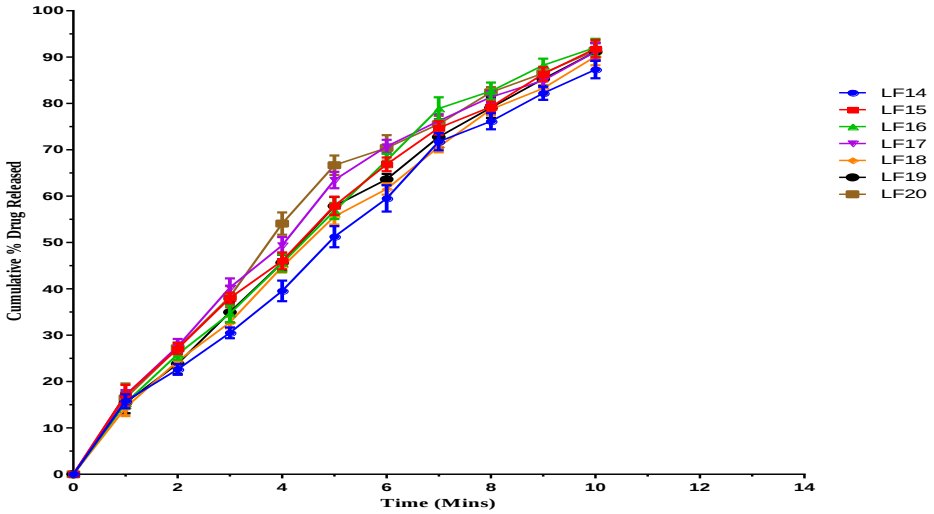

Figure 15: *In vitro* Drug Release Profile of Fast Disintegrating Tablets of Lornoxicam LF14-LF20

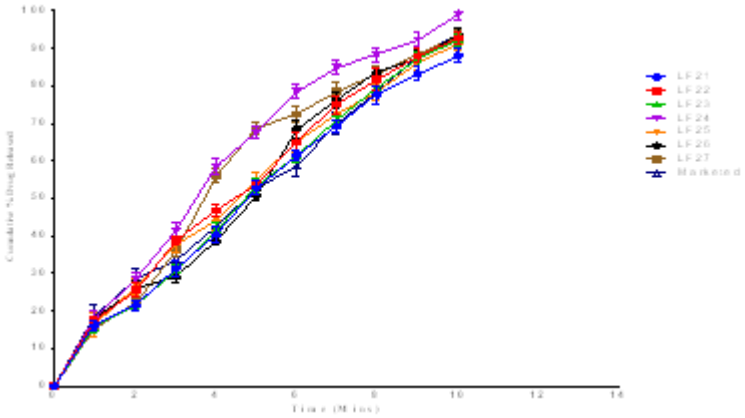

Figure 16: *In vitro* Drug Release Profile of Fast Disintegrating Tablets of Lornoxicam LF21-LF27

Design of Experiment

This method is mainly used to explain the effect of one factor on another factor, whether this effect is significant or not, if significant how it influences the response. In this present work the effect of one factor (Plantago ovate mucilage) on other two factors (Locust Bean Gum, Gum Karaya, and Plantago ovate mucilage) is explained.

In the graph (Figure 17) the effect of Plantago Ovata Mucilage on % cumulative drug release is examined and it clearly indicates that there is a very significant effect of Plantago Ovata Mucilage on % cumulative drug release. From the *in vitro* drug release study observed that as concentration of superdisintegrants increase, % drug release was increased to certain level beyond it as the concentration of superdisintegrants increase, % drug release was decreased. But prediction of results of % drug release, response surface plot was plotted for graphical representation of results. So, Figure 17 showed common effect of superdisintegrants concentration.

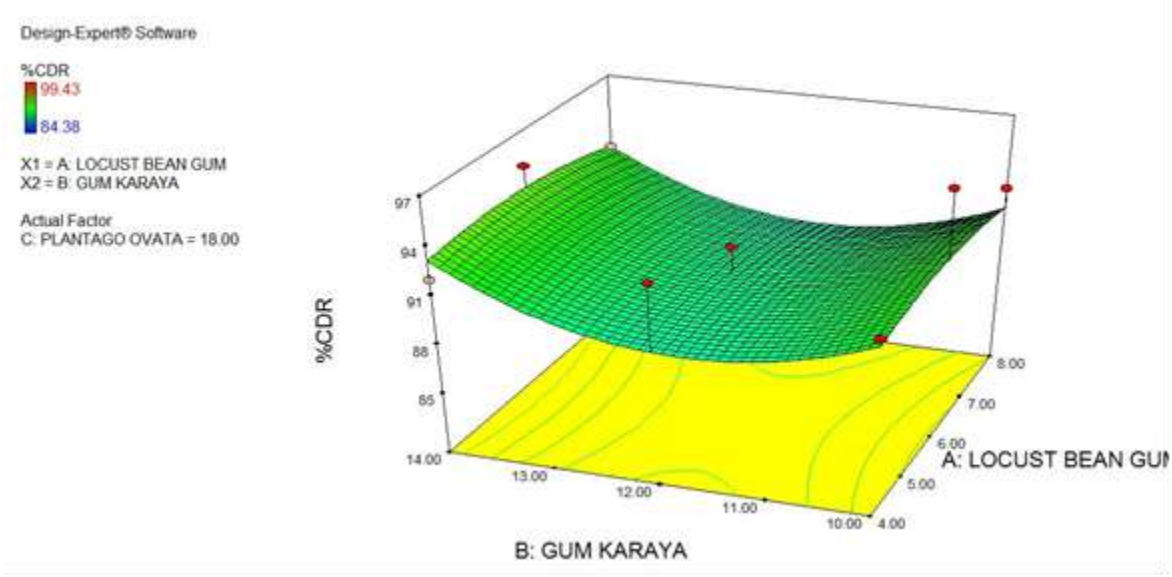

Figure 17: Response surface plot showing the influence of amount of Superdisintegrants on the release profile of Lornoxicam for % Cumulative Drug Release.

In the graph (Figure 18) the effect of Plantago Ovata Mucilage on disintegration time release is examined and it clearly indicates that there is a very significant effect of Plantago Ovata Mucilage on Disintegration Time. From the Disintegration Time study observed that as concentration of superdisintegrants increase, Disintegration Time was decreased.

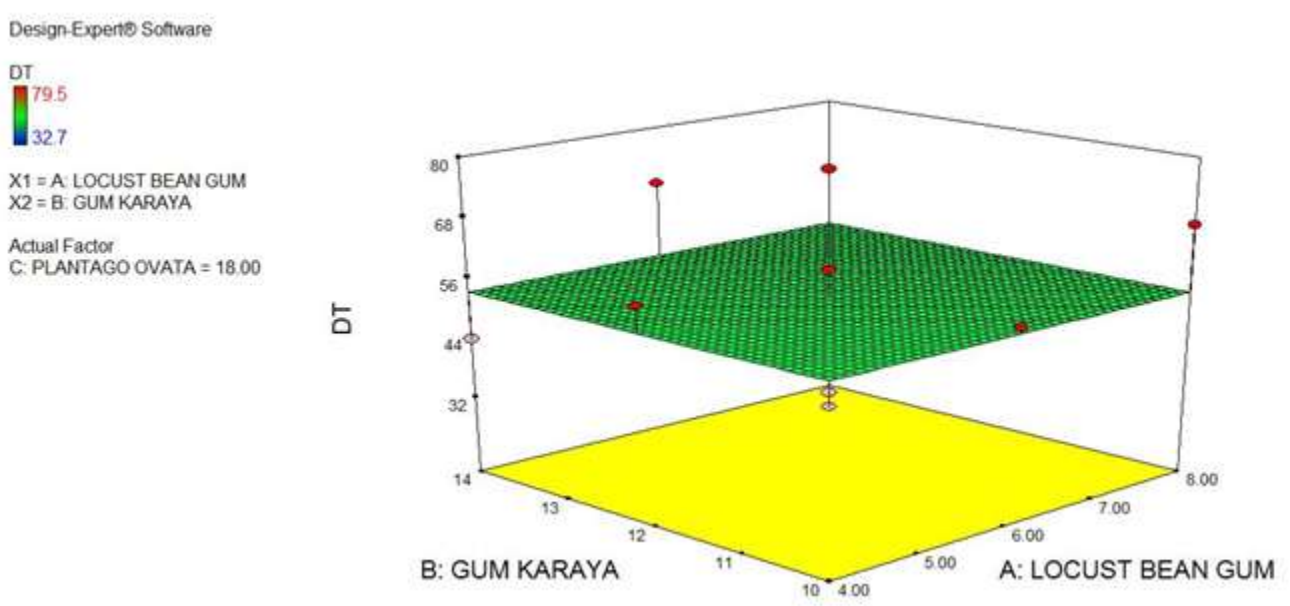

Figure 18: Response surface plot showing the influence of amount of superdisintegrants on Disintegration Time of Lornoxicam

Stability Studies

The developed formulation was subjected to stability studies for 6 months according to ICH guidelines to evaluate its stability and the integrity of the dosage form. From these results, it was concluded that, theoptimized formulation is stable and retained their original properties of hardness, disintegration test and *in vitro* dissolution studies with minor differences (Table 8).

Table 8: Stability studies of optimized formulation

Retest Time for Optimized formulation (LF24)	**#Hardness (Kg/Cm^2)**	**Disintegration test (Sec)**	***In-vitro* drug release profile (%)**
0 days	4.3±0.13	33±1.31	99.21±1.87
30 days	4.3±0.11	33±0.09	99.20±1.23
60 days	4.3±0.08	34±0.15	99.20±1.15
120 days	4.3±0.04	34±0.11	99.18±1.20
180 days	4.3±0.04	34±0.05	99.18±1.13

*Values are expressed in mean± SD :(n=6)

CONCLUSION

From the present study it can be concluded that the solid dispersion incorporated fast disintegrating tablets of Lornoxicam has shown the increased dissolution rate and aqueous solubility and to enable faster onset of action. Solid dispersions are prepared with polymers like Kolliwax GMS, Soluplus and HPMC in three different ratios 1:1:1, 1:2:1 and 1:3:1. Formulations were characterized for drug content studies, drug release studies, and drug-polymer interactions using Fourier transform infrared spectroscopy (FTIR) spectrum. The solid dispersions can be evaluated by *in vitro* dissolution studies. The optimized solid dispersion SD9 was further used to prepare fast disintegrating tablet by direct compression method using 3^3 Response surface method with natural superdisintegrants like locust bean gum, gum karaya, Plant ago ovata. The values of pre-compression parameters evaluated, were within prescribed limits and indicated good free flowing properties. The data obtained of post-compression parameters such as weight variation, hardness, friability, content uniformity, disintegration time (33 sec) and percentage drug release was maximum in LF24 (99.21±1.87%) and was found to superior over conventional formulation. It can be concluded that fast disintegrating tablets using Lornoxicam solid dispersion could be used to improve better patient compliance in the effective management of pain and inflammation.

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