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FORMULATION AND EVALUATION OF SELF EMULSIFYING DRUG DELIVERY SYSTEM (SEDDS) OF IBUPROFEN

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Keywords:

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ABSTRACT: Aim of present investigation was to develop self emulsifying drug delivery system of ibuprofen to enhance solubility, dissolution rate which may improve therapeutic performance and drug loading capacity so as to develop alternative to traditional oral formulations to improve bioavailability. In this study Labrafac, Tween 80 and PEG 200 were selected as oil, surfactant and co-surfactant respectively. Formulation development and screening was done based on results obtained from phase diagrams and characteristics of resultant microemulsions. The developed SEDDS were evaluated for droplet size analysis, zeta potential, polydispersibility index, viscosity, refractive index, % transmittance, drug content and *in vitro* diffusion profiles. All formulations of ibuprofen SEDDS showed globule size in micrometer range, good stability with no phase separation, creaming or cracking and rapidly formed emulsion which was clear. All formulations showed more than 90% of drug release within 30 min. The SEDDS showed improved dissolution rate compared to marketed product. Anti-inflammatory studies were conducted in Wistar strain male albino rats and ibuprofen SEDDS showed more significant activity than the marketed product. Thus, the study confirmed that the SEDDS formulation can be used as a possible alternative to traditional oral formulations of ibuprofen to improve its bioavailability.

INTRODUCTION: Oral bioavailability of a drug depends on its solubility and/or dissolution rate, and dissolution may be the rate-determining step for the onset of therapeutic activity. Therefore, poorly aqueous soluble drugs are usually characterized by a low bioavailability due to less absorption, which is a major concern of pharmaceutical industries worldwide.

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Various approaches available to improve drug solubility as well as drug dissolution of poorly aqueous soluble drugs include micronization[1], formation of inclusion complexes with cyclodextrins[2], formation of amorphous drugs[3], and formation solid dispersions of drugs using various hydrophilic carriers[4] and lipid-based formulations.

Self-emulsifying drug delivery systems is one of the most recognized and economically feasible formulation concepts for solving these measures. SEDDS are isotropic mixtures of natural or synthetic oil, surfactant(s) with or without a co-surfactant. Upon mild agitation these systems can form fine oil in water emulsions in aqueous media, such as dissolution media or gastrointestinal

fluids[5]. Self-emulsifying formulations spread readily in such aqueous media providing the drug in fine droplets which in turn enhance the dissolution rate of lipophilic drugs by increasing their aqueous solubility. However, studies have shown that the self-emulsification process is specific to the nature of the oil/surfactant pair, surfactant concentration, oil/surfactant ratio and temperature at which self-emulsification occurs[6, 7].

Ibuprofen, a phenyl propionic acid derivative, is widely used as first line non-steroidal anti-inflammatory, analgesic, and antipyretic agents with a half-life of 1.8-2 hours[8]. It is poorly aqueous soluble and its oral absorption is dissolution rate limited, which leads to a potential bioequivalence problem. Thus, the improvement of ibuprofen dissolution for its immediate release is desirable for rapid ibuprofen absorption, which is prerequisite for quick onset of its pharmacological actions. The present study is to formulate ibuprofen in a SEDDS to increase its solubility in water and hence improving its dissolution rate which in turn may enhance ibuprofen oral bioavailability.

MATERIALS & METHODS:

Ibuprofen was obtained as a gift sample from Hetero Drugs, Hyderabad. Capmul MCM, Captex were obtained from Abitec group, USA, Labrafac PG was obtained from Gattefosse, Mumbai, Tween 80, PG, PEG 400, glycerol, ethyl oleate were purchased from Loba chemie Pvt ltd, Mumbai. All other reagents and chemicals used were of analytical grade.

Preparation of SEDDS

Selection of oils, surfactants and cosurfactants

The oils, surfactants and cosurfactants were selected based on solubility of the drug. The study was carried out by taking 2 ml of oil/ surfactant / in glass vial containing excess amount of drug. The mixtures were mixed manually for 30 min in order to facilitate proper mixing of drug with the vehicles.

The vials were sonicated for 2 h and kept in water bath for 48 h for equilibration. The vials were centrifuged at 3000 rpm for 20 min, followed by filtration. The filtrate was suitably diluted with methanol and drug dissolved in various vehicles was analysed by UV spectrophotometer[9].

Construction of pseudoternary phase diagram[10]

Pseudoternary phase diagrams were constructed to examine the formation of oil in water emulsions using four components: oil, surfactant, cosurfactant and aqueous system. Based on the solubility study, the oil, surfactant and cosurfactant were selected. Surfactant and cosurfactant (Smix) in each group were mixed in different weight ratios (1:0, 1:1, 1:2, 1:3, 1:4, 2:1, 3:1, 4:1). These Smix ratios were chosen in increasing concentration of surfactant with respect to cosurfactant and increasing concentration of cosurfactant with respect to surfactant for comprehensive study of the phase diagrams.

For each phase diagram, oil and specific Smix ratio was mixed thoroughly in different weight ratios from 1:1 to 2:1 in different glass vials. Ten combinations of oil and Smix, 1:1, 1:2, 1:3, 1:4, 1:5, 1:6, 1:7, 1:8, 1:9 and 2:1 were made so that maximum ratios were covered for the study. Phase diagrams were constructed using aqueous titration method. In the phase diagrams, only emulsion points were plotted (shaded area), so that there is no overcrowding of the phases in the diagram, as for formulation development, only the microemulsion n region is of interest.

Selection of formulations from Phase diagrams

From each phase diagram constructed, different formulations were selected from emulsification region so that drug could be incorporated into it on the following basis. 200 mg of ibuprofen was dissolved in oil phase. The oil phase used was in the increment of 5% (10%, 15%, 20%, 25%, etc) from the emulsion region. For each 5 % of oil selected, the formula that used the minimum concentration of Smix for its formulation was selected from the phase diagram.

Evaluation of SEDDS

Thermodynamic stability tests[11]

Selected formulations were subjected to different thermodynamic stability tests (Centrifugation, Heating cooling cycle and Freeze thaw cycle), to overcome selecting metastable formulation.

Centrifugation: Selected formulations from phase diagrams were centrifuged at 3500 rpm for 30 min and observed for phase separation, creaming and cracking. Formulations that are stable were taken for heating cooling cycle.

Heating cooling cycle (H/C cycle): Stability of nanoemulsions on variation of temperature was studied by H/C cycle. Six cycles between refrigerator temperature 4°C and 45°C with storage at each temperature for not less than 48 h. Formulations, that are stable at these temperatures, were subjected to Freeze thaw cycle**.**

Freeze thaw cycle: Three freeze thaw cycles between -21°C and +25°C with storage at each temperature for not less than 48 h was carried out for the formulations. Formulations, which passed these thermodynamic stress tests, were further taken for the dispersibility tests for assessing the efficiency of self emulsification.

Dispersibility tests

The efficiency of dispersibility was assessed using a USP XXII dissolution apparatus II. Each formulation (0.5 ml) was added to 500 ml distilled water maintained at 37±0.5°C, with paddle rotating at 50 rpm for gentle agitation. The *in vitro* performance of the formulations was visually assessed using the grading system as shown below[12].

Grade A: Rapidly forming (within 1 min) nanoemulsion, having a clear or bluish appearance.

Grade B: Rapidly forming, slightly less clear emulsion, having a bluish white appearance.

Grade C: Fine milky emulsion that formed within 2 min.

Grade D: Dull, greyish white emulsion having slightly oily appearance that is slow to emulsify (longer than 2 min).

Grade E: Formulation, exhibiting either poor or minimal emulsification with large oil globules present on the surface.

The Formulations that passed the thermodynamic stability and dispersibility tests in Grade A and B were selected for further studies.

Effect of pH and robustness to dilution

Formulations were subjected to 50, 100, 1000 and 3000 fold dilution with distilled water, 0.1M HCl and simulated intestinal fluid (pH 6.8). The resultant diluted emulsions were checked manually for any physical changes such as (coalescence of droplets, precipitation or phase separation) after 24 h storage[13].

Globule size measurement

The mean globule size and polydispersity index (P.I.) of the resulting emulsions were determined by photon correlation spectroscopy (which analyses the fluctuations in light scattering due to Brownian motion of the particles) using a Zetasizer 3000 (Malvern Instruments Worcestershire, UK) Light scattering was monitored at 25ºC at a 90ºangle[11].

Zeta potential determination

The zeta potential of the diluted formulation was measured using a zeta meter system (Malvern instrument, Worcestershire, UK).

Viscosity

Brookfield DV III ultra V6.0 RV cone and plate rheometer (Brookfield Engineering Laboratories, Inc, Middleboro, MA, spindle # CPE40) was used to determine the viscosity of different formulations at 25±1.0°C[14].

Refractive index and percent transmittance

The refractive index of the system was measured using Abbe's refractometer. The percent transmittance of the system was measured using UV spectrophotometer (Shimadzu, Japan) keeping distilled water as blank at 221 nm[15].

Differential scanning calorimetry

The samples (about 3.00 mg) were placed in standard aluminum cups, and dry nitrogen was used as effluent gas. All samples were scanned at a temperature ramp speed of 5°C /min and the heat flow from 0 to 250°C.

Drug content estimation

SEDDS containing ibuprofen equivalent to one dose was added in 100 ml volumetric flask containing methanol and mixed it well. The extracted solution was suitably diluted and analyzed for drug content using UV-spectrophotometer at 221 nm[15].

Drug Release Studies

The *in vitro* drug release of formulations was determined by using USP dissolution apparatus-II (paddle method). The dissolution medium, according to the monograph of ibuprofen in USP, is a pH 7.4 Phosphate buffer. 5 ml of dissolution medium were withdrawn every 10 min over 60

min. The amount of dissolved drug was determined using UV Spectrophotometer method (UV 1205 Shimadzu, Japan) at 221nm[15].

Evaluation of anti-inflammatory activity

The anti-inflammatory activity of prepared ibuprofen SEDDS was evaluated by the carrageenan-induced rat hind paw edema method[16]. The experimental protocol was designed and approval of Institutional Animal Ethics Committee (IAEC) (Reg. No. IAEC/SUCP/08/2013) 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[17].

Anti-inflammatory activity of the ibuprofen SEDDS was compared to the marketed product. Animals were divided into three groups of six animals each. Group I (control) received water. Group II, received 25 mg/kg ibuprofen SEDDS and Group III received 25 mg/kg marketed product. After one hour, 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 after five hour 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.

% 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:

Selection of oils, surfactants and cosurfactants

The oil, surfactant and cosurfactant are selected based on the solubility of Ibuprofen. The oil and surfactants selected for the preparation of SEDDS should have the ability to solubilize the drug at a high level in order to obtain a concentrated form that can be loaded in the solid matrices[18].

The solubility of Ibuprofen in various vehicles is depicted in **Table 1**. The Ibuprofen show highest solubility in Labrafac PG (Oil), Tween 80 (Surfactant) and PEG 200 (Co-surfactant) hence are selected for the preparation of SEDDS.

The Labrafac PG contains a mixture of medium chain fatty acid that favours complete solubilization of drug in the vicinity of triglyceride chains attributable to the shorter chain length[19]. Tween 80 is a non-ionic surfactant with high hydrophilic-lipophilic balance (HLB) i.e., 15. Non-ionic surfactants are often used in SEDDS preparation, as they are less toxic and less affected by pH and ionic strength. PEG 200 is used as cosurfactant, it is very well accepted that cosurfactant along with surfactants assemble at the interfacial layer reduces the surface tension and tend to fluidize the interfacial surfactant film and thus broadens the area of emulsification region[19].

TABLE 1: SOLUBILITY OF IBUPROFEN IN VARIOUS OILS/SURFACTANTS

Oil/surfactant	Solubility (mg/ml)
Ethyl oleate	173.2±2.1
Captex 200	255.4±1.6
Capmul MCM	291.7±2.1
Labrafac PG	330.2±1.3
Tween 20	256.6±1.9
Tween 80	314.89±2.1
PEG 200	793.5±1.7
PEG 800	780.1±1.9
Triethanolamine	216.7±0.8
SPAN 80	134.8±0.4

Mean ± S.D, n=3

Although PEG 200 and PEG 400 have similar characteristics and HLB value, PEG 200 was used since it solubilises more ibuprofen than PEG 800. Hence, these excipients are selected for the further studies.

Construction of Pseudo ternary phase diagram

Pseudo-ternary phase diagrams are constructed to optimize the concentration of the Labrafac PG (oil), Tween 80 (surfactant) and PEG 200 (cosurfactant) and to identify their effect on the emulsion formation. It is important to determine the self emulsification area in order to ensure successful aqueous dilution without 'breaking' the emulsion. The phase diagrams show only emulsification region, to avoid the overcrowding of phase diagram. The phase diagrams for different oil-

Smix-water systems are shown in **Figure 1**. The interfacial free energy between Labrafac PG and the water was decreased due to hydrophilicity of Tween 80 that contained on the surface of the Labrafac PG droplets that provides a mechanical barrier to prevent oil droplets from coalescence resulting in a thermodynamically stable emulsion[20].

In **Figure 1** (Smix ratio 1:0), when surfactant alone was used only a small area of emulsion is formed with oil solubilized upto 15% with 24% of Smix. In case of self emulsifying system without cosurfactant, instantaneous formation of turbid gel was observed on addition to water. Therefore, this mixture without co-surfactant was considered as 'bad' emulsifying system as spontaneous emulsification was not observed. When surfactant and cosurfactant were taken in equal ratio (Smix 1:1), a large area of nanoemulsion is formed and the oil solubilization increased to 29%.

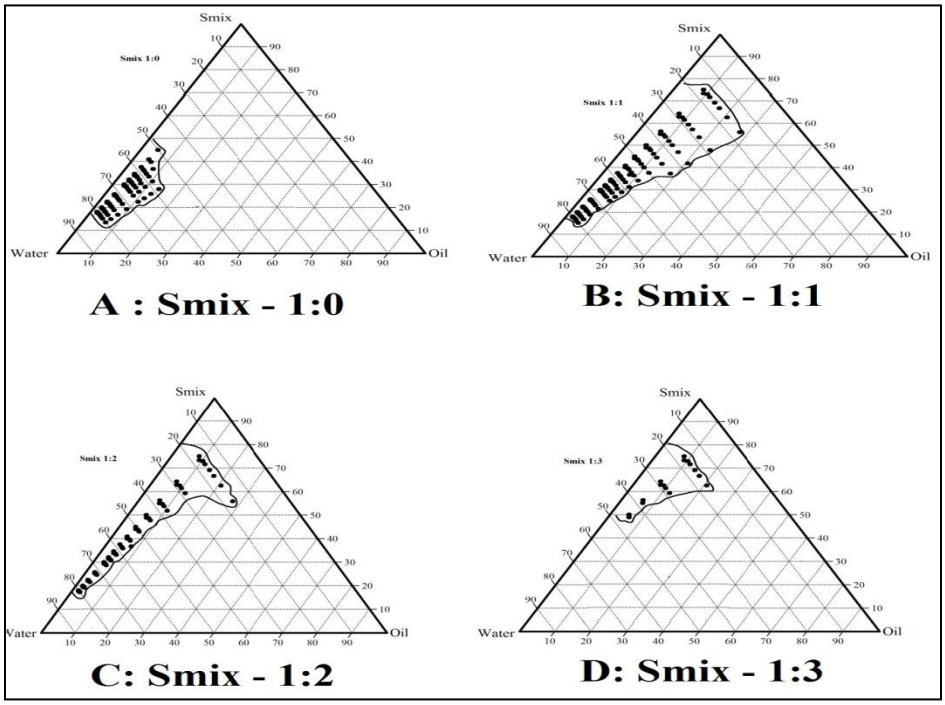

FIGURE 1: PSEUDO-TERNARY PHASE DIAGRAM OF IBUPROFEN

The presence of co-surfactants decrease the bending stress of the interface and allow an interfacial film with sufficient flexibility to assume different curvatures required to form a emulsion over a wide range of compositions[21]. As the concentration of cosurfactant was increased with respect to surfactant, there was no change in the oil solubilisation but there is gradual increase in self emulsification area.

Selection of formulations from phase diagrams

From each phase diagram different concentrations of oil that formed a emulsion was selected at 5% increments (10%, 15%, 20%, 25%, 30%, 35%, 40%), large number of formulations could be selected covering the emulsion area of the phase diagram. Formulations containing minimal amount of Smix were chosen for further studies. The optimised formulations were chosen which has low surfactant concentration; short self-emulsifying time and optimum droplet size[22], as high concentration of surfactants produce toxic effects during long term oral administration.

Thermodynamic stability tests

Formulations selected from ternary phase diagram (o/w emulsion region) were subjected to thermodynamic stability in order to eliminate metastable formulations in minimum possible time. The results of formulations which passed thermodynamic test are presented in **Table 2** along with their concentrations. Emulsions are thermodynamically stable systems which are formed at a particular concentration of oil, surfactant and water, with no phase separation, creaming or cracking. It is the thermodynamic stability which differentiates nano or micro emulsions from macroemulsions which have kinetic instability and eventually results in phase separation.

TABLE 2: THERMODYNAMIC STABILITY TEST AND DISPERSION TEST

Smix	Oil	Smix	Aqueous	Centrifuge	H/C cycle	Freeze Thaw	Disperse Grade	Inference
1:0	10	15	75	Pass	Fail	Fail	D	Fail
(A)	15	24	61	Pass	Fail	Fail	D	Fail
1:1	10	26	64	Pass	Fail	Fail	A	Fail
(B)	15	34	51	Pass	Fail	Fail	A	Fail
	20	36	44	Pass	Fail	Fail	A	Fail
	25	48	27	Fail	Fail	Fail	A	Fail
1:2	10	44	46	Pass	Fail	Fail	A	Fail
(C)	15	57	28	Pass	Pass	Pass	A	Pass
	20	58	22	Pass	Pass	Pass	A	Pass
	25	55	20	Pass	Fail	Fail	A	Fail
1:3	10	54	36	Pass	Fail	Fail	A	Fail
(D)	15	58	27	Pass	Fail	Fail	A	Fail
	20	60	20	Pass	Pass	Pass	A	Pass
1:4	10	54	36	Pass	Fail	Fail	A	Fail
(E)	15	57	28	Pass	Fail	Fail	A	Fail
	20	60	20	Fail	Fail	Fail	A	Fail
	25	56	29	Pass	Fail	Fail	B	Fail

Dispersibility tests

Dispersibility tests were carried to find the formation of emulsions from the prepared SEDDS after oral administration. The results of dispersibility tests are given in the table 2. Majority of the formulations emulsify as soon as they come in contact with dissolution media. The formulations containing surfactants alone (Smix 1:0) take longer time to emulsify, because of absence of cosurfactant, formation of interfacial film is rarely achieved. The similar result were observed with higher oil concentration (Smix 4:1), due to lack of availability of cosurfactant in the formation of interfacial film.

On the basis of the thermodynamic stability studies and dispersibility tests, three formulations were selected for further characterization based on thermodynamic stability tests and dispersibility test **(Table 3)**.

TABLE 3: COMPOSITION OF OPTIMIZED FORMULATIONS

Formulation Code	Smix ratio	Oil %	Surfactant %	Co-Surfactant %
F1	1:2	15	19	38
F2	1:2	20	19.3	38.7
F3	3:1	30	36	12
Ibuprofen	200 mg			

Effect of pH and robustness to dilution

High inter-subject variation exists in the volume of GI fluid particularly in case of fed and fasted states. The success of prepared SEDDS depends on the infinite dilutability and formation of micro droplets, as the process of dilution by the GI fluids lead to gradual desorption of surfactant located at the globule interface. The process is thermodynamically driven by the requirement of the surfactant to maintain an aqueous phase concentration equivalent to its critical micelle concentration.

The optimized oil and Smix concentrations are robust to all dilutions with various dissolution media. Robustness to dilution, with excess of water, 0.1M HCl, standard pH 1.2 and pH 6.8 phosphate buffers, show no precipitation or phase separation. No significant effect of pH on the optimized formulations F1, F2 and F3 was observed. It confirms the preparations were robust to high dilution and variations in pH.

Globule size determination

The crucial factor in the self emulsification performance of the emulsion is its droplet size, because it determines the rate and extent of drug release as well as drug absorption. The mean droplet size of formulations was in the micrometer range. The mean globule size of the optimized formulations is shown in **Table 4**. These

formulations showed the narrow size distribution and the difference in the droplet size among the formulations was not statistically significant. F1 showed the lowest globule size **(Figure 2)** than F2 and F3.

An increase in the ratio of the oil phase resulted in a proportional increase in globule size, because of the simultaneous decrease in the Smix proportion. It is well accepted that the addition of surfactants to the emulsion systems causes the interfacial film to stabilize and condense, while the addition of co-surfactant causes the film to expand; thus, the relative proportion of surfactant to co-surfactant has varied effects on the droplet size[23].

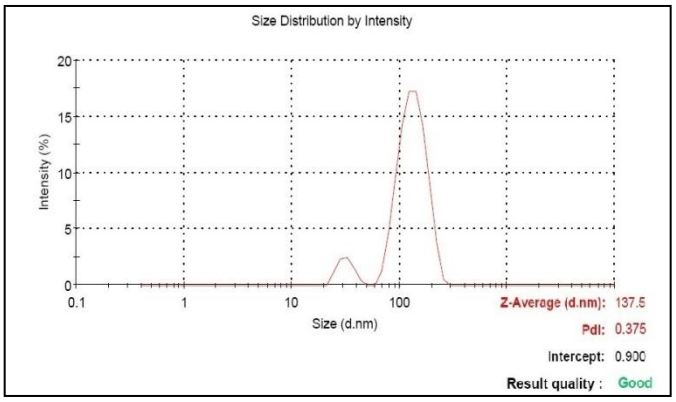

FIGURE 2: GLOBULE SIZE DISTRIBUTION OF F1

A smaller droplet size improves drug release and provides larger interfacial area across which drug can diffuse into the gastrointestinal fluids and thus increases drug absorption[24]. The polydispersibility value was less than one in all formulations indicating narrow size distribution.

TABLE 4: GLOBULE SIZE, ZETA POTENTIAL, POLYDISPERSIBILITY INDEX OF FORMULATIONS

Formulation Code	Globule size (nm)	Zeta potential (mV)	Polydispersibilty index
F1	137.5	-32.67	0.281
F2	147.7	-39.54	0.236
F3	156.5	-27.7	0.281

Polydispersibility is the ratio of standard deviation to mean droplet size, so it indicates the uniformity of droplet size within the formulation. The higher the polydispersibility, the lower the uniformity of the droplet size in the formulation.

Zeta potential

Many studies have reported that the zeta potential played an important role in the interactions with mucus of the gastrointestinal tract. According to the reports, the intestinal cell interior carry negative charges with the presence of mucosal fluid, the positive charged droplets could have better interaction with the mucus of the gastrointestinal tract[25]. The Zeta potential of the optimized formulations is given in **Table 4.** Zeta potential of formulations increased with increase in surfactant concentration.

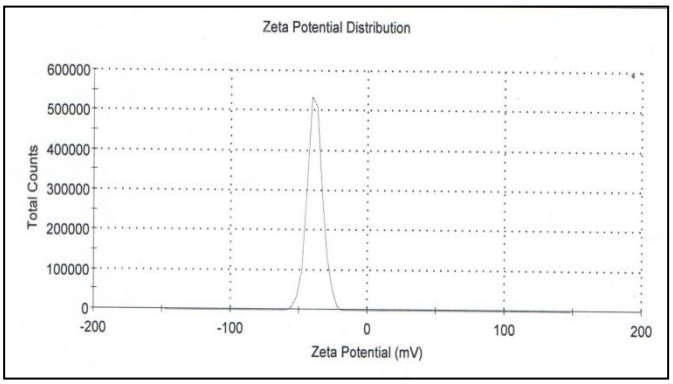

FIGURE 3: ZETA POTENTIAL VALUE FOR F3

Surfactant decreases the globule size that makes higher surface area, lead to increase in zeta potential value. Because the droplets have a lower zeta potential, aggregations will not take place and they are likely to facilitate the intestinal absorption of ibuprofen.

TABLE 5: VISCOSITY, REFRACTIVE INDEX, % TRANSMISSION OF FORMULATIONS

Formulation	Viscosity (cps)	Refractive index	% Transmission*
F1	21.2±0.2	1.46±0.2	98.2±1.6
F2	24.6±0.6	1.458±0.4	98.7±0.8
F3	29.3±0.3	1.458±0.3	97.4±1.2

Mean ± S.D, n=3

Viscosity

The viscosity of prepared formulation are in the following order, F3 > F2 > F1 (table 5). The viscosity of all the formulations was in the range of 21.2-29.3 cps. The viscosity of formulation related to the concentration of oils and surfactants used. There are reports indicating that SEDDS having lower viscosity tend to form o/w type of emulsion system.

Refractive index and percent transmittance

The refractive index of the prepared formulation was similar to the refractive index of the water (1.333). In addition, the formulation showed more than 95% percent transmittance. The refractive index and percent transmittance data **(Table 5)**

indicates the formulation was transparent. The observed transparency of the system is due to the fact that the maximum size of the droplets of the dispersed phase is not larger than 1/4th of the wavelength of visible light. Thus, emulsion scatters little light and therefore appears transparent or translucent.

Differential scanning calorimetry

The DSC thermograms of pure ibuprofen and ibuprofen SEDDS are presented in **Figure 4.** The DSC thermograms show pronounced melting peak for ibuprofen, at 77.5°C. The absence of ibuprofen peak in SEDDS was due to presence of drug in molecularly dissolved state in the lipid excipients.

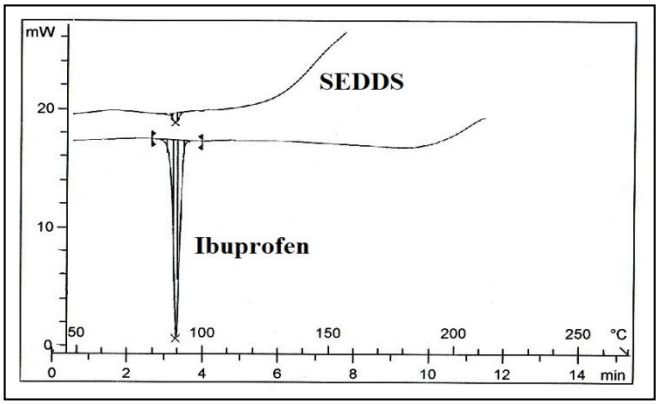

FIGURE 4: DSC THERMOGRAMS OF IBUPROFEN AND IBUPROFEN SEDDS

Drug content estimation

Drug content of all the optimized formulations was more than 98% and there was no significant difference among the formulations.

***In vitro* drug release**

The *in vitro* drug release studies were carried in order to ensure the fast release of the drug to the dissolution medium. Furthermore, *in vitro* drug release studies also depecits the self emulsification efficiency of the developed system.

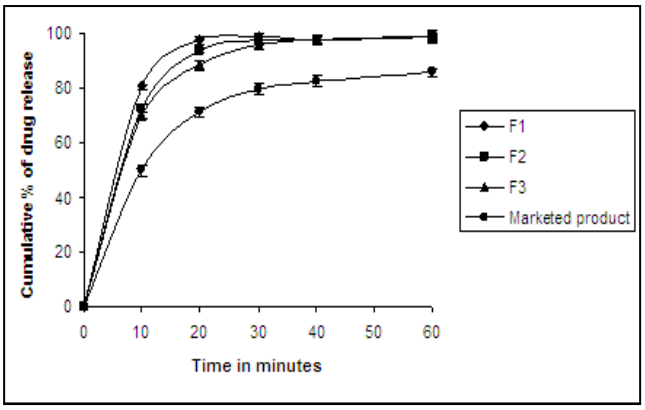

FIGURE 5: *IN VITRO* DRUG RELEASE STUDIES

The *in vitro* drug release of F1, F2, F3 and marketed product were studied in pH 7.4 Phosphate buffer. F1, F2 and F3 formulations showed more than 90% of drug release within 30 min. The result of drug release correlates with the results of globule size determination. As the globule size decreases, the surface area exposure to dissolution media increases, that result in the faster release of the drug. F1 showed the maximum release hence it's selected for anti-inflammatory activity.

Table 6 shows the results of percentage inhibition of carrageenan-induced paw edema in rats treated with marketed formulation and prepared SEDDS. A significant ($p<0.05$) inhibition of carrageenan induced paw edema was observed in animals treated with SEDDS in comparison with marketed product during the entire 5 h duration of the study. This may be due to increased absorption (permeation) of drug from SEDDS over marketed product, leading to better absorption and onset of action of drug. Hence, SEDDS showed better anti-inflammatory activity over the marketed product.

TABLE 6: ANTI-INFLAMMATORY ACTIVITY OF IBUPROFEN SEDDS AND MARKETED PRODUCT

Group	Percentage inhibition of edema at various time intervals				
	1h	2 h	3 h	4 h	5 h
II (treated with F1)	58.25±2.38	65.32±3.21	72.9±4.37	82.95±4.16	87.73±6.12
III (treated with marketed product)	48.28±4.11	53.94±5.33	62.87±3.91	71.34±6.28	73.07±5.71

Mean ± S.D, n=6

Therefore, the results of the *in vivo* studies clearly demonstrate that the SEDDS showed better anti-inflammatory activity over the marketed product, thus confirming the better therapeutic efficacy of the SEDDS.

CONCLUSION: Self-emulsifying drug delivery systems are a promising approach for the formulation of drug compounds with poor aqueous solubility. SEDDS of ibuprofen showed improved dissolution rate and absorption. DSC study showed

that the drug is stable in formulation. SEDDS of ibuprofen found to be having better anti-inflammatory activity in the rats when compared to marketed product due to improved solubility, which have been shown to substantially improve oral bioavailability.

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