Int J Pharm Bio Sci 2015 April; 6(2): (P) 381 - 395

Research Article **Pharmaceutics**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

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

C. APARNA*[1], DR.PRATHIMA SRINIVAS[1] AND DR. K.S.K. RAO PATNAIK[2]

[1] *Department of Pharmaceutics, Sri Venkateshwara college of Pharmacy And Research centre, Hyderabad, Telangana, India.*
[2] *College of Technology, Osmania university, Hyderabad, Telangana India.*

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

C. APARNA
Department of Pharmaceutics, Sri Venkateshwara college of Pharmacy And Research centre, Hyderabad, Telangana, India.

***Corresponding author**

INTRODUCTION

Lipid-based formulations are well known approach to enhance water solubility and oral bioavailability of BCS ClassII 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 selfemulsifying drug deli very 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[1] 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 [2]. 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[3]. 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 Caproyl 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 [4]. 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-1.

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[5] 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, 60and 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.

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

where, V control = mean edema of rats in control group;
V 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[a] (mg/ml)	Surfactant	Solubility[a] (mg/ml)	Cosurfactant	Solubility[a] (mg/ml)
Caproyl90	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	-	-	-	-

[[a]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 transcutol 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 $S_{mix.}$ Ingroup 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.

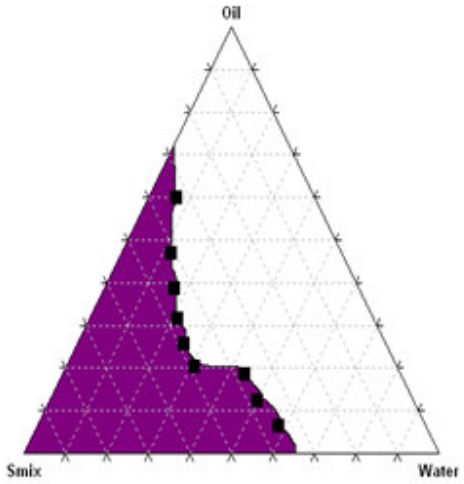


Fig 1(a)

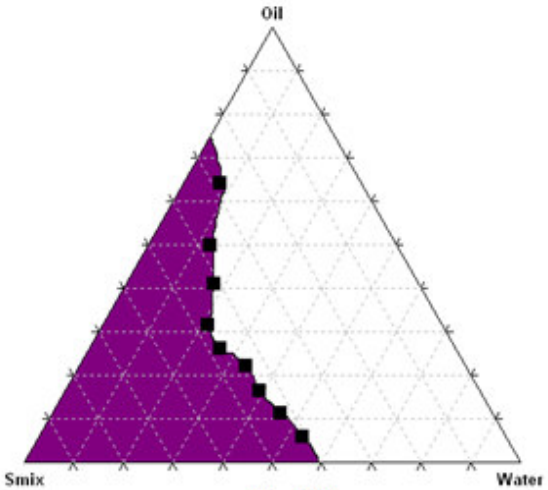


Fig 1(b)

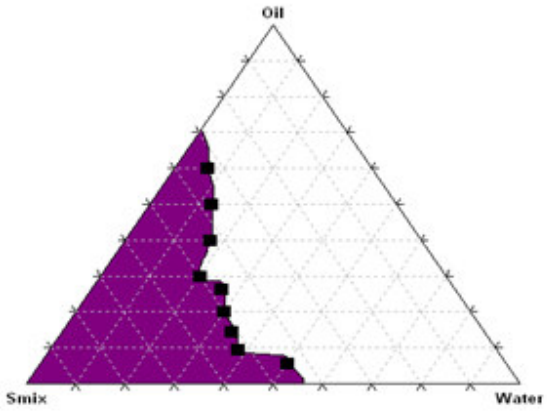


Fig 1 (c)

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.

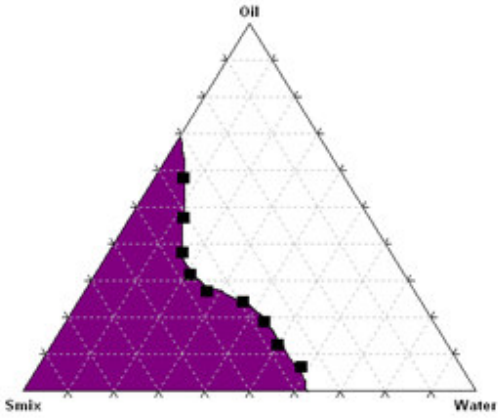


Fig 2(a)

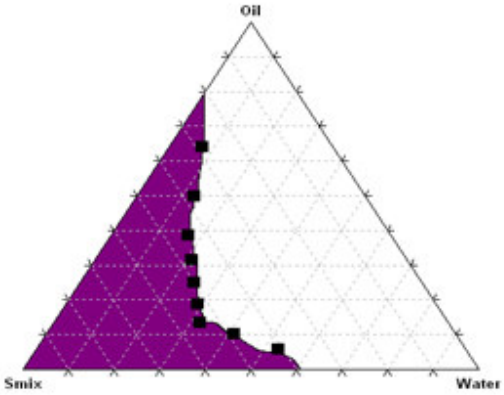


Fig 2 (c)

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 Caproyl 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 (Shimazdu 8400S). The FTIR spectrum of pure Lornoxicam has three characteristic peaks at 3421 cm^{-1} , 1631 cm^{-1} , (1157cm^{-1} and 1383cm^{-1} and 1327cm^{-1} representing N-H stretch, C=O, O=S=O functional group respectively and the FTIR spectrum of Lornoxicam SEDDS formulation has 3419cm^{-1} , 1631cm^{-1} . (1172cm^{-1} and 1379cm^{-1} and 1352cm^{-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.

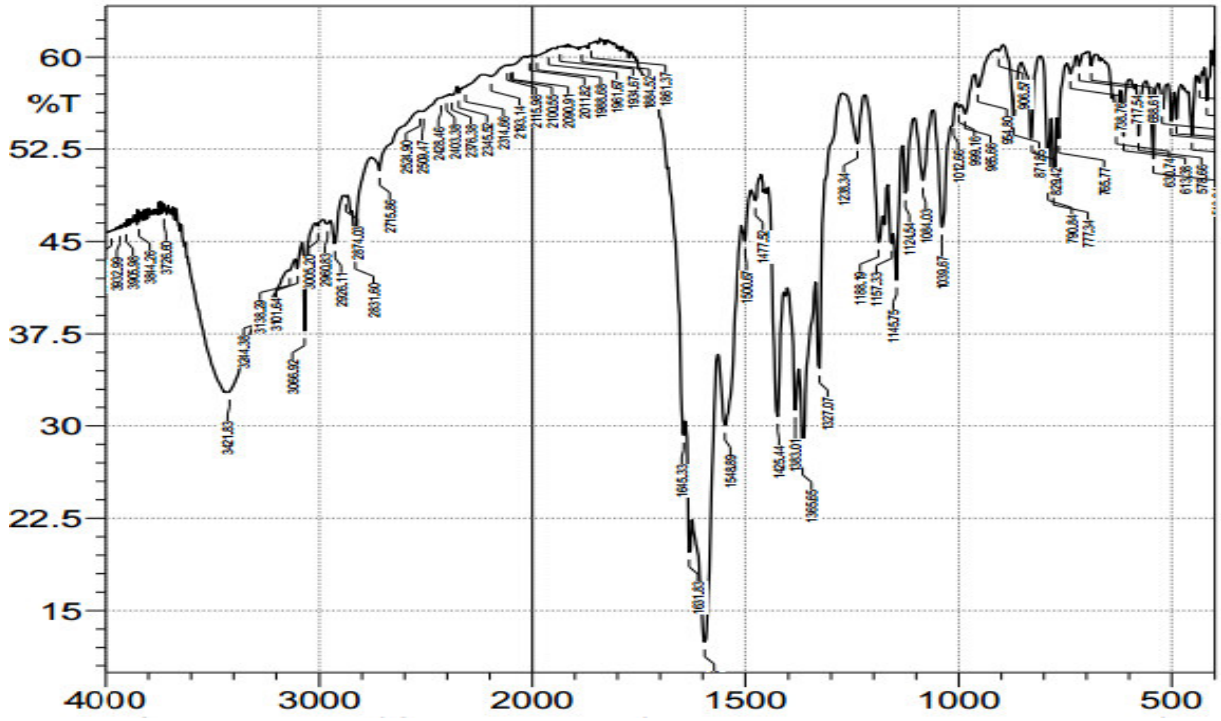
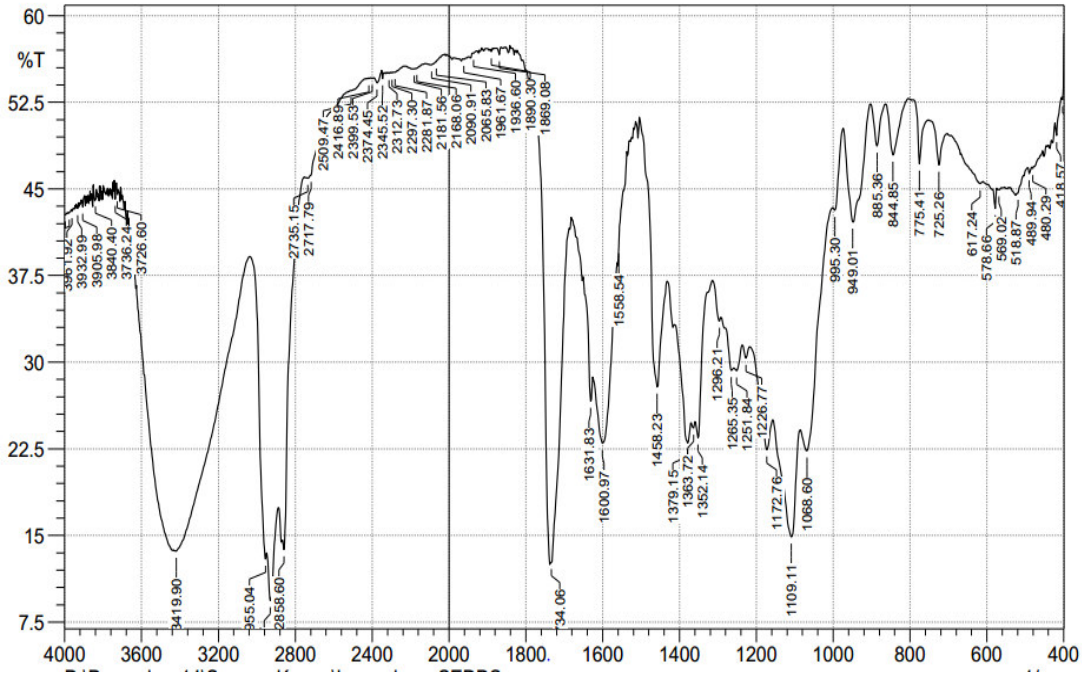


Figure 4
FTIR spectrum of Lornoxicam SEDDS



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[a] F1	%DR[a]F2	%DR[a]F3	%DR[a]F4	%DR[a]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

[[a]Data expressed as mean ± SD (n=3)]

Table 7
Invitro Drug Release Of Formulations F6 to F10

Time(hrs)	%DR[a] F6	%DR[a] F7	%DR[a] F8	%DR[a] F9	%DR[a] 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

[[a]Data expressed as mean ± SD (n=3)]

Figure 5
Percentage drug release of formulations F1 – F5

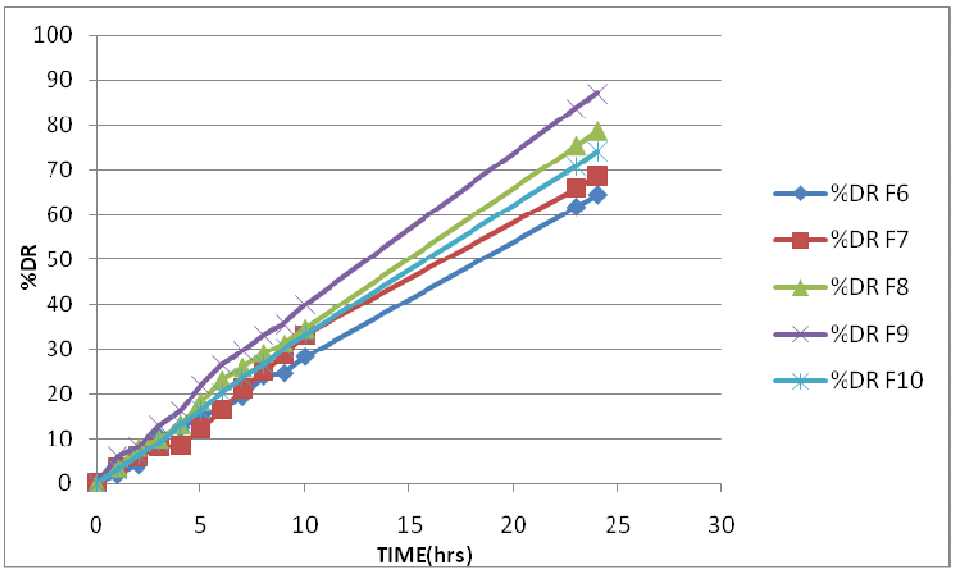
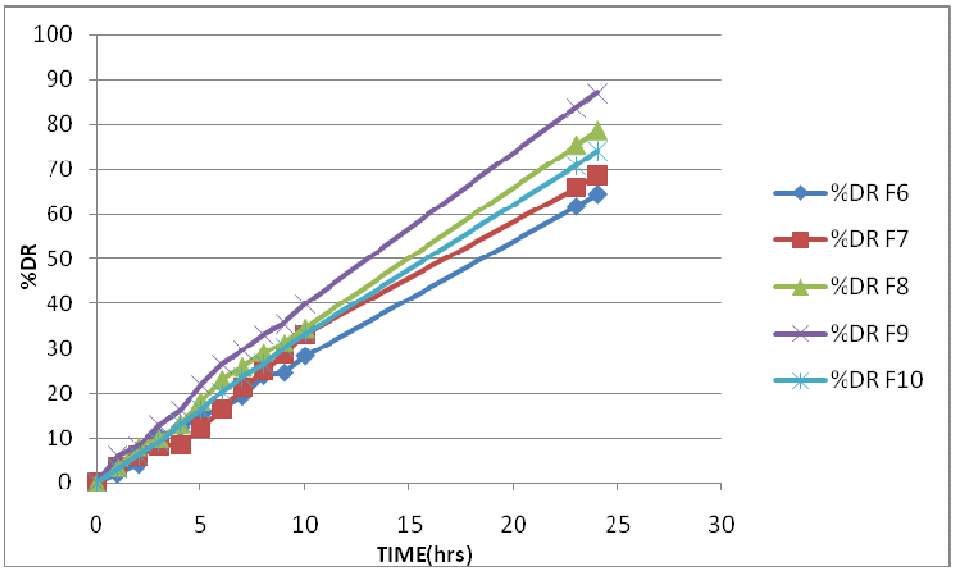


Figure 6
Percentage drug release of formulations F6 – F10



Comparision of SEDDS (F9) vs Marketed formulation (Lornoxi tablet)

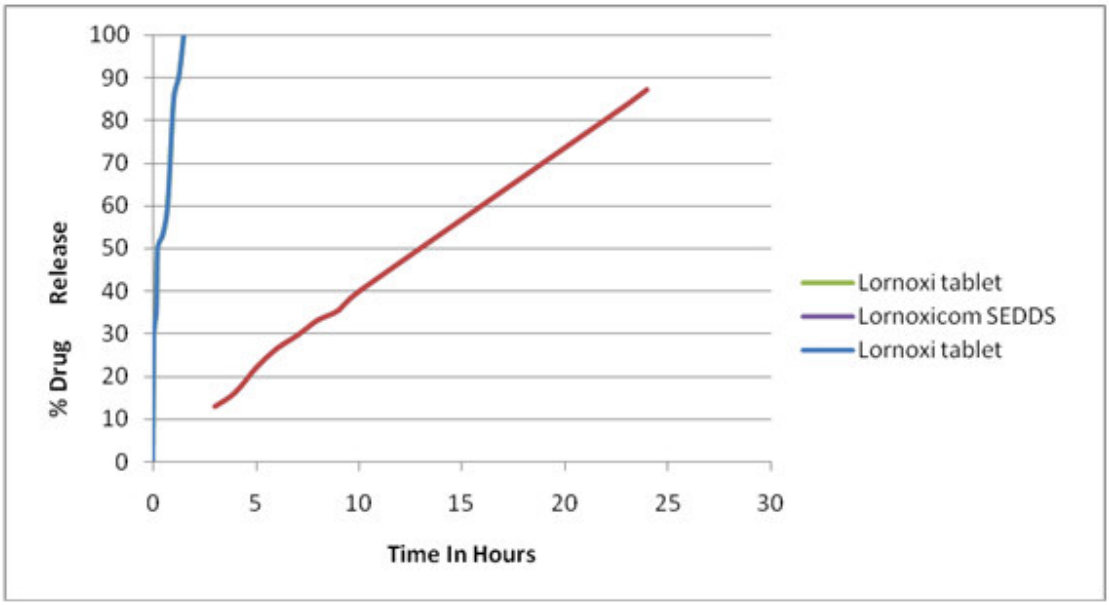
Drug release profile of optimized formulation was compared to marketed formulation (dose - 8 mg.)

Table 8
Comparison of SEDDS Formulation to Marketed Formulation

Time	Lornoxi tablet - %DR[a]	Lornoxicam SEDDS	Time	Lornoxi tablet	Lornoxicam SEDDS %DR[a]
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

[[a]Data expressed as % DR[a] ± 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

Lornoxicam SEDDS.nzt

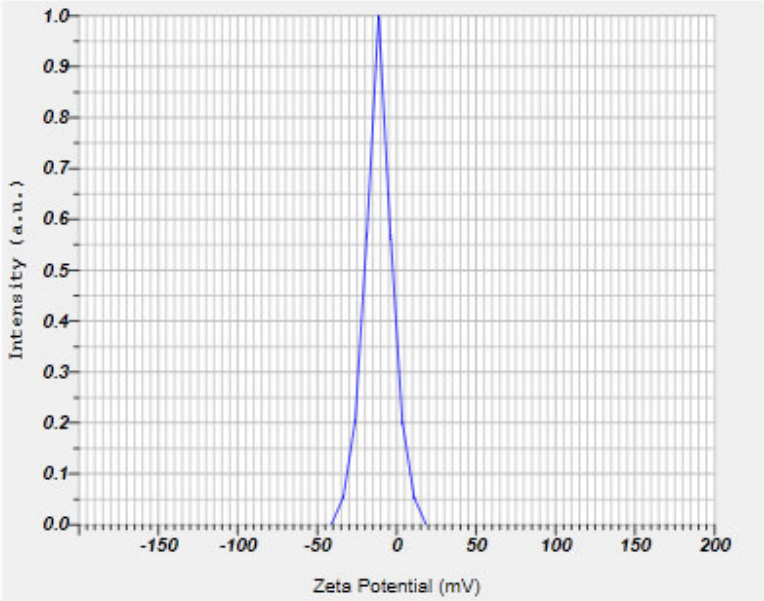
Measurement Results

Date	: 22 December 2014 13:56:04
Measurement Type	: Zeta Potential
Sample Name	: Lornoxicam SEDDS
Temperature of the holder	: 25.0 deg. C
Viscosity of the dispersion medium	: 0.894 mPa.s
Conductivity	: 0.131 mS/cm
Electrode Voltage	: 3.4 V

Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-11.4 mV	-0.000088 cm2/Vs
2	--- mV	--- cm2/Vs
3	--- mV	--- cm2/Vs

Zeta Potential (Mean)	: -11.4 mV
Electrophoretic Mobility mean	: -0.000088 cm^2/Vs



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

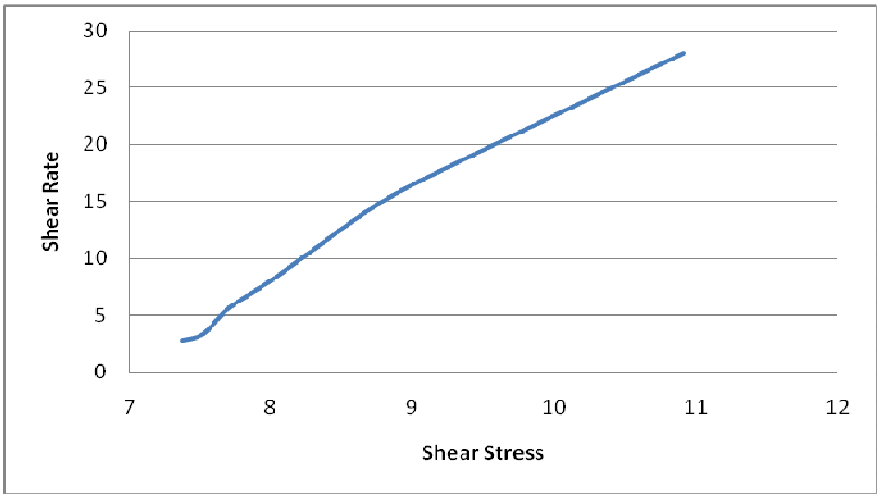


Figure 9
Rheogram Of F9
The graph in Fig. 9 is nearly linear indicating Newtonian flow.

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

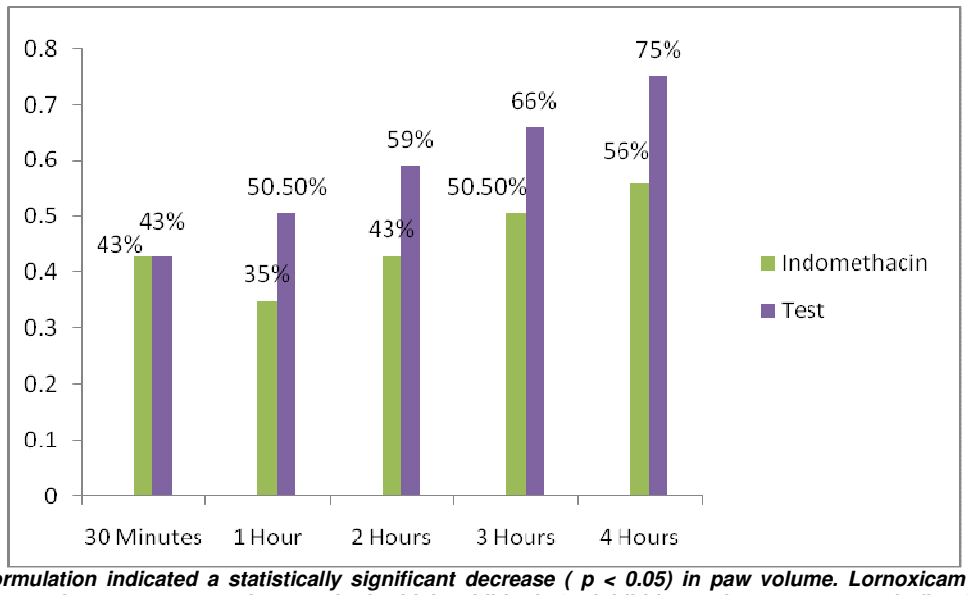
	30 Minutes	1 Hour	2 Hours	3 Hours	4 Hours
Normal (Control) (n=6)	0.26± 0.06	0.26±0.06	0.3±0.05	0.26±0.06	0.26±0.06
Indomethacin (n=6)	0.53±0.06	0.6±0.0	0.53±0.06	0.46±0.06	0.4±0.06
Test (n=6)	0.53±0.06	0.46±0.06	0.33±0.02	0.31±0.03	0.23±0.01
		p = 0.0418	p =0.01	p = 0.0493	p = 0.01

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 4hours 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-inflamatory studies indicate that the test formulation showed significant inhibition in paw edema compared to the standard formulation.

ACKNOWLEDGEMENT

The authors acknowledge Osmania University and Sri Venkateshwara College of Pharmacy for their support in completion of present study.

REFERENCES

1. Sheikh Shafiq, Faiyaz Shakeel, Sushma Talegaonkar, Farhan J. Ahmad, Roop K. Khar, Mushir Ali. Development and bioavailability assessment of ramipril nanoemulsion formulation. European Journal of Pharmaceutics and Biopharmaceutics, 2007; 66: 227–243.
2. Preeti K Suresh et al. Formulation And In-vitro Characterization Of Self-Nanoemulsifying Drug Delivery System Of Cinnarizine / Pharmacie Globale (IJCP) 2011, 9 (08)
3. Balfour JA1, Fitton A, Barradell LB Lornoxicam. A review of its pharmacology and therapeutic potential in the management of painful and inflammatory conditions.. Drugs. 1996 Apr;51(4):639-57.
4. Sheikh Shafiq-un-Nabi, Faiyaz Shakeel, Sushma Talegaonkar, Javed Ali, Sanjula Baboota, Alka Ahuja,Roop K. Khar et al. Formulation Development and Optimization Using Nanoemulsion Technique:A Technical Note. AAPS PharmSciTech, 2007; 8.
5. Kavita Sapraa, Ashu Saprab, S K Singha, Saloni Kakkarb, Self Emulsifying Drug Delivery System: A Tool in Solubility

Enhancement of Poorly Soluble Drugs, Indo Global Journal of Pharmaceutical Sciences, 2(3): 2012, 313-332.

6. V.Kiran kumar, M. Aruna Devi and D.V.R.N.Bikshapathi, Development of Solid self emulsifying drug delivery system containing Efavirenz: *In-vitro* and *in-vivo* evaluation Int J Pharm Bio Sci 2013 Jan; 4(1): (P) 869 – 882.
7. Shukla Jill B, Koli Akshay R., Ranch Ketan M and Parikh Rajesh K., Self Micro Emulsifying Drug Delivery System, Pharma science monitor: International journal of pharmaceutical sciences Vol-1, Issue-2, 2010,213-225.
8. Shobhit Kumar, Satish Kumar Gupta and Pramod Kumar Sharma, Self-Emulsifying Drug Delivery Systems (SEDDS) for Oral Delivery of Lipid Based Formulations - A Review, African Journal of Basic & Applied Sciences, 4 (1) 2012: 07-11.
9. Shinde Ganesh, Kuchekar Shantanu, Kamble Pravin, Kuchekar Ashwin , Kshirsagar Rajesh ,Kuchekar Bhanudas, Self Emulsifying Drug Delivery System: A Novel Approach for Hydorphobic drugs, International Journal of pharmaceutical science, Jan-Apr 2011:3(1):988-1005.
10. Rajesh B. V, Reddy T.K., Srikanth G., Mallikarjun V, Nivethithai P.Sharma:Lipid Based Self-Emulsifying Drug Delivery Systems (SEDDS) for Poorly water soluble drugs- A Review, Journal of Global Pharma Technology, 2010; 2(3): 47-55.
11. Tayal Ayushi, Jamil Faraz, Sharma Ritika, Self-Emulsifying Drug Delivery Systems : A Review, IRJP 2012, Vol. 3(5).
12. M. P. Khinchi, Akanksha Gupta, M. K. Gupta, D. Agrawal, N. Sharma, A. Malav, A. Singh, Self Emulsifying Drug Delivery System, Asian Journal of Biochemical and Pharmaceutical Research,Issue 2 (Vol. 1) 2011.
13. Kanika Sarpal, Yogesh B. Pawar and Aravind K. Bansal, Self Emulsifying Drug Delivery System:A Strategy to Improve Oral Bioavailability, CRIPS Vol.11 No.3 July-September 2010.
14. Rakesh Kumar Sharma, Solubility Enhancement of Lipophilic Drugs- Solid Self Emulsified Drug Delivery Systems, International Journal of Research in Pharmaceutical and Biomedical Sciences, Vol. 4 (1) Jan– Mar 2013,NT.J.PH.SCI.,JAAPR, 2011;3(1):988-1005
15. JessyShaji, Digambar Jadhav, Newer Approaches to Self Emulsifying Drug Delivery System, International Journal of Pharmacy and Pharmaceutical Sciences,Vol2, Suppl 1, 2010.
16. Singh, B., *et al*., Self-Emulsifying Drug Delivery Systems (SEDDS): Formulation Development, Characterization, and Applications. Critical reviews in therapeutic drug carrier systems, 2009. 26(5):
17. A. Bhattacharyya and M. Bajpai, Development and Oral Bioavailability of self emulsifying formulation of Ketoconazole, International journal of pharmaceutical sciences and nanotechnology, Volume5:issue4:January-March2013.
18. Maulik J. Patela, Natvarlal M. Patela, Ritesh B. Patelb, Rakesh. P. Patelb, Formulation and evaluation of self-micro emulsifying drug delivery system of Lovastatin,Asian Journal of Pharmaceutical Sciences, 2010, 5 (6): 266-275.
19. Kokare C.R, Kumbhar S.A, Archana patil, Formulation and Evaluation of self emulsifying drug delivery system of Carbamazepine, Indian Journal of Pharmaceutical Education and Research, 2012-2013.
20. Swayam Prakash Patel, Girish jani, Solid Self-Emulsifying Drug Delivery Systems :An Emerging Dosage Form for Poorly Bioavailable Drugs, Inventi Rapid: NDDS, Vol. 2012.