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## FORMULATION AND EVALUATION OF ORAL SELF EMULSIFYING DRUG DELIVERY SYSTEM OF LORNOXICAM

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### ABSTRACT

The objective of the present study is to formulate Self emulsifying drug delivery system (SEDDS) of lornoxicam, an anti-inflammatory drug to sustain the drug release and to reduce the side effects. The study involves combining oils with food grade non ionic emulsifiers to form concentrates that can incorporate large quantities of water and remain as a single phase liquid. Solubility studies were performed to select oils, surfactants and co-surfactants for the formulation. of the drug (BCS class II). In this study, self emulsifying formulations (Batch F1 to F20) of drug Lornoxicam were made using different concentration of Capryol 90, Tween 20, Tween 80, Transcutol P, Propylene glycol. Systematic optimization was carried out , with a goal to minimize self emulsification time, to sustain the percentage drug release and reduce the side effects. The best emulsification grade was with batch F9. The *in vitro* drug release of Lornoxicam SEDDS was sustained (87.12% for 24 hours) when compared to marketed formulation Lornoxi (tablet) (100% at 90 mins). Pharmaco dynamic studies performed by paw volume method indicated significant ( $p < 0.05$ ) inhibition in paw edema (75%) for the test formulation after 4hours as compared to the standard formulation (56%).

**KEYWORDS:** Lornoxicam, Self Emulsification, Optimization, Solubility, *In vitro* drug release



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## INTRODUCTION

Lipid-based formulations are well known approach to enhance water solubility and oral bioavailability of BCS Class II drugs. Various strategies are explored for lipid soluble drugs including the use of surfactants, lipids, permeation enhancers, micronization, salt formation, cyclodextrins, nanoparticles and solid dispersion.

Recently, due to good and reliable result, there is a great emphasis on self-emulsifying drug delivery systems (SEDDS) to improve the oral bioavailability of lipophilic drugs. SEDDS formulations are isotropic mixtures of an oil, a surfactant, a cosurfactant (or cosolvents), and a drug. The basic principle of this system is its ability to form fine oil-in-water (o/w) micro emulsion under gentle agitation following dilution by aqueous phases. This spontaneous formation of an emulsion in the GI tract presents the drug in a solubilized form, and the small size of the formed droplet provides a large interfacial surface area for drug absorption. Further, the presence of oily phase in the formulation helps improve bioavailability by affecting the drug absorption<sup>1</sup>. The ability of certain lipid compounds and their metabolites to initiate changes in the gastrointestinal fluid to favor improved drug absorption. The inhibition of cellular efflux mechanisms and pre-absorptive metabolism by gut membrane-bound cytochrome enzymes, further augmenting the absorption enhancing properties of these formulations. Certain lipidic excipients are associated with selective drug uptake into the lymphatic transport system, thereby reducing the effect of first-pass drug metabolism in the liver<sup>2</sup>. This indicates the advantage of formulating lornoxicam as SEDDS. Lornoxicam is a new nonsteroidal anti-inflammatory drug (NSAID) of the oxicam class having a short half life of 3-4hrs with analgesic, anti-inflammatory and antipyretic properties. Lornoxicam differs from other oxicam compounds in its potent inhibition of prostaglandin biosynthesis, a property that explains the particularly pronounced efficacy of the drug<sup>3</sup>. Lornoxicam has side effects similar to other NSAIDs, most commonly mild ones like gastrointestinal disorders

(nausea and diarrhea) and headache. Severe but rare side effects include bleeding, bronchospasms and the extremely rare Stevens–Johnson syndrome. To overcome these side effects lornoxicam can be formulated and given in the form of a self-emulsifying drug delivery system. Oral absorption of several drugs has been enhanced by SEDDS with different mechanisms. This study is done to sustain the activity of Lornoxicam and reduce the side effects. For the present study 8mg dose was selected for the formulation. The objective of the study was to design, optimize and evaluate the SEDDS of lornoxicam.

## MATERIALS AND METHODS

### *Materials*

Lornoxicam was obtained as gift sample from M/s Optimus Pharma, Hyderabad. Capryol 90 was purchased from Gattefosse Mumbai, India, Tween 20 and Tween 80 were supplied by S.D fine chemicals and Transcutol P was supplied by Avra labs Hyderabad. All other reagents used were of suitable analytical grade and used as supplied.

### *Solubility Studies*

The solubility of drug in various oils (Capryol 90, Isopropyl myristate, Oleic acid, Olive oil and Linseed oil), surfactants (Tween 20 and Tween 80) and cosurfactants (Transcutol P, Propylene glycol, PEG 400 and Glycerol) was determined as follows: 5ml of each of the selected vehicles was added to each cap vial containing an excess amount of drug, and mixed using a cyclic mixer. The vials were then kept at 25±1°C in an Orbital shaker for 72h to reach equilibrium. The samples were removed after achieving equilibrium and centrifuged at 3000 rpm for 15 minutes. The supernatant was taken and filtered through a membrane filter (0.45-µm 13mm Whatman, Mumbai, India). The filtrate was diluted with the pH 7.4 buffer and the concentration of drug was determined using UV-Visible spectrophotometer (Lab India) at 373nm.

### **Construction of phase diagrams**

The pseudo ternary phase diagrams were constructed by aqueous titration method using Capryol 90 as oil, Tween 20 and Tween 80 as surfactants, Transcutol P and Propylene glycol as cosurfactants. Surfactant and cosurfactant (Smix) were mixed in different weight ratios (1:1, 1:2 and 1:3). These Smix ratios were chosen in increasing concentration of cosurfactant with respect to surfactant for study of the phase diagrams needed for nanoemulsion formation. For each phase diagram, oil and Smix were combined in different weight ratios from 1:9 to 9:1 in different glass vials. Slow titration with the aqueous phase was done to each weight ratio of oil and Smix, and visual observations were made for transparent and easily flowable nanoemulsions. The pseudo ternary phase diagrams were constructed using Triplot V4 software (4.1.2. version).

### **Preparation of SEDDS**

SEDDS were prepared by aqueous phase titration method<sup>4</sup>. The composition of the nanoemulsions was chosen according to the pseudo ternary phase diagram. The drug was first dissolved in the oil, and later subjected for sonication. Surfactant and cosurfactant mixture was prepared and added in the chosen concentration to the drug and oil mixture, later water was added drop wise with continuous stirring until clear nanoemulsion formed.

### **Characterization of SEDDS.**

#### **Drug - Excipient compatibility studies**

Fourier transform infrared analysis (SHIMADZU) was conducted to study the drug excipient interactions. Samples were scanned in the range from 400-4000cm<sup>-1</sup>.

#### **Particle size and zeta potential measurement**

The formulation (0.1 ml) was dispersed in 50 ml of water in volumetric flask and gently mixed by inverting the flask. Globule size and zeta potential of the nanoemulsion was determined by particle size analyzer (Horiba) that analyzes the fluctuations in light scattering due to Brownian motion of the particles. Light

scattering was monitored at 25 °C at a 90° angle.

### **Thermodynamic Stability Studies**

Selected formulations were subjected to different thermodynamic stability tests<sup>5</sup> to assess their physical stability.

1. Heating-cooling cycle: Six cycles between refrigerator temperature (4°C) and 45°C with storage at each temperature for not less than 48h were conducted, and the formulations were examined for stability at these temperatures.

2. Centrifugation test: Formulations were centrifuged at 3500 rpm for 30 min, and examined for phase separation.

3. Freeze-thaw cycle: The formulations were subjected to freeze-thaw cycles between -4°C and +40°C for not less than 48hours at each temperature and observed for any phase separation.

### **Percent Transmittance**

The percent transmittance of the nano emulsion was measured using UV-Visible double beam spectrophotometer keeping distilled water as blank at 560nm.

### **Viscosity**

Viscosity of the samples was measured as such without dilution using Brookfield viscometer (LVDV-II+P) fitted with an S-34 spindle at 25°C. A sample volume of 10ml was used. The nano emulsion formulations were subjected to different rpm (5, 10, 20, 30, 50, 60 and 100) and the rheological behavior of the disperse system was examined by constructing rheograms of shear stress vs. shear rate.

### **In vitro drug release studies**

Formulation containing single dose of the drug was placed in the dialysis bag, which was immersed in 50ml of 0.1 N HCl for 2hrs and replaced with pH 7.4 buffer maintained at 37°C and stirred with a magnetic stirrer. Samples were withdrawn at predetermined time intervals. In order to maintain sink conditions, an equal volume of medium was replaced. The samples were analyzed by the UV-Visible

spectrophotometer at 373nm to determine the concentration of the drug.

### Evaluation of anti-inflammatory activity

The anti-inflammatory activity of prepared lornoxicam SEDDS was evaluated by the carrageenan-induced rat hind paw edema method. The experimental protocol was designed and approval of Institutional Animal Ethics Committee (IAEC) (Reg. No. 1722/ PO / A / 13 / IAEC / CPCSEA EXP-049 ) was obtained. Wistar strain male albino rats weighing between (150-200 g) were used. The animals were in a light controlled 12 hours cycle with free access to food and water. Animals were fasted overnight before experiment with free access to water. Anti-inflammatory activity of the lornoxicam SEDDS

was compared to the marketed product. Animals were divided into three groups of six animals each. Group I (control) received normal saline. Group II, received standard drug Indomethacin and Group III received lornoxicam SEDDS. Paw edema was induced by injecting 50 µl of 1% w/v carrageenan into the sub planar region of the left hind paw. Paw volume was determined at different time intervals in all groups. Difference in the paw volume, determined before and after injection of the edema-provoking agent indicated the severity of edema. Volumes of right hind paw of controls and treated animals were measured with a plethysmometer and the percentage inhibition of inflammatory reaction was determined for each animal by comparison with control and calculated by the following formula.

$$\% \text{ inhibition of edema} = (V_{\text{control}} - V_{\text{test}}) \times 100 / V_{\text{control}}$$

where,  $V_{\text{control}}$  = mean edema of rats in control group;  
 $V_{\text{test}}$  = mean edema volume of rats in tested group.

## RESULTS AND DISCUSSION

### Solubility Studies

The solubility of drug in various oils (Capryol 90, Isopropyl myristate, Oleic acid, Olive oil and Linseed oil), surfactants (Tween 20 and Tween

80) and cosurfactants (Transcutol P, Propylene glycol, PEG 400 and Glycerol) was determined and is presented in Table-1 Based on these studies Capryol90 was selected as the oil Tween 20 and Tween 80 as surfactants and Transcutol P as cosurfactant.

**Table 1**  
**Solubility Studies**

| Oil         | Solubility <sup>a</sup> (mg/ml) | Surfactant | Solubility <sup>a</sup> (mg/ml) | Cosurfactant | Solubility <sup>a</sup> (mg/ml) |
|-------------|---------------------------------|------------|---------------------------------|--------------|---------------------------------|
| Capryol90   | 22.50±1.23                      | Tween 20   | 30.21±1.68                      | Transcutol P | 8.03±0.11                       |
| IPM         | 36.09±1.50                      | Tween 80   | 10.62±0.92                      | PG           | 6.50±0.24                       |
| Oleic acid  | 20.28±1.23                      | -          | -                               | PEG 400      | 7.35±0.24                       |
| Olive oil   | 32.56±2.33                      | -          | -                               | Glycerine    | 4.98±0.16                       |
| Linseed oil | 40.08±1.83                      | -          | -                               | -            | -                               |
| Alotic oil  | 70.15±2.50                      | -          | -                               | -            | -                               |

[<sup>a</sup>Data expressed as mg/ml ± SD (n=3)]

### Construction of phase diagrams

The pseudo ternary phase diagrams were constructed by aqueous titration method using Capryol 90 as oil, Tween 20 and Tween 80 as surfactants and Transcutol P and Propylene glycol as co-surfactants. Surfactant and co-surfactant (Smix) were mixed in different weight ratios (1:1, 1:2 and 1:3). These Smix ratios were chosen in increasing concentration of co-

surfactant with respect to surfactant for study of the phase diagrams needed for SEDDS formation. For each phase diagram, oil and Smix were combined in different weight ratios from 1:9 to 9:1 in different glass vials. Slow titration with the aqueous phase was done to each weight ratio of oil and Smix, and visual observations were made for transparent and easily flowable SEDDS. The pseudo ternary

phase diagrams were constructed using Triplot V4 software (4.1.2. version) Pseudo ternary phase diagrams were constructed for 1:1, 1:2 and 1:3  $S_{mix}$  ratios. So that nano emulsion regions could be identified. In construction of phase diagrams Capryol 90 was used as oil, tween 20, tween80 were used as surfactants and transcutool P, Propylene glycol were used as cosurfactants. In group I Capryol 90 was used as oil, tween 20 was used as surfactant and Transcutol P was used as cosurfactant. When the  $S_{mix}$  ratio was 1:1 the maximum amount of oil that could be emulsified was found to be 60% (w/w) using 33% (w/w) of  $S_{mix}$ . When the proportion of cosurfactant was doubled ( $S_{mix}$  1:2) the nanoemulsion region was slightly decreased when compared to  $S_{mix}$  of 1:1 and the maximum amount of oil that could be emulsified was found to be 63% (w/w) using 38% (w/w) of  $S_{mix}$ . When the proportion of  $S_{mix}$  was increased by three times ( $S_{mix}$  1:3) the nanoemulsion region was further decreased and the maximum amount that could be

emulsified was found to be 58% (w/w) using 32% (w/w) of  $S_{mix}$ . In group II Capryol 90 was used as oil, Tween 80 was used as surfactant and Transcutol P was used as cosurfactant. When the  $S_{mix}$  was 1:1 the maximum amount of oil that could be emulsified was found to be 59% (w/w) using 33% (w/w) of  $S_{mix}$ . When the proportion of cosurfactant was doubled ( $S_{mix}$  1:2) the nanoemulsion region was increased when compared to  $S_{mix}$  1:1 and the maximum amount of oil that could be emulsified was found to be 63% (w/w) using 30% (w/w) of  $S_{mix}$ . When the proportion of  $S_{mix}$  was increased by three times ( $S_{mix}$  1:3) the nanoemulsion region was decreased when compared to  $S_{mix}$  1:2 and the maximum amount of the oil that could be emulsified was found to be 62% (w/w) using 28% (w/w) of  $S_{mix}$ . Based on the pseudo ternary phase diagrams, the formulations in which the amount of oil phase completely solubilized the drug and which could accommodate the optimum quantity of  $S_{mix}$  and distilled water were selected for the study.

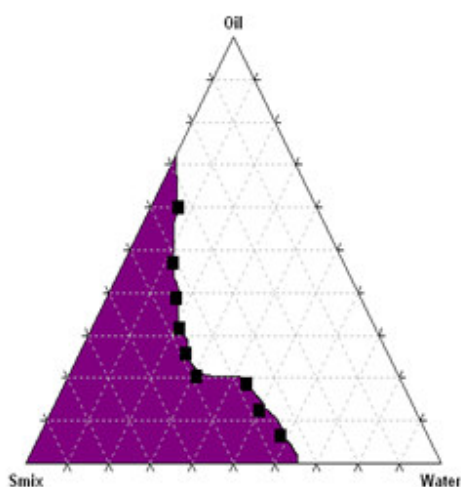


Fig 1(a)

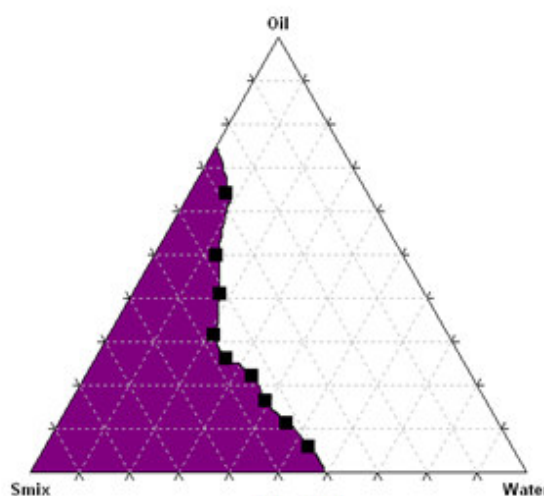


Fig 1(b)

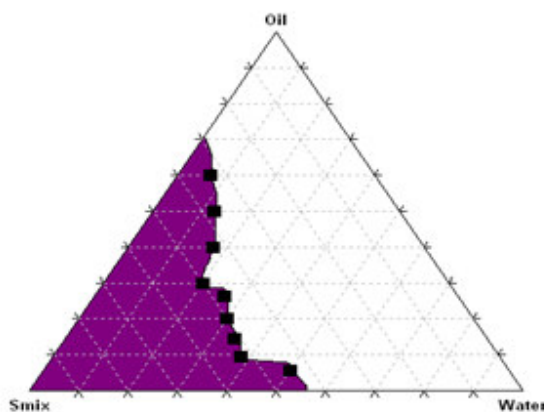


Fig 1 (c)

*Pseudo ternary phase diagrams involving Capryol 90, Tween 20 and Transcutol P as the oil, surfactant and cosurfactant respectively (group I). Ratio of surfactant to cosurfactant in Fig 1 (a) is 1:1, Fig 1 (b) is 1:2 and Fig 1(c) is 1:3.*

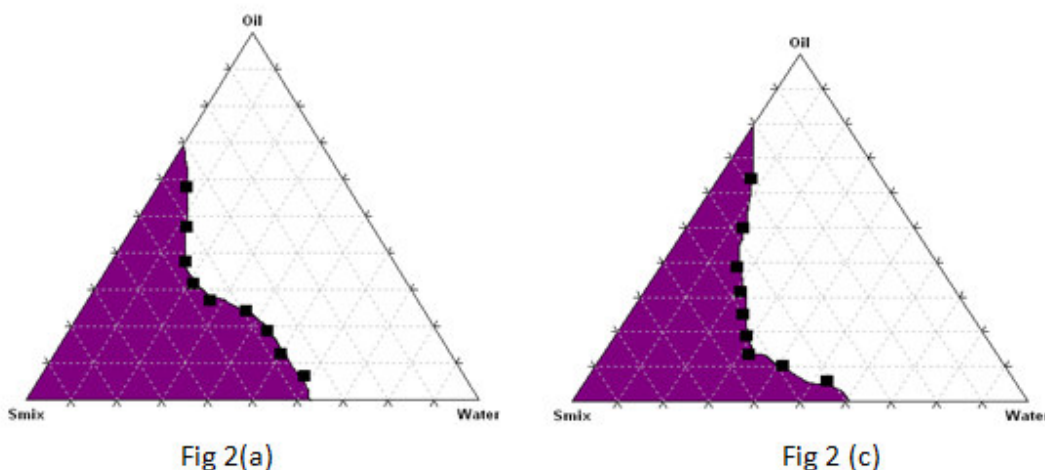


Fig 2(a)

Fig 2 (c)

*Pseudo ternary phase diagrams involving Capryol 90, Tween 80 and Transcutol P as the oil, surfactant and cosurfactant respectively (group II). Ratio of surfactant to cosurfactant in Fig 2(a) is 1:1, Fig 2(b) is 1:2 and Fig 2(c) is 1:3.*

### Preparation of SEDDS

SEDDS formulations were prepared by water titration method. The formulations are presented in Table 2, 3, 4 & 5 .

**Table 2**  
**Formulations with Capryol 90, Tween 20, Transcutol P and water(%w/w)**  
**(Surfactant to cosurfactant ratio is 1:2)**

| Formulation code | Oil   | Surfactant | Cosurfactant | Water |
|------------------|-------|------------|--------------|-------|
| F1               | 64.28 | 9.523      | 19.04        | 7.14  |
| F2               | 50.00 | 12.50      | 25.00        | 12.50 |
| F3               | 41.17 | 13.72      | 27.44        | 17.64 |
| F4               | 31.50 | 15.76      | 32.46        | 21.00 |
| F5               | 30.70 | 14.80      | 29.57        | 30.00 |



**Table 3**  
**Formulations with Caproyl 90, Tween 20, Transcutol P and water(%w/w)**  
**(Surfactant to cosurfactant ratio is 1:3)**

| Formulation code | Oil   | Surfactant | Cosurfactant | Water |
|------------------|-------|------------|--------------|-------|
| F6               | 58.08 | 8.332      | 24.99        | 8..60 |
| F7               | 48.20 | 9.375      | 28.125       | 14.30 |
| F8               | 40.01 | 10.712     | 32.137       | 17.14 |
| F9               | 30.00 | 12.50      | 37.50        | 20.00 |
| F10              | 27.33 | 12.125     | 36.375       | 26.53 |

**Table 4**  
**Formulations with Caproyl 90, Tween 80, Transcutol P and water(%w/w)**  
**(Surfactant to cosurfactant ratio is 1:2)**

| Formulation code | Oil   | Surfactant | Cosurfactant | Water |
|------------------|-------|------------|--------------|-------|
| F11              | 63.28 | 10.523     | 20.04        | 8.14  |
| F12              | 47.07 | 14.05      | 28.08        | 10.76 |
| F13              | 39.88 | 14.80      | 29.30        | 15.66 |
| F14              | 32.40 | 15.31      | 30.59        | 21.62 |
| F15              | 25.30 | 15.77      | 31.23        | 27.30 |

**Table 5**  
**Formulations with Caproyl 90, Tween 80, Transcutol P and water(%w/w)**  
**(Surfactant to cosurfactant ratio is 1:3)**

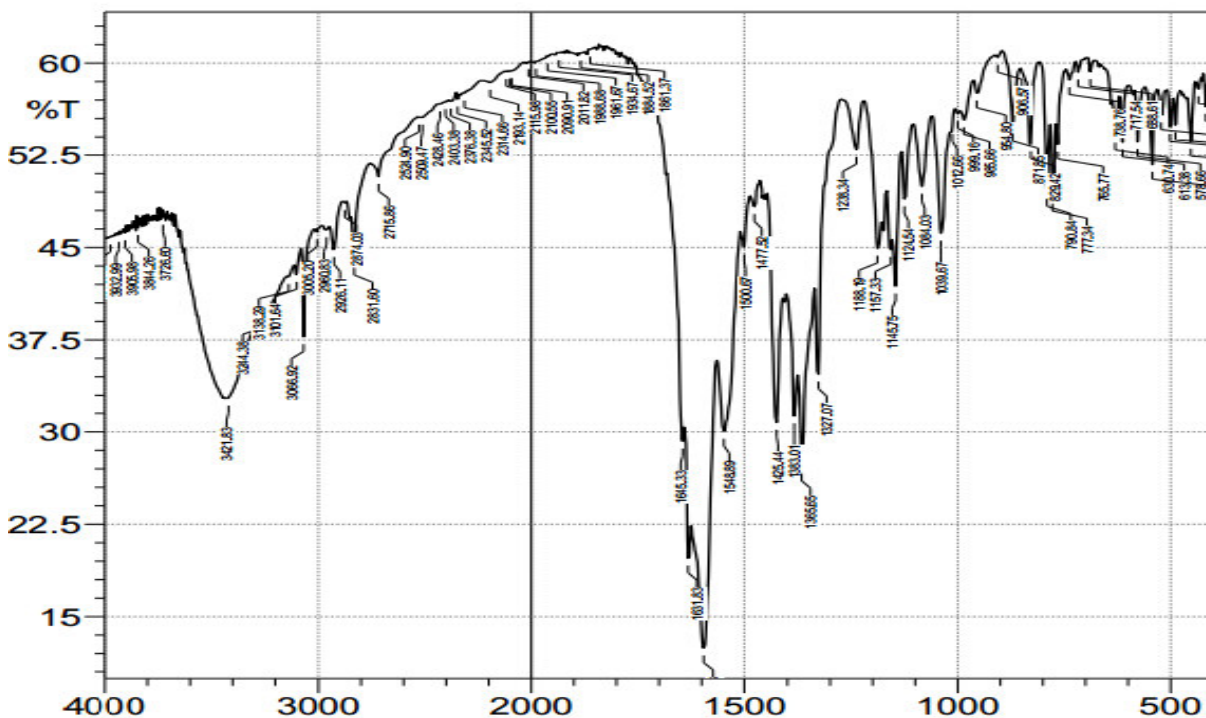
| Formulation code | Oil   | Surfactant | Cosurfactant | Water |
|------------------|-------|------------|--------------|-------|
| F16              | 62.38 | 7.14       | 21.42        | 9.04  |
| F17              | 40.00 | 9.40       | 28.20        | 12.40 |
| F18              | 36.88 | 11.10      | 33.30        | 18.66 |
| F19              | 30.57 | 11.83      | 35.51        | 22.10 |
| F20              | 26.50 | 12.55      | 38.40        | 25.30 |

#### **FTIR studies**

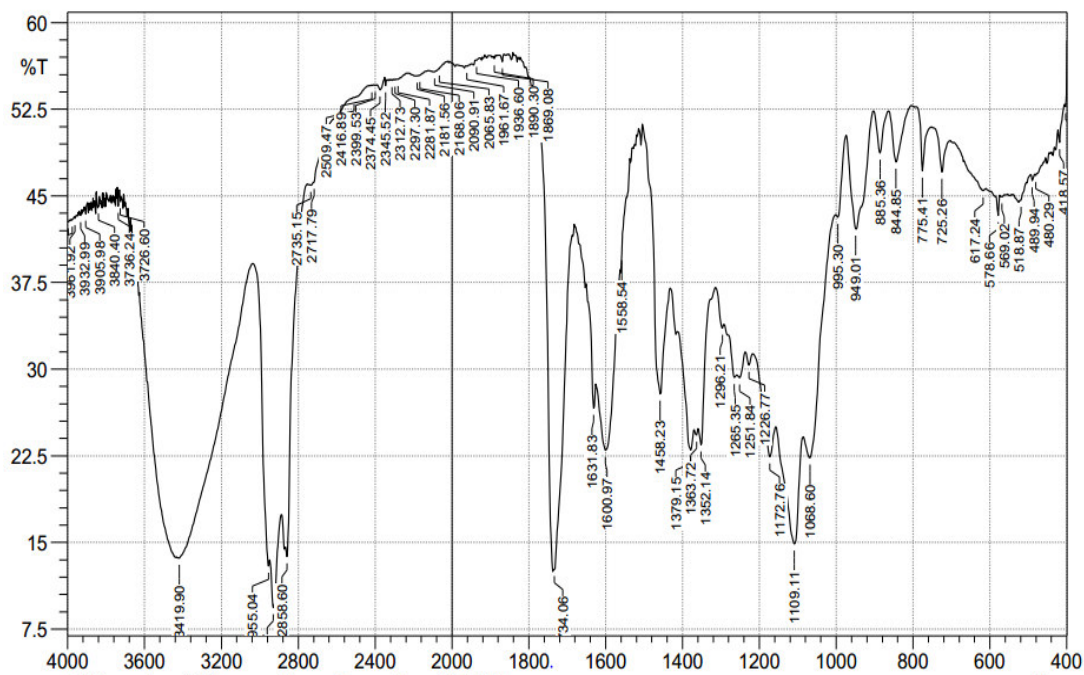
FTIR spectrums of formulations were obtained by means of an FTIR spectrophotometer (Shimadzu 8400S). The FTIR spectrum of pure Lornoxicam has three characteristic peaks at  $3421\text{ cm}^{-1}$ ,  $1631\text{ cm}^{-1}$ , ( $1157\text{ cm}^{-1}$  and  $1383\text{ cm}^{-1}$  and  $1327\text{ cm}^{-1}$  representing N-H

stretch, C=O, O=S=O functional group respectively and the FTIR spectrum of Lornoxicam SEDDS formulation has  $3419\text{ cm}^{-1}$ ,  $1631\text{ cm}^{-1}$ , ( $1172\text{ cm}^{-1}$  and  $1379\text{ cm}^{-1}$  and  $1352\text{ cm}^{-1}$ ) The spectra indicate that there is no interaction between lornoxicam and excipients used in the formulation.

**Figure 3**  
*FTIR spectrum of Lornoxicam pure drug.*



**Figure 4**  
*FTIR spectrum of Lornoxicam SEDDS*



**Thermodynamic Stability Studies**

Nanoemulsions are thermodynamically stable and are formed at a particular concentration of oil, surfactant and water, making them stable to phase separation; creaming or cracking. The selected nanoemulsion formulations were subjected to various thermodynamic stability tests, which included heating-cooling cycle, centrifugation, and freeze-thaw cycle tests. It is the thermostability which differentiates nanoemulsion from emulsions that have kinetic stability and will eventually show phase separation. The results showed that all the

formulations F1 - F10 had good physical stability and were selected for further studies.

**Evaluation of SEDDS****In vitro drug release studies**

The studies were performed to compare the release rate of the drug from various formulations. The formulation F5 ( 82.85% in 24 hours) and F9 ( 87.12% in 24hours ) showed high drug release (DR) as compared to the other formulations , the results are presented in table 6 & 7

**Table 6**  
**Invitro Drug Release Of Formulations F1 to F5**

| Time(hrs) | %DR <sup>a</sup> F1 | %DR <sup>a</sup> F2 | %DR <sup>a</sup> F3 | %DR <sup>a</sup> F4 | %DR <sup>a</sup> F5 |
|-----------|---------------------|---------------------|---------------------|---------------------|---------------------|
| 0         | 0.00                | 0.00                | 0.00                | 0.00                | 0.00                |
| 1         | 2.37±0.02           | 3.31±0.12           | 4.27±0.68           | 2.99±0.03           | 3.91±0.04           |
| 2         | 5.67±0.01           | 5.99±0.09           | 6.60±0.45           | 6.15±0.01           | 6.29±0.01           |
| 3         | 8.23±0.09           | 8.12±0.07           | 10.16±0.03          | 10.56±0.52          | 11.50±0.93          |
| 4         | 11.99±0.08          | 10.76±0.11          | 12.54±0.07          | 12.25±0.80          | 13.19±0.08          |
| 5         | 13.20±0.08          | 14.39±0.13          | 15.97±0.10          | 15.12±0.02          | 17.62±0.23          |
| 6         | 14.89±0.35          | 16.05±1.25          | 17.04±0.34          | 19.13±0.5           | 22.63±0.91          |
| 7         | 16.78±0.23          | 18.46±0.85          | 20.20±0.11          | 22.35±1.02          | 25.34±0.08          |
| 8         | 18.56±0.06          | 23.75±0.23          | 24.21±0.24          | 26.15±0.09          | 29.90±1.23          |
| 9         | 20.24±0.03          | 26.19±0.24          | 28.34±0.35          | 29.32±0.80          | 31.24±1.28          |
| 10        | 23.15±0.12          | 28.05±0.45          | 31.15±0.08          | 32.56±1.2           | 36.67±1.35          |
| 23        | 50.13±0.89          | 61.93±1.30          | 67.96±1.35          | 69.74±1.35          | 79.49±1.38          |
| 24        | 53.25±1.23          | 64.05±1.56          | 70.15±0.96          | 73.45±1.38          | 82.85±1.96          |

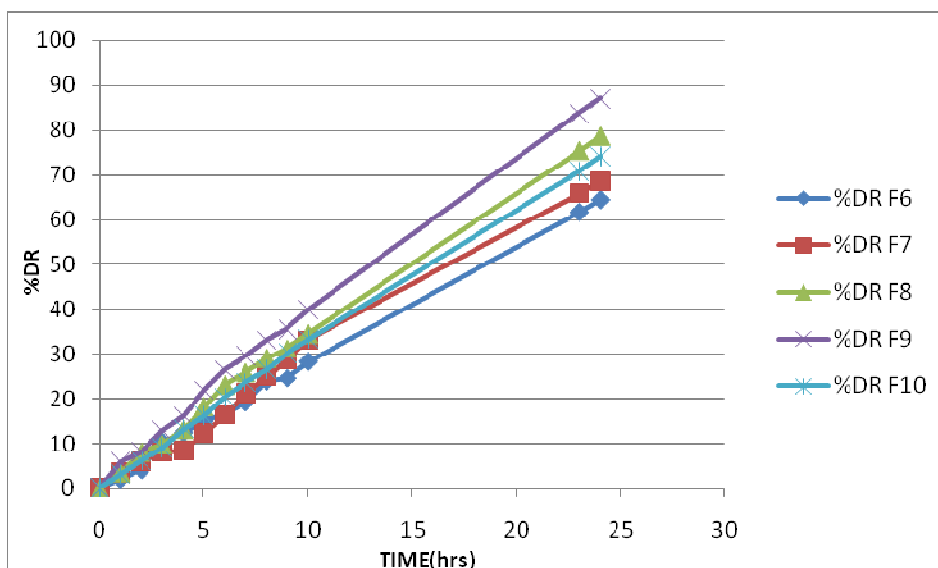
[<sup>a</sup>Data expressed as mean ± SD ( n=3 )]

**Table 7**  
**Invitro Drug Release Of Formulations F6 to F10**

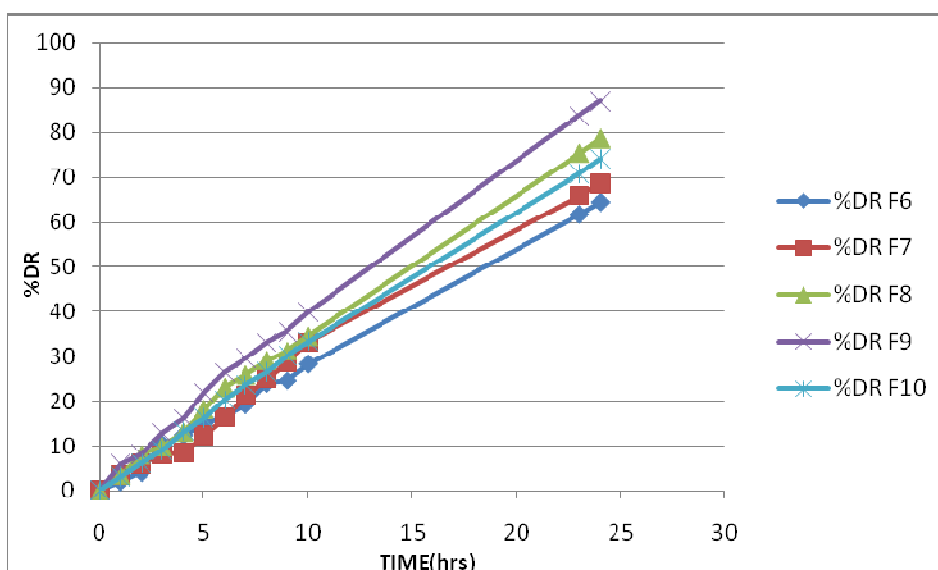
| Time(hrs) | %DR <sup>a</sup> F6 | %DR <sup>a</sup> F7 | %DR <sup>a</sup> F8 | %DR <sup>a</sup> F9 | %DR <sup>a</sup> F10 |
|-----------|---------------------|---------------------|---------------------|---------------------|----------------------|
| 0         | 0.00                | 0.00                | 0.00                | 0.00                | 0.00                 |
| 1         | 2.01±0.08           | 3.36±0.07           | 3.45±0.31           | 5.86±0.07           | 3.20±0.65            |
| 2         | 4.06±0.12           | 5.96±0.03           | 7.99±0.57           | 8.13±0.65           | 6.09±1.23            |
| 3         | 10.31±0.16          | 7.99±0.90           | 9.78±0.68           | 12.92±0.38          | 8.96±0.08            |
| 4         | 12.35±0.07          | 8.45±0.25           | 13.05±0.83          | 16.15±0.87          | 13.25±0.65           |
| 5         | 14.95±0.65          | 12.36±0.91          | 18.15±0.19          | 21.96±1.23          | 16.29±0.38           |
| 6         | 16.56±1.20          | 16.27±0.98          | 22.99±0.27          | 26.41±1.60          | 20.23±0.87           |
| 7         | 19.19±1.34          | 21.16±1.23          | 25.78±1.80          | 29.56±0.87          | 23.60±0.24           |
| 8         | 23.96±0.89          | 24.90±0.96          | 29.02±0.23          | 33.12±0.35          | 26.45±1.36           |
| 9         | 24.52±1.20          | 28.56±1.35          | 31.23±0.95          | 35.5±1.25           | 30.12±0.97           |
| 10        | 28.24±1.27          | 33.01±0.95          | 34.41±0.87          | 39.90±1.80          | 33.32±0.85           |
| 23        | 61.6±2.3            | 65.78±1.78          | 75.30±1.34          | 83.67±2.50          | 70.75±1.25           |
| 24        | 64.35±2.5           | 68.50±1.65          | 78.53±1.38          | 87.12±1.87          | 74.21±1.67           |

[<sup>a</sup>Data expressed as mean ± SD ( n=3 )]

**Figure 5**  
**Percentage drug release of formulations F1 – F5**



**Figure 6**  
**Percentage drug release of formulations F6 – F10**



**Comparison of SEDDS (F9) vs Marketed formulation (Lornoxi tablet)**

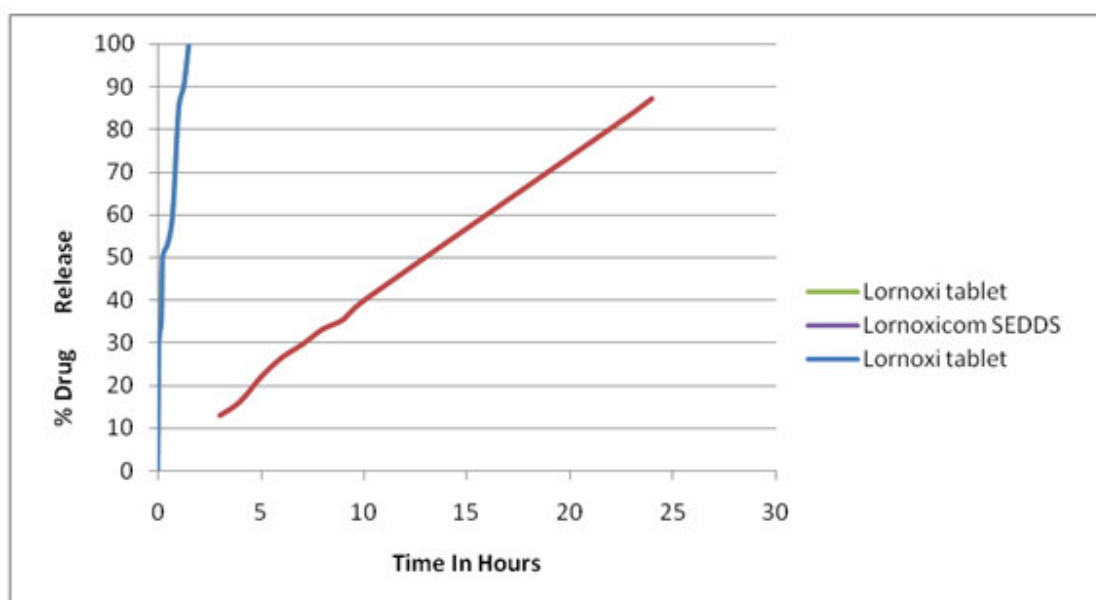
Drug release profile of optimized formulation was compared to marketed formulation (dose - 8 mg.)

**Table 8**  
**Comparison of SEDDS Formulation to Marketed Formulation**

| Time | Lornoxi tablet - %DR <sup>a</sup> | Lornoxicam SEDDS | Time | Lornoxi tablet | Lornoxicam SEDDS %DR <sup>a</sup> |
|------|-----------------------------------|------------------|------|----------------|-----------------------------------|
| 0    | 0                                 | 0                | 3    | -              | 12.92±0.38                        |
| 0.08 | 30±1.34                           | -                | 4    | -              | 16.15±0.87                        |
| 0.16 | 35±0.86                           | -                | 5    | -              | 21.96±1.23                        |
| 0.25 | 50±1.90                           | -                | 6    | -              | 26.41±1.60                        |
| 0.5  | 53±1.20                           | -                | 7    | -              | 29.56±0.87                        |
| 0.75 | 60±1.35                           | -                | 8    | -              | 33.12±0.35                        |
| 1    | 85±0.98                           | 3.91             | 9    | -              | 35.5±1.25                         |
| 1.25 | 90±1.02                           | -                | 10   | -              | 39.90±1.80                        |
| 1.5  | 100                               | -                | 23   | -              | 83.67±2.50                        |
| 2    | -                                 | 6.29             | 24   | -              | 87.12±1.87                        |

[<sup>a</sup>Data expressed as % DR<sup>a</sup> ± SD ( n=3 )]

**Figure 7**  
**Comparison profile of Percentage Drug Release Of [Lornoxicam SEDDS vs Lornoxi tablet]**

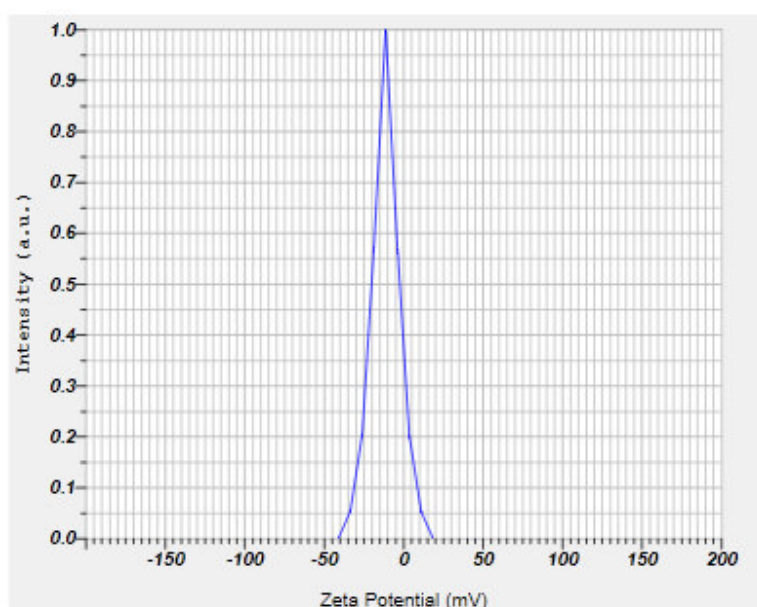
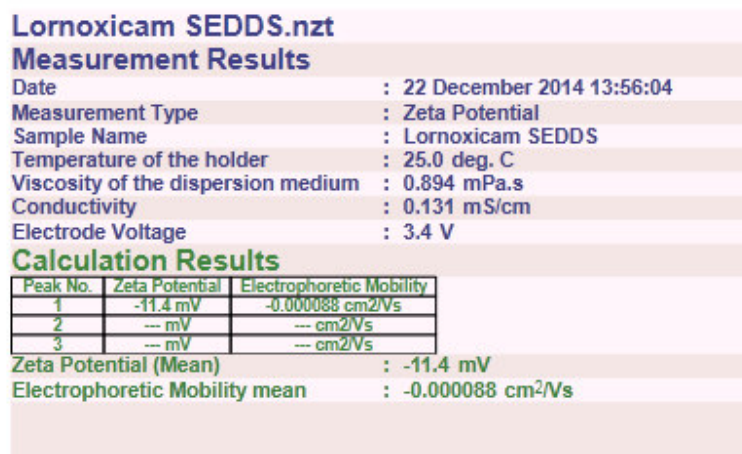


The marketed formulation showed 100% drug release in 90 minutes whereas the optimized SEDDS formulation could sustain the activity for 24 hours.

**Particle size and zeta potential**

The zeta potential of microemulsion was determined using nano zeta sizer. Charge on emulsion droplets and their mean zeta potential value (± SD) were obtained from the instrument HORIBA. It was found to be -11.4 mV. Average particle size was found to be 85.5nm.

**Figure 8**  
**Zeta potential of the optimized formulation**



**Percentage Transmittance**

The percent transmittance of the all formulations was measured at 560nm keeping distilled water as a blank. The percentage transmittance of the optimized formulation F9 was found to be 94.2% . The results of

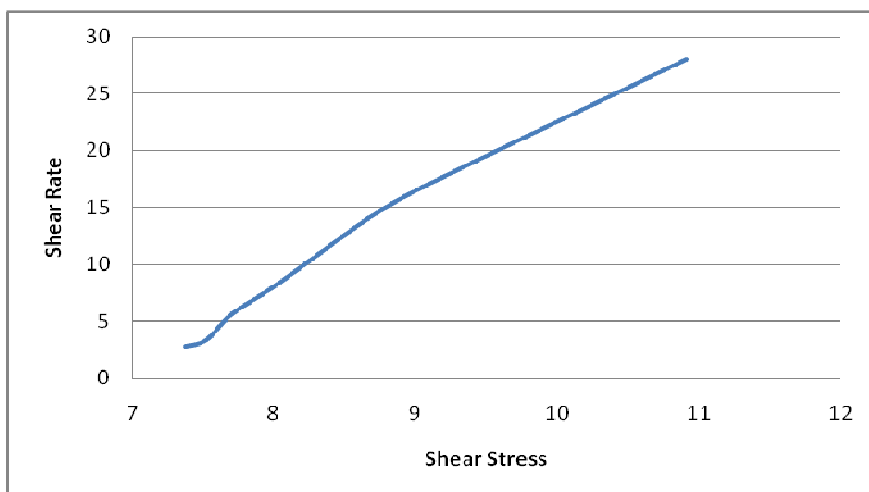
percentage transmittance revealed that the formulation was transparent.

**Viscosity measurement**

Viscosity measurement of the optimized formulations (F9) was performed by Brookfield viscometer

**Table 9**  
**Rheological Behavior of F9**

| RPM | VISCOSITY | SHEAR STRESS | SHEAR RATE |
|-----|-----------|--------------|------------|
| 6   | 369       | 7.03         | 1.68       |
| 10  | 255       | 7.37         | 2.80       |
| 12  | 207       | 7.52         | 3.36       |
| 20  | 128       | 7.70         | 5.60       |
| 30  | 86        | 8.04         | 8.40       |
| 50  | 54        | 8.66         | 14.0       |
| 60  | 47        | 9.05         | 16.8       |
| 100 | 32        | 10.91        | 28.0       |



**Figure 9**  
**Rheogram Of F9**  
The graph in Fig. 9 is nearly linear indicating Newtonian flow.

**Anti Inflammatory Activity Of Lornoxicam SEDDS**

The study was done after induction of edema by carrageen. Paw volume and percentage decrease in paw edema was compared between control and test group. Paw volume in control, standard and test groups is presented in Table 10 shown below

**Table 10**  
**Paw Volume After Induction**

|                        | 30 Minutes | 1 Hour     | 2 Hours   | 3 Hours    | 4 Hours   |
|------------------------|------------|------------|-----------|------------|-----------|
| Normal (Control) (n=6) | 0.26±0.06  | 0.26±0.06  | 0.3±0.05  | 0.26±0.06  | 0.26±0.06 |
| Indomethacin (n=6)     | 0.53±0.06  | 0.6±0.0    | 0.53±0.06 | 0.46±0.06  | 0.4±0.06  |
| Test (n=6)             | 0.53±0.06  | 0.46±0.06  | 0.33±0.02 | 0.31±0.03  | 0.23±0.01 |
|                        |            | p = 0.0418 | p = 0.01  | p = 0.0493 | p = 0.01  |

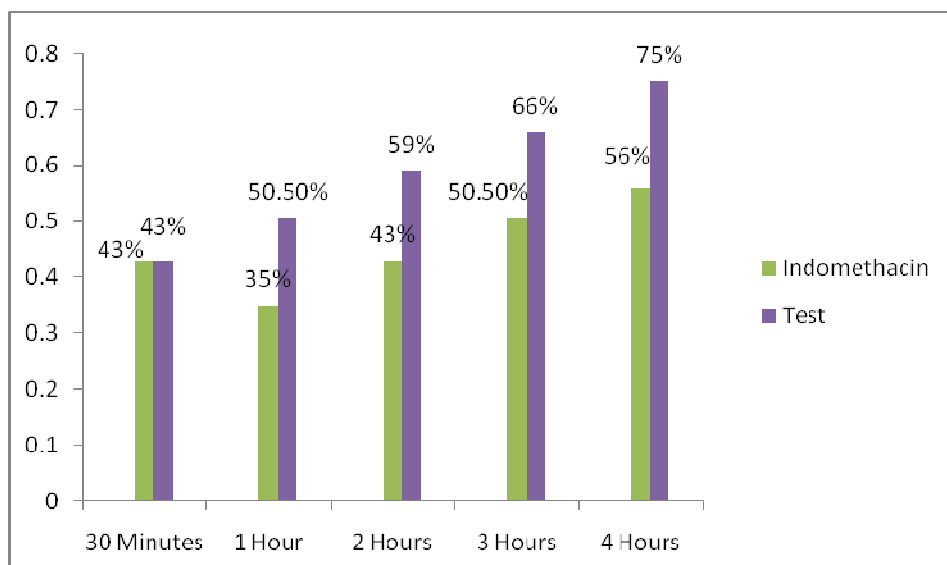
\*p < 0.05 considered significant [ Data expressed as mean ± SEM]

**Table 11**  
**Percentage Inhibition of paw edema**

|                         | 30 Minutes | 1 Hour | 2 Hours | 3 Hours | 4 Hours |
|-------------------------|------------|--------|---------|---------|---------|
| Normal (Control)        | 0.00       | 0.00   | 0.00    | 0.00    | 0.00    |
| Indomethacin (Standard) | 43%        | 35%    | 43%     | 50.5%   | 56%     |
| Lornoxicam SEDDS (Test) | 43%        | 50.5%  | 59%     | 66%     | 75%     |

**Figure 10**

**Comparison Of Percentage decrease in paw edema between control and test groups.**



The optimized test formulation indicated a statistically significant decrease ( $p < 0.05$ ) in paw volume. Lornoxicam SEDDS showed 75% inhibition in paw edema at 4 hours as compared to standard which exhibited 56% inhibition at the same as seen in fig 10.

## CONCLUSION

In this study lornoxicam was formulated to sustain the drug release and reduce its side effects. The SEDDS formulation contained Caproyl 90 (30%), Tween 20 (12.5%), Transcutal P (37.5%) and water (20%). The optimized formulation was compared to the marketed formulation by both invitro and invivo studies. The invitro studies revealed that the SEDDS formulation could sustain the

activity for 24hrs. Anti-inflammatory studies indicate that the test formulation showed significant inhibition in paw edema compared to the standard formulation.

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