Design and Development of Novel Self Emulsifying Floating Drug Delivery System of Ibuprofen

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Abstract:

The present study focuses on the design and development of a novel self-emulsifying floating drug delivery system (SEFDDS) for Ibuprofen, a poorly water-soluble drug belonging to the Biopharmaceutical Classification System (BCS) Class II. Poor aqueous solubility of such drugs often results in low oral bioavailability and variable therapeutic response. The aim of this research is to enhance the solubility, dissolution rate, gastric residence time, and bioavailability of Ibuprofen through the development of a floating self-emulsifying drug delivery system.

Self-emulsifying drug delivery systems (SEDDS) are isotropic mixtures of oils, surfactants, and co-surfactants that spontaneously form fine oil-in-water emulsions upon mild agitation in gastrointestinal fluids. Incorporation of floating characteristics into the formulation helps prolong gastric retention time, thereby improving drug absorption and therapeutic effectiveness. The developed formulation was prepared using suitable lipids, surfactants, and floating agents, and evaluated for parameters such as emulsification time, droplet size, buoyancy behavior, drug content, in-vitro dissolution, and stability.

The results demonstrated that the optimized formulation exhibited rapid self-emulsification, good floating ability, enhanced dissolution rate, and improved drug release compared to conventional dosage forms. Thus, the novel self-emulsifying floating drug delivery system represents a promising approach for improving the oral bioavailability and therapeutic performance of poorly water-soluble drugs like Ibuprofen.

Key words: Ibuprofen self-emulsifying system phase diagram zeta potential, anti-inflammatory activity.

1. INTRODUCTION:

Nearly 35-40% of new drug candidates have poor water solubility; oral delivery of such drugs is associated with the problem of low bioavailability. To overcome these issues various formulation strategies have been exploited like complexation, particle size reduction, use of lipids, surfactants, cyclodextrins and micelles. Advanced approaches include self micro emulsifying drug delivery system and self micro-emulsifying nanoparticles. Self-emulsifying drug delivery systems are isotropic mixtures of drug, lipids and surfactants, usually with one or more hydrophilic co-solvents or co-emulsifier with droplet size ranging from few nanometers to several microns.[1,2,3]

Recently, much attention has been paid to lipid-based formulations with particular emphasis on self-emulsifying drug delivery systems (SEDDS) to improve the oral bioavailability of lipophilic drugs. Upon mild agitation followed by dilution in aqueous media, such as gastrointestinal (GI) fluids, these systems can form fine oil- in-water (o/w) emulsions or microemulsions (SMEDDS). Fine oil droplets would pass rapidly from the stomach and promote wide distribution of the drug throughout the GI tract, thereby minimizing the irritation frequently encountered during extended contact between bulk drug substances and the gut wall. When compared with emulsions, which are sensitive and meta-stable dispersed forms, SEDDS are physically stable formulations that are easy to manufacture. Self emulsifying drug delivery systems

(SEDDS) easily form micro emulsions with mild agitation, and have been identified as a promising technology for drug delivery (independent of the delivery mode) because they have a large solubilization capacity, small particle size, and excellent stability, and they can enhance permeation across the intestinal membrane, provide reproducible and increased bioavailability, and eliminate or reduce food effects[3].

According to the Biopharmaceutical Classification System (BCS) classification, two classes of drugs show poor aqueous solubility namely BCS II and BCS IV. BCS II drugs possess poor aqueous solubility but have good permeation properties. Most of the times, such drugs are withdrawn at its lead optimization stage of drug discovery and reworked to improve its physico-chemical properties. Developing a formulation for a drug belonging to BCS II is often challenging as it requires improved dissolution characteristics.[1, 4]

Nearly 35–40% of new drug candidates have poor water solubility, leading to low oral bioavailability. To overcome this, strategies such as complexation, particle size reduction, and the use of lipids, surfactants, cyclodextrins, and micelles are employed. Advanced systems like self-emulsifying drug delivery systems (SEDDS) and SMEDDS have gained importance.

SEDDS are isotropic mixtures of drugs, lipids, and surfactants that form fine oil-in-water emulsions upon mild agitation in gastrointestinal fluids, improving drug distribution and reducing irritation. They are more stable and easier to manufacture than conventional emulsions and enhance solubility, permeability, and bioavailability while minimizing food effects.

According to the Biopharmaceutical Classification System (BCS), Class II and IV drugs exhibit poor solubility. BCS Class II drugs, despite good permeability, require improved dissolution, making their formulation particularly challenging.

1.1 BIOPHARMACEUTICAL CLASSIFICATION SYSTEM:

The SEDDS formulation has been well accepted for drugs with poor aqueous solubility and high permeability, classified as Class II drugs by BCS system. The rate and extent of absorption of class II compounds is highly dependent on the performance of the formulated product. These drugs can be successfully formulated for oral administration, but care needs to be taken with formulation design to ensure consistent bioavailability. Essentially the options available involve either reduction of particle size of crystalline drug or formulation of the drug in solution, as anamorphous system or lipid formulation.[1, 3, 4]

1.2 LIPID FORMULATION CLASSIFICATION SYSTEM (LFCS):

In recent years the LFCS has been discussed more widely within the pharmaceutical industry to seek a consensus which can be adopted as a framework for comparing the performance of lipid based formulation. The main purpose of the LFCS is to enable in vivo studies to be interpreted more rapidly, and subsequently to facilitate the identification of the most appropriate formulation for specific drugs, i.e. with reference to their physicochemical properties. Table 1 indicates the fundamental differences between Type I, II, III and IV formulations. [5, 9]

1) Formulation of Type I systems:

Type I systems are comprised of only one excipients which is a triglyceride or a mixture of a triglyceride with amonoordiglyceride. Highly lipophilic drugs with log P >5 can be delivered by this formulation. Examples of commercially available type I formulations (in soft gelatin capsules) are Progesterone dissolved in peanut oil (Prometrium®), testosterone undecanoate dissolved in oleic acid (Restandol®) and valproic acid dissolved in corn oil (Depakene®).

2) Formulation of Type II formulations:

These formulations contain a lipophilic surfactant (HLB<12) in addition to the triglycerides. Surfactants aid in the emulsification of these systems as well as provide solvent capacity for the drug. If the surfactant is not sufficiently hydrophilic, it exists as a dispersed phase, either within or separated from the oily components. A SEDDS comprising of a medium chain triglyceride and a polyoxyethylene-(25)-glyceryl trioleate (Tagat TO) is an example of type II

system.

3) Formulation of Type III systems:

Addition of a hydrophilic surfactant (HLB>12) and /or water soluble co-solvent to the triglyceride makes the formulation self-emulsifying. Addition of co-solvent has a double effect: (a) along with the surfactant it is able to form a very fine dispersion with droplet size of less than 100 nm and (b) it increases the solvent capacity of the formulation since it can dissolve large quantities of a drug.

4) Formulation of Type IV system:

These systems are comprised of just surfactants or a mixture of surfactant and a co-solvent. If the drug is formulated in a pure solvent, there are chances of drug being precipitated as amorphous or fine crystalline particles. If the drug is formulated in pure surfactants, there will be less chance of precipitation but owing to formation of a liquid crystalline state at the oil-water interface, surfactants will take more time to disperse in water. Commercially examples of such a system is Amprenavir (Agenerase®, GSK) which is formulated in a blend of tocopheryl polyethylene glycol 1000 succinate (TPGS), PEG 400, and propylene glycol.

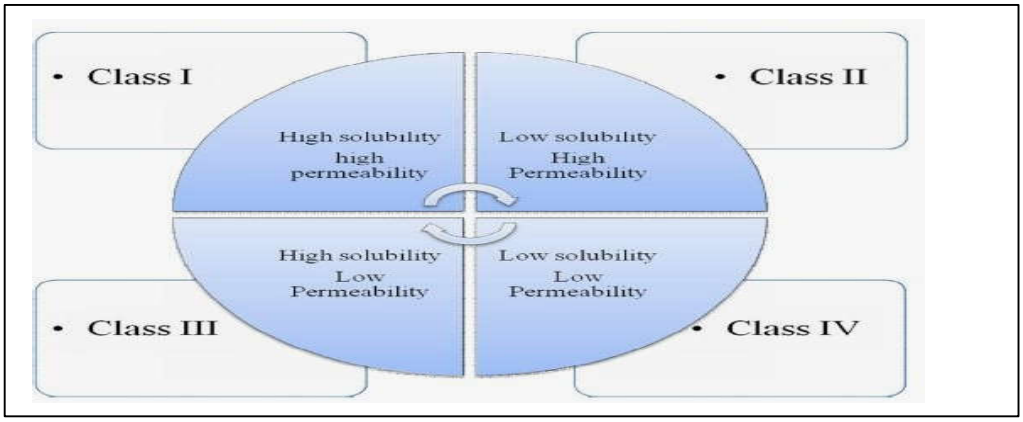


Figure No.1Biopharmaceutical Classification System

Characteristic features, advantages and disadvantages of the four essential types of Lipid Formulation:

Table 1: The Lipid Formulation Classification System:

LCFS type	Materials	Characteristics	Advantages	Disadvantages
Type I	Oils without surfactants (e.g. tri-, di- and monoglyceroides)	Non-dispersing, require digestion	GRAS status, simple, excellent capsule compatibility	Poor solvent capacity unless the drug is highly lipophilic
Type II	Oils and water insoluble surfactants	SEDDS without water soluble components	Unlike lytolose solvent capacity on dispersion	Turbid o/w emulsion (0.25-2μm)
Type IIIA	Oils, surfactants, co-solvents (both water- insoluble and water soluble excipients)	SEDDS/SMED DS with water soluble components	Clear or almost clear dispersion, drug absorption without digestion	Possible loss of solvent capacity on dispersion, less Easily digested
Type IIIB	Water- soluble surfactants and co-solvents , oils	SMEDDS with water-soluble components and Low oil content	Clear dispersion, drug absorption without digestion	Likely loss of solvent capacity on dispersion

Type IV	Water- soluble surfactants and co-solvents (no oils)	Oil-free formulation based on surfactant and co-solvents	Good solvent capacity for many drugs, disperses to Micellar solution	Loss of solvent capacity on dispersion, may not be digestible

Table 2: Typical properties of Type I, II, IIIA and IIIB lipid formulations:

	Increasing hydrophilic content			
	Type I	**Type II**	**Type III A**	**Type III B**
Typical composition (%) Triglycerides or Mixed glycerides	100	40-80	40-80	<20
Surfactant	--	20-60 (HLB<12)	20-60 (HLB<11)	20-50 (HLB>11)
Hydrophilic Co-solvent	--	--	0-40	20-50
Particle size dispersion(nm)	Coarse	100-250	100-250	50-100
Significance aqueous dilution	Limited Importance	Solvent Capacity unaffected	Some loss of solvent Capacity	Significant phase changes and potential loss of solvent capacity
Significance Digestibility	Crucial Requirement	Not crucial but likely to occur	Not crucial but may be inhibited	Not required and not likely to occur

1.3 Self Emulsifying Drug Delivery System:

The Self Dispersing Lipid Formulations are of two kinds namely, Self-Emulsifying Drug Delivery Systems (SEDDS) formed using surfactants of HLB < 12 and Self-Micro Emulsifying Drug Delivery Systems (SMEDDS) formed with surfactants of HLB > 12. Both SEDDS and SMEDDS are stable preparations and improvethedissolutionofthedrugduetoincreasedsurfaceareaondispersion.

Therefore, they are not dependent on bile secretion for absorption. The emulsified form itself is readily absorbable. This ensures a rapid transport of poorly soluble drugs into the blood.[10]

1.3.1 Advantages:

Potential advantages of these systems (SEDDS) include-

1. Enhanced oral bioavailability enabling reduction in dose.
2. More consistent temporal profiles of drug absorption.
3. Selective targeting of drug (s) to ward specific absorption windowing GIT.
4. Protection of drug (s) from the hostile environment in gut.
5. Control of delivery profiles.
6. Reduced variability including food effects.
7. Protection of sensitive drug substances.
8. High drug payloads.
9. Liquid or solid dosage forms.[11,12]

1.3.2 Drawbacks of SEDDS: Includes

1. Chemical instabilities of drugs and high surfactant concentrations.
2. The large quantity of surfactant in self-emulsifying formulations (30-60%) irritates GIT. Consequently, the safety aspect of the surfactant vehicle had to be considered.
3. Moreover, volatile co solvents in the conventional self-emulsifying formulations are

known to migrate into the shells of soft or hard gelatin capsules, resulting in the precipitation of the lipophilic drugs.[10,11]

1.3.3 Properties of SEDDS:

1. They are able to self emulsify rapidly in gastro-intestinal fluids & under the influence of gentle agitation provided by Peristaltic and other movements of gastro intestinal tract, they form a fine o/w emulsion.
2. They can effectively incorporate drug (hydrophobic or hydrophilic) within the oil surfactant mixture.
3. They can be used for liquid as well as solid dosage forms.
4. They require lower dose of drug with respect to conventional dosage forms.[1]

1.4 Self Emulsifying Drug Delivery System:

Self-Emulsifying drug delivery systems (SEDDS) are isotropic mixtures of oil, hydrophilic surfactant and/or a co-surfactant, and a solubilized drug. They can be encapsulated in

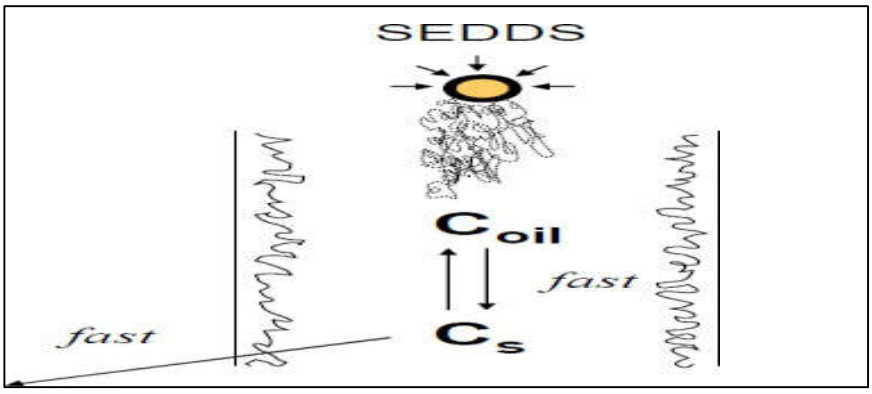


Figure No. 2 Mechanism of Drug Partitioning in SEDDS

hard or soft gelatin capsules or can be converted to solid state (Solid SEDDS). These formulations spontaneously form a fine oil-in-water emulsion in case of SEDDS and a nano-emulsion in the case of SEDDS upon dilution with water. In the GI tract, they are readily dispersed, where the motility of the stomach and small intestine provides the gentle agitation necessary for emulsification. SEDDS produces coarse emulsions while SEDDS produces droplets of size less than 100nm. SEDDS improves the rate and extent of absorption of hydrophobic drugs, whose absorption is considered to be dissolution rate-limited.

Upon aqueous dilution the drug remains in the oil droplets or as amicellar solution since the surfactant concentration is very high in such formulations. The drug in the oil droplet may partition out in the intestinal fluid as shown in figure -2. [13-16]

Selection of suitable self emulsifying formulation depends upon the assessment of

1. The solubility of the drug in various components,
2. The area of the self-emulsifying region as obtained in the phase diagram.
3. The droplet size distribution of the resultant emulsion following self emulsification. [14]

In recent years several successful oral pharmaceutical products have been marketed as lipid systems, notably cyclosporine A (originally marketed as sandimmune E' and now as the improve product Neoral E') and the two HIV protease inhibitors, ritonavir and saquinavir. [15]

1.5. Role of SEDDS Sin improvement of oral absorption:

SEDDS partially avoids the additional drug dissolution step prior to absorption in the GI tract. They increase the amount of solubilized drug in the intestinal fluids resulting in good drug absorption. Apart from this, absorption of the drug may also been enhanced by using lipid based excipients in the formulation. There are several mechanisms through which increased absorption can be achieved; the following schematic diagram describes these mechanisms. [17]

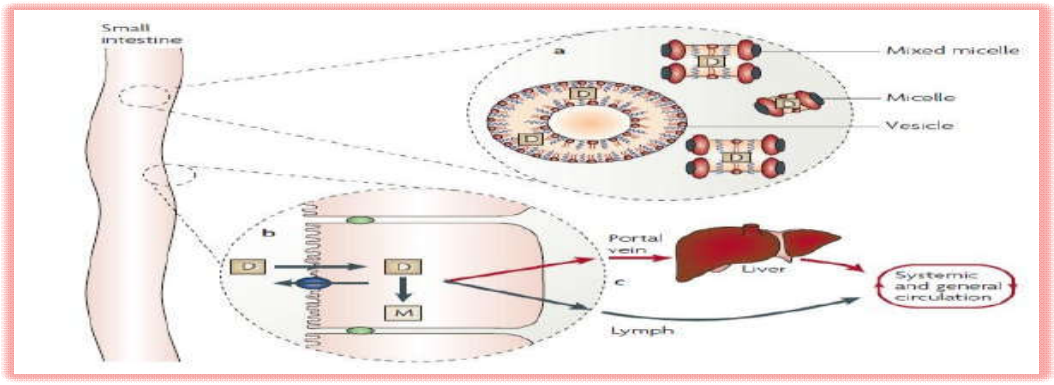


Figure No.3: Pathways for drug absorption from lipid based formulations

1) **Retardation of gastric emptying time:** Surfactants are believed to play a role in retardation of gastric transit time, thereby increasing the time available for the drug to dissolve and get absorbed. Surfactants may slow down gastric emptying for a period of time by formation of viscous mass in the gastric and intestinal lumen. Labrasol (a caprylo caproyl macrogol glyceride) was shown to improve bioavailability of an investigational compound by retarding gastric emptying time.

2) **Increase in effective drug solubility in lumen:** When exogenous lipid excipients are encountered in the gastric environment, they are digested by gastric lipases.

Triglycerides are digested to diglycerides and fatty acids. The duodenum secretes bile salts (BS), phosphatidylcholine (PL) and cholesterol (Ch) from the gall bladder and pancreatic lipases from pancreas. These agents in combination with lipid digestion products get adsorbed to the surface of emulsion droplet and transform into small, stable droplets. They also produce a series of colloidal particles such as micelles, mixed micelles, and vesicles as shown in figure 3. The drug contained in the oil droplet partitions into these micellar structures making them a drug reservoir at the absorption site. These results in an increased solubilization capacity of the drug in the GI tract.[18] the micelles and nanoemulsions can be absorbed through following mechanisms: pinocytosis, diffusion, or endocytosis. In case of SEDDS, it has been shown that digestion of the resultant nanoemulsion acts independently of bile salts and the polarity of the oil droplets are not significant because the drug reaches the capillaries within the oil droplets.

3) **Lymphatic transport of the drug**: Most of the drugs delivered using SEDDS are absorbed systematically via portal vein except for certain type of drugs. Lymphatic transport of the drug occurs when the drug is highly lipophilic (logP>5) and shows high solubility in triglycerides (>50mg/ml). Such drugs are absorbed via lymph vessels in the intestine which are responsible for absorption of lipids. Since the drug is cleared by the lymph vessels, they bypass the liver metabolism. This results in an increased bioavailability of these drugs. The bioavailability of Ontazolast, an extensively first-pass metabolized drug was improved when delivered in a lipid based formulation. The drug was absorbed via lymphatic pathway and thus bypassed first-pass metabolism.[19, 20]

4) **Enterocyte based drug transport**: Few endogenous lipid transporters have been identified which are responsible for intestinal passage of lipophilic drugs. At low lipid concentrations drugs are actively transported, while at high lipid concentrations drugs are passively permeated. P-glycoprotein (P-gp) is an efflux transporter present in enterocytes that acts as a substrate for many lipophilic drugs. Surfactants are reported to inhibit these P-gp efflux transporters resulting in an increase in permeability of poorly permeated drugs[21]. Labrasol was identified as the most effective surfactant in inhibiting the P-gp.

5) **Increasing membrane permeability:** Lipids are responsible for causing fluidization of intestinal cell membrane and opening of tight junctions resulting in increased membrane permeability. Labrasol has a dual property of increasing membrane permeability by both the mechanisms, while Cremphor EL and Tween 80 act by opening the tight junction barrier[22, 23].

Surfactants also penetrate into the intestinal cell membrane and disrupt the structural organization of the membrane leading to an increased permeability.

1.5.1 Factors affecting SEDDS:

a) Drug that are administered at very high doses are not suitable for SEDDS unless they exhibit extremely good solubility in at least one of the component of SEDDDS, preferably lipophillic phase.

- High-dose drugs are unsuitable for SEDDS unless they have very high solubility, preferably in the lipid phase.
- Drug solubility in the oily phase is crucial; reliance on surfactants may cause precipitation upon dilution.
- Equilibrium solubility studies help predict precipitation, though crystallization may be slow in the GI environment.

b) The ability of SEDDS to maintain the drug in solubilized form is greatly influenced by the solubility of the drug in oily phase. If the surfactant or co- surfactants contributing to great extent in drug solubilization, then there could be a risk of precipitation, as dilution of SEDDS lead to lowering of solvent capacity of surfactant or co-surfactant.

c) Equilibrium solubility measurement can be carried out to anticipate potential cases of precipitation in the gut. However, crystallization could be slow in solubilizing and colloidal stabilizing environment of the gut.

d) The polarity of lipid phase is one of the factors that govern the release from the micro-emulsion. HLB, chain length and degree of un-saturation of the fatty acids, molecular weight of the hydrophilic portion and concentration of the emulsifier govern polarity of the droplets. In fact, the polarity reflects the affinity of the drug for oil and/or water, and the type of forces involved. The high polarity will promote rapid rate of release of the drug into the aqueous phase

1.6 Mechanism of self-emulsification:[24, 25]

Self emulsifying processes are related to the free energy, ΔG given by:

$$\Delta G = \Sigma N \pi r^2 \sigma$$

Where, N=Number of droplets with radius r σ = Interfacial energy

It is apparent from the above equation that spontaneous formation of interface between oil & water phase is not favorable due to higher energy level. The system commonly classified as SEDDS have not yet been shown to emulsify spontaneously in true thermodynamic sense.

1.7 Construction of Ternary Phase Diagrams:

Pseudo ternary phase diagrams of oil, surfactant/co-surfactant (S/CoS), and water were plotted using the water titration method or dilution method. In the water titration method the mixtures of oil and S/CoS at fixed ratios were diluted with water in a drop wise manner. For each phase diagram at a specific ratio of S/CoS (i.e.1:1,1:2,:2:1wt/wt),a transparent and homogenous mixture of oil and S/CoS was formed by vortexing for 5 minutes. Then each mixture was titrated with water and visually observed for phase clarity and flowability. The concentration of water at which gel formation, turbidity to transparency and transparency to turbidity transitions cooured was noted. These values were then used to determine the boundaries of the microemulsion domain corresponding to the chosen value of oils, as well as the S/CoS mixing ratio. Phase diagrams were then constructed using **TRIPLOT** and **CHEMIX** software can also be used for the same purpose.

Water Titration Method: The pseudo-ternary phase diagrams were also constructed by titration of homogenous liquid mixtures of oil, surfactant and co-surfactant with water at room temperature. Oil phase, Surfactant and the co-surfactant (surfactant: co-surfactant ratio) were prepared varied from 9:1 to1:9 and weighed in the same screw- cap glass tubes and were

vortexed. Each mixture was then slowly titrated with aliquots of distilled water and stirred at room temperature to attain equilibrium. The mixture was visually examined for transparency. After equilibrium was reached, the mixtures were further titrated with aliquots of distilled water until they showed the turbidity. Clear and isotropic samples were deemed to be within the micro-emulsion region. No attempts were made to completely identify the other regions of the phase diagrams. Based on the results, appropriate percentage of oil, surfactant and co- surfactant was selected, correlated in the phase diagram and were used for preparation of SMEDDS. [26]

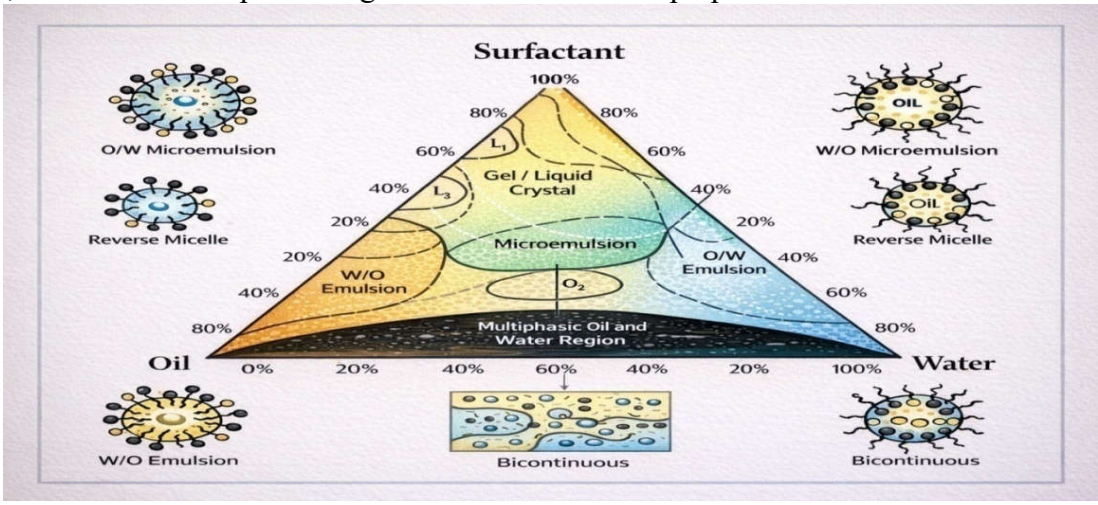


Figure No.4.Example of Phase Diagram

1.8 Excipient suitable for self emulsifying drug delivery system:[27]

Chemically, Lipids are considered as one of the most versatile excipient classes available today. There are various sub categories of lipid available and there is constant influx of new lipid based excipient in the market. This provides flexibility to the formulator in term of selecting a suitable excipient but the same time formulator should be caution while selecting particular excipient. Pouton et. al[12].

Described few factors that should be considered while selecting the lipid excipient. These are:

- ❖ Regular issues–Irritancy, Toxicity
- ❖ Solvent capacity
- ❖ Miscibility
- ❖ Morphology at room temperature
- ❖ Self dispersibility
- ❖ Digesibility and fate of digested product
- ❖ Capsule compatibility
- ❖ Purity, Chemical stability and
- ❖ Cost

Apart from this factor, Lipids have been shown to increase the bioavailability of drug. [27]

Excipients used in Self Emulsifying Drug Delivery System:

The self-emulsifying process is depends on:

- •The nature of the oil–surfactant pair
- •The surfactant concentration
- •The temperature at which self emulsification occurs.

A) Oils:-

Oils are the most important excipients in the SEDDS formulation, because they may be able to solubilize the lipophilic drug in definite quantity, and facilitate self- emulsification. By this, the amount of lipophilic drug transport can be increased via the intestinal lymphatic system, therefore absorption from the GI tract also increased by basing on the nature of triglyceride oils. At present Novel semi-synthetic medium- chain triglyceride oils have surfactant properties and are widely

used instead of the regular medium- chain triglyceride. Deckelbaum (1990) showing that MCT is more soluble and have a higher mobility in the lipid/water interfaces than LCT allied with a more rapid hydrolysis of MCT.[11,28]

Examples: Mono, di, tri-glycerides, DL-alpha-Tocopherol, Fractionated triglyceride of palm seed oil(medium-chain triglyceride), Medium chain mono-and di-glycerides, Corn oil, Olive oil, Oleic acid, Sesame oil, Soyabean oil, Peanut oil.

Table 3: Type of oils used in marketed SEDDS

Type of oil	Marketed Product	Drug
Corn oil	Depakene capsule	Valproic acid
Olive oil	Sandimmune oral solution	Cyclosporine
Peanut oil	Prometrium soft gelatin capsule	Progesterone
Sesame oil	Marinol soft gelatin capsule	Dronabinol

B) Surfactant:

Numerous compounds exhibiting surfactant properties might be working for the design of self-emulsifying systems, but the choice is limited at the same time as very few surfactants are orally suitable, because Safety is a major determining factor in choosing a surfactant The most extensively suggested ones being the non-ionic surfactants with a relatively high hydrophilic lipophilic balance (HLB).

The strength of surfactant usually ranges between 30–60%w/w of the formulation for the formation of stable SEDDS. Surfactants contain high HLB and hydrophilicity, which assists the instantaneous formation of o/w droplets and fast dispersion of the formulation in the aqueous media. Amphiphilic surfactants can solubilize the high amounts of hydrophobic drug compounds.

Nonionic surfactants are less toxic and possess good emulsion stability over wider range of ionic strength and pH than ionic surfactants, but may cause changes in intestinal lumen permeability.[28,36]

The least possible surfactant concentration should be used so as to prevent gastric irritation.[29-31]

Increase in surfactant concentration causes a decrease in droplet size associated with stabilization of surfactant molecules at the oil-water interface, while the reverse is possible due to enhanced water penetration into oil droplets leading to breakdown of oil droplets. [32-34]

Examples: Tween80, Labrasol, LabrafacCM10, Cremophore, Span80, LabrafilM 2125 Cs, Labrafil M1944 Cs, Tween 20.

Table 4: Type of surfactants used with different drugs in SEDDS

Surfactant	Marketed Product	Drug
Span80,Tween 80	Gengraf soft gelatin capsule	Cyclosporine
CremophorRH40	BCNU self emulsifying implant	Carmustine
D-alpha Tocopheryl Poly ethylene Glycol 1000Succinate (TPGS)	Agenerase Soft Gelatin capsule, Agenerase oral solution	Amprenavir
LabrafilM1944CS	Sandimmune oral solution.	Cyclosporine

C) Co-surfactant/Co-solvents:

Water soluble co-solvents are widely used in lipid based dosage forms. Ethanol, polyethylene glycol (PEG), propylene glycol, and glycerol are examples of co-solvents used. Their role is: (a) to increase the solvent capacity of the drugs which are freely soluble in them. But this is associated with the risk of drug precipitation when SEDDS are dispersed in water, (b) to dissolve large quantities of the hydrophilic surfactant in the oil. SEDDS requires use of high concentration

of surfactants to ensure proper dispersion of the formulation (c) To increase the stability of nanoemulsion by wedging themselves between surfactant molecules.

There are several key issues that have to be considered before using a particular co-solvent. The co-solvents are miscible with the oil only up to a certain limit. There are some incompatibilities of using alcohol since it may penetrate into soft and hard gelatin shell causing precipitation of the drug.[35]

Examples: Spans, Capyrol90, Lauroglycol, Diethylene glycol, monoethyl ether (transcutol), Propylene glycol, Polyethylene glycol, Polyoxyethylene, Propylene carbonate, Tetrahydrofurfuryl alcohol polyethylene glycol ether (Glycofurol), etc., might help to dissolve large amounts of hydrophilic surfactants or the hydrophobic drug in the lipid base.

Table 5: Type of Co-surfactants used in marketed SEDDS:

Co-surfactants	Marketed preparation	Drug
PolyEthyleneGlycol	Targretin soft gelatin Capsule	Bexarotene
Propylene glycol	Lamprene soft gelatin capsule	Clofazimine
Ethanol	Sandimmune soft gelatin capsule	Cyclosporine
Glycerin	Sandimmune soft gelatin capsule.	Cyclosporine

Formulation of SEDDS:

With a large variety of liquid or waxy excipients available, ranging from oils through biological lipids, hydrophobic and hydrophilic surfactants, to water-soluble co-solvents, there are many different combinations that could be formulated for encapsulation in hard or soft gelatin or mixtures which disperse to give fine colloidal emulsions

The following should be considered in the formulation of a SEDDS:

- The solubility of the drug in different oil, surfactants and co solvents.
- The selection of oil, surfactant and co solvent based on the solubility of the drug and the preparation of the phase diagram
- The preparation of SEDDS formulation by dissolving the drug in a mixture of oil, surfactant and co-solvent. The addition of a drug to a SEDDS is critical because the drug interferes with the self emulsification process to a certain extent, which leads to a change in the optimal oil–surfactant ratio. So, the design of an optimal SEDDS requires pre formulation-solubility and phase- diagram studies.[37]

Table 6: Examples of self- emulsifying systems designed by oral delivery of Lipophilic drugs:

Sr. No.	Drug	Formulation	Reference product	Increase in Bio avaibility (In Folds)
1	Vitamin E	SEDDS	Natophenol soft Gelatin capsule	2.0
2	Ontazolast	SEDDS	Aqueous suspension	13.0
3	Carvedilol	SEDDS	Conventional tablet	4.13
4	Co-enzyme Q10	SEDDS	Powder	2.0
5	Phenytoin	SEDDS	Dilantin suspension	2.3
6	Halofantrine	SEDDS, LCT	SMEDDS, MCT	1.3
7	1,3-bis (2-chloro ethyl) -1- nitroso urea (BCNU)	SEDDS	Intact BCNU	-
8	Ketoprofen	SEDDS (gelled)	-	-
9	Itraconazole	SEDDS	-	-
10	Diclofenac Sodium	Self- emulsifying	Pure drug	Increased

		tablet		dissolution rate
11	Methyl Paraben, Propyl paraben	Self-emulsifying pellets	Pure drug	Increased dissolution rate

1.9 Characterization:

The primary means of self-emulsification assessment is visual evaluation. The efficiency of self-emulsification could be estimated by determining the rate of emulsification, droplet-size distribution and turbidity measurements.

1) Visual assessment:

This may provide important information about the self-emulsifying and micro-emulsifying property of the mixture and about the resulting dispersion.[1,38]

2) Turbidity measurement:

Nepheloturbidimetric evaluation is done to monitor the growth of emulsification. Fixed quantity of Self emulsifying system is added to fixed quantity of suitable medium (0.1N hydrochloric acid) under continuous stirring (50 rpm) on magnetic plate at ambient temperature, and the increase in turbidity is measured using a turbid meter. However, since the time required for complete emulsification is too short, it is not possible to monitor the rate of change of turbidity (rate of emulsification),This is to identify efficient self-emulsification by establishing whether the dispersion reaches equilibrium rapidly and in a reproducible time.[38,39]

3) Droplet Size Analysis Particle Size Measurements:

This is a crucial factor in self-emulsification performance because it determines the rate and extent of drug release as well as the stability of the emulsion. Photon correlation spectroscopy, microscopic techniques are mainly used for the determination of the emulsion droplet size. The reduction of the droplet size to values below 50 μm leads to the formation of SEDDSs, which are stable, isotropic, clear o/w dispersions. [1.39]

4) Zeta potential measurement:

This is used to identify the charge of the droplets. In conventional SEDDSs, the charge on an oil droplet is negative due to presence of free fatty acids.[38]

5) Determination of emulsification time:

The self-emulsification time is determined by using USP dissolution apparatus IIat50 r/ min, where 0.5 g of SEDDS formulations is introduced into 250 ml of 0.1N HCL. The time for emulsification at room temperature is indicated as self-emulsification time for the formulation. [1]

6) Refractive Index and Percent Transmittance:

Refractive index and percent tranmittance proved the transparency of formulation. The refractive index of the system is measured by refractometer by placing drop of solution on slide and it compare with water (1.333)**.** The percent transmittance of the system is measured at particular wavelength using UV spectrophotometer keeping distilled water as blank. If refractive index of system is similar to the refractive index of water (1.333) and formulation have percent transmittance > 99 percent, then formulation have transparent nature. [1,38.39]

7) Viscosity Determination:

The SEDDS system is generally administered in soft gelatin or hard gelatin capsules. So, it can be easily pourable into capsules and such system should not too thick to create a problem. The rheological properties of the micro emulsion are evaluated by Brookfield viscometer. This viscosities determination conform whether the system is w/o or o/w. If system has low viscosity then it is o/w type of the system and if high viscosities then it are w/o type of the system. [38, 39]

1.10 Solid Self Emulsifying Drug Delivery System (S-SEDDS):

As SEDDS may exist in liquid or solid dosage form, but due to better stability as well as ease in handling and transporatation, solid SEDDS are generally preferred over liquid SEDDS. Conventional solid SEDDS are capsules, solid dispersion and dry emulsions but recently, a number of solid SEDDS have been prepared such as pellets, microsphere, tablets, beads, implants &

suppositories. [40]

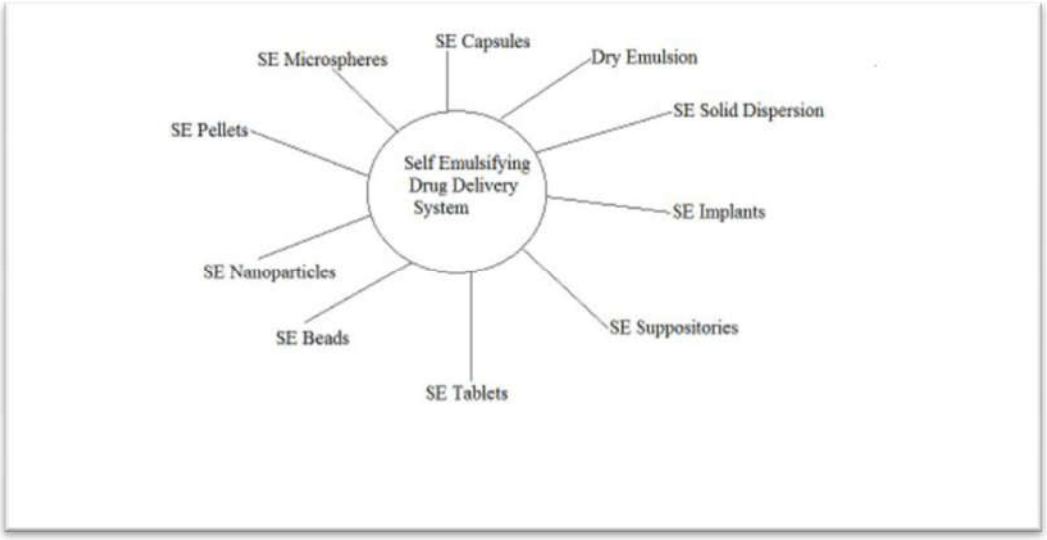


Figure No 5. Solid Self Emulsifying Drug Delivery System

- **Advantages of Solid Self Emulsifying Drug Delivery System:**
  - It acts as substitute for traditional oral formulations of lipophilic drugs.
  - It enhances the dissolution rate and hence, bioavailability of hydrophobic drugs.
  - It provides better consistent temporal profiles of drug absorption.
  - It helps in selective drug targeting toward a specific site in the GI tract.
- **Disadvantages of Solid Self Emulsifying Drug Delivery System:**

- Due to presence of high surfactant concentrations there may be chances of instabilities of drugs.
- Also the high content of surfactant in self emulsifying formulations irritates the gastrointestinal tract. This problem may be avoided by utilizing optimum less amount of surfactants.
- Sometime co-solvents remain into the formulation and cause degradation of drugs.
- It may allow less drug loading.

- **Conversion of Liquid SEDDS to Solid SEDDS:**

Liquid SEDDS can be filled in soft or hard gelatin capsule. Recently, there have been efforts by research groups working on SEDDS to convert liquid SEDDS to solid state SEDDS. These Solid SEDDS can be made into tablets or be encapsulated. The primary reason to formulate SEDDS in a solid form is to consolidate the advantages of Liquid SEDDS with convenience of solid oral dosage forms. [1,2]

Oral solid dosage forms have the followingadvantages[42]:

a. Low production cost
b. Convenience of process control
c. High stability and reproducibility and
d. Better patient compliance.

Generally, the formulated SEDDS are liquid in state, but sometimes it could be in a semisolid state depending on the physical state of excipients used. Researchers have adopted various techniques to obtain this conversion. Solid SEDDS also offers added versatility in terms of possible dosage forms.

The following description elaborates various Liquid to Solid SEDDS conversion techniques. [1, 2,40,41]

- **Spray drying:** Spray drying is the most widely used technique to convert liquid SEDDS into solid state. In this method the Liquid SEDDS is mixed with a solid carrier in a suitable solvent. The solvent is then atomized into a spray of fine droplets. These droplets are introduced

into a drying chamber, where the solvent gets evaporated forming dry particles under a controlled temperature and airflow conditions. The process parameters required to be controlled are inlet and outlet temperature, feed rate of solvent, and aspiration and drying air flow rate. The dry particles can then be either filled into capsules or made into tablets after addition of suitable excipients. Various solid carriers that have been used for this purpose are: Aerosil 200 suspended in ethanol and aqueous solution of Dextran[43].

• **Adsorption to solid carriers:** The Liquid SEDDS can be made to adsorb onto free flowing powders that possess very large surface area and are capable of adsorbing high quantities of oil material. The adsorption can be done either by mixing Liquid SEDDS and the adsorbent in a blender or by simple physical mixing.

The resulting powders can be either filled into capsules or can be made into tablets after addition of appropriate excipients. The adsorbents are capable of adsorbing Liquid SEDDS up to 70%w/w of its own weight. Solid carriers used for this purpose can be microporous inorganic substances, high surface area colloidal inorganic substances or cross-linked polymers. Categories of solid adsorbents used are: silicates, magnesium trisilicate, talcum, crospovidone, cross-linked sodium carboxymethyl cellulose and cross-linked polymethyl methacrylate. Oral solid heparin and gentamicin SEDDS were prepared using three kinds of adsorbents: microporous calcium silicate (Florite RE), magnesium aluminometa silicate (Neusilin US2) and silicon dioxide (Sylysia 320). [40, 41]

• **Encapsulation of Liquid and Semisolid SEDDS:** It is one of the simplest techniquesforconversionofLiquidSEDDStosolidoraldosageform.Liquid SEDDS can be simply filled in capsules, sealed using a microspray or a banding process.

For a semisolid SEDDS, it is a four step process:

- Heating the semisolid excipients toatleast20°Caboveitsmelting point;
- Adding the drug in the molten mixture while stirring;
- Filling the drug loaded molten mixture into the capsule shell and
- Cooling the product to room temperature.

The compatibility of the excipients used with the capsule shell should be well investigated. Lipid excipients compatible with the capsule shell are described in the work by Cole et al. Capsule filling of SEDDS is suitable for low dose highly potent drugs and allows high drug incorporation. [1, 2, 40]

• **Extrusion Spheronization:**

This is a solvent free technique that converts Liquid SEDDS into pellets using extrusion and spheronization processes. In this method the Liquid SEDDS is first mixed with a binder, followed by addition of water until the mass is suitable for extrusion. The extruded mass is then spheronized to form uniform sized pellets. The pellets are then dried and size separated. The relative quantity of water and Liquid SEDDS used in the process has an effect on size distribution, extrusion force, surface roughness of pellets, and disintegration time. High drug incorporation can be achieved by using this technique. Abdalla et al. used microcrystalline cellulose (MCC) as abinder in preparation of progesterone self-emulsifying pellets. A mixture of silicon dioxide, glyceryl behenate, pregelatinized starch, sodium croscarmellose, and MCC were used by Setthacheewakul et al. in the preparation curcumin loaded SMEDDS pellets [44].

Extrusion–spheronization is a solvent-free method used to convert liquid SEDDS into pellets. The liquid SEDDS is mixed with a binder and water, and then extruded and spheronized to form uniform pellets, which are dried and sized. Process variables like water and SEDDS content affect pellet properties. This technique allows high drug loading and commonly uses excipients like MCC and other additives.

• **Melt Granulation:**

Melt Granulation is another solvent free technique for converting Liquid SEDDS. In this method, Liquid SEDDS is mixed with a binder that melts or softens at relatively low temperature. This melted mixture can be granulated. This technique is advantageous since it does not require

addition of a liquid binder and subsequent drying unlike conventional wet granulation. The variables to be controlled in this process are impeller speed, mixing time, binder particle size, and the viscosity of the binder. A mixture of mono-, di- and triglycerides and esters of polyethylene glycol (PEG) called as Gelucire are used as binders to prepare immediate release pellets by melt granulation and as a self-emulsifying drug delivery system by capsule moulding or as powder obtained by cryogenic grinding.[40,41]

Melt granulation is a solvent-free technique where liquid SEDDS is mixed with a low-melting binder to form granules. It avoids the need for liquid binders and drying. Key process variables include impeller speed, mixing time, binder size, and viscosity. Lipid-based binders like Gelucire are commonly used for preparing SEDDS formulations.

Design and development of novel self emulsify floating drug delivery system for Ibuprofen.

The Objectives are:

1	To investigate influence of the oil, surfactant & co-surfactant types on the drug solubility & their ratios forming efficient & stable SEDDS.
2	To formulate &evaluate liquid SEDDS of Ibuprofen.
3	To develop a novel solid SEFDDS of Ibuprofen.
4	To study effect of liquid SEDDS & solid SEFDDS formulation on solubility by comparing with marketed formulation.
5	To perform stability study.

NEED OF WORK:

a. Ibuprofen is NSAID BCS Class II drug which have high permeability through stomach but due to its solubility limitation it can't enter to systemic circulation also gastric emptying time of drug ranging from 30 min to 2 hrs after this time drug goes into small intestine where it is solubilize but can't permeate through intestinal membrane, which give rational for the development of Self Emulsifying floating drug delivery system of Ibuprofen.

b. Self Emulsifying Floating Drug Delivery System (SEFDDS) increases the oral bioavailability of drug by increasing its solubility & also it's gastric residence time.

2. DRUG AND EXCIPIENT PROFILE:

2.1: Drug Profile

2.1.1: Ibuprofen.

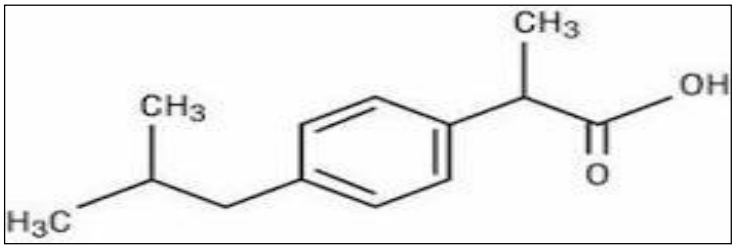


Figure No. 6: Structure of Ibuprofen

Table 7: Excipients profile Lemongrass Oil

IUPAC name	2-[4-(2-methylpropyl)phenyl] propanoic acid
Molecular formula	$C_{13}H_{18}O_2$
Molecular weight	206.3gm
Melting Point	75-77.5 ^{0} C
BCS class	Class II
Bioavailability	87%
Half life	2-4 hours
Description	White crystalline powder with characteristic odour

Dissociation Constant	5.2
Solubility	Soluble in ethanol, chloroform, ether, acetone, methanol and ethyl acetate. Insoluble in water
Dosage forms Oral suspension, oral tablets, oral chewable, oral capsules, compounding power, intravenous solutions	Capsule:- 200mg , Suspension:- 100mg / 5ml Tablet :- 100mg, 200mg, 400mg, 600mg
Adverse effects	Nausea, dyspepsia, gastrointestinal ulceration ,raised enzymes liver, diarrhea, constipation, nosebleed, headache, dizziness, rash, salt and fluid retention, and hypertension. Infrequent adverse effects include: esophageal ulceration, heart failure, hyperkalemia, renal impairment, confusion and bronchospasm. Ibuprofen can exacerbate asthma, sometimes fatally
Uses	uprofen is used primarily for fever (including post-immunisation fever), mild-to-moderate pain (including pain relief after surgery), painful menstruation, osteoarthritis, dental pain, headaches and pain from kidney stones. It is used for inflammatory diseases such as juvenile idiopathic arthritis and rheumatoid arthritis. It is also used for pericarditis and patent ductus arteriosus
Drug Interactions	rinking alcohol when taking ibuprofen may increase risk of stomach bleeding. Ibuprofen can interfere with the anti-platelet effect of low-dose aspirin, potentially rendering aspirin less effective when used for cardioprotection and stroke prevention." Allowing sufficient time between doses of ibuprofen and immediate-release (IR) aspirin can avoid this problem
Mechanism Of Action	Ibuprofen is a non-selective inhibitor of cyclooxygenase, an enzyme invovled in prostaglandin synthesis via the arachidonic acid pathway. Antipyretic effects may be due to action on the hypothalamus, resulting in an increased peripheral blood flow, vasodilation, and subsequent heat dissipation. Inhibition of COX-1 is thought to cause some of the side effects of ibuprofen including GI ulceration. Ibuprofen is administered as a racemic mixture. The R-enantiomer undergoes extensive interconversion to the S-enantiomer *in vivo*. The S-enantiomer is believed to be the more pharmacologically active enantiomer**.**
Stability and storage conditions	Stored in well closed light resistant container at 20-25^{0}C (68-770F). Keep out of the reach of children.

2.2 Excipients Profile:

2.2.1. Lemongrass Oil:

Table 8: Excipients profile Lemongrass Oil

Synonym	lemongrass; Citral terpenes; Lemon grass oil; Oil of lemongrass; Indian melissa oil
Chemical Name	1,2-dimethoxy-4-prop-2-enylbenzene
Empirical Formula	$C_{15}H_{84}O_5$

Molecular Weight	777.20966 g/mol
Functional category	Antipyretic, Energetic for body & mind, Antiseptic, Antifungal, Astringent, Pessimistic thoughts and used in fear and Analgesic.
Description	Pale yellow to Orange brown liquid
Odour	Fresh grassy, lemon and citral type
Specific Gravity at 25^0C	0.8725 – 0.8965
Refractive Index at 25^0C	1.485 – 1.494
Solubility	Soluble in 0.5 to 1.5 vol. of 80% alcohol
Pharmacopoeial Specification	Acid value – 12.86% Ester value – 49.64 % Saponification Value– 205.66
Safety	It is used in the oral pharmaceutical formulations and it is generally regarded as relatively nontoxic and non-irritant at level employed as excipients, It has medicinal & nutritional values.
Regulatory Status	GRAS listed (Generally regarded as safe).

2.2.2. Lauroglycol 90:

Table 9: Excipients profile Lauroglycol 90

Synonym	PGML;G 917;E 2580;Ai3-00968;Acaritouch; EMALEX PGML;LAUROGLYCOL;Atlas G 917;Emcol PL 50; Atlas G 3851
Chemical Name	Propylene glycol monolaurate (type II) EP/NF
Empirical Formula	C15H30O3
Molecular Weight	258.4
Functional category	Bioavailability Enhancer, Solubilizer & oily vehicle
Description	Colourless liquid, *Lauroglycol90* is used in oral and topical formulations. It is a co-surfactant for microemlsions in topical formulations.It can also act as a solubilizer/penetration enhancer in topical formulations.
HLB Value	5
Flash Point	178ºC
Relative Density	0.92 gm/ml
Solubility	Insoluble in water, soluble in organic solvent
Pharmacopoeial Specification	Vapour Pressure- 0.162 Pa/^{0}C @ 25 ^{0} C Saponification value –230-250
Safety	It is used in the oral & topical pharmaceutical formulations and Human pharmaceutical products, veterinary products including food producing animals
Regulatory Status	GRAS listed (Generally regarded as safe). It is reported in FCC, USFA, JSFA, EP, USP-NF, FDA IIG

2.2.3. Polysorbate 80:

Table 10: Excipients profile Polysorbate 80

Synonym	Tween 80
Chemical Name	Polyoxyethylene 20 sorbitanmonooleate
Empirical Formula	$C_{64}H_{124}O_{26}$
Molecular Weight	1310gm/mole
Functional category	Emulsifying agent; non-ionic surfactant; solubilizing

	agent; wetting, dispersing/suspending agent
Description	Oily yellowish, bitter taste
HLB Value	15
Flash Point	> 300 deg F
Relative Density	1.08 gm/ml
Solubility	Miscible with water, soluble in alcohol, toluene, Insoluble in mineral oil
Pharmacopoeial Specification for Polysorbate 80	Acid value – 2.0% Hydroxyl value – 65-80 Moisture content – 3.0 Saponification value – 45-55
Safety	It is used in the oral pharmaceutical formulations and it is generally regarded as relatively nontoxic and non-irritant at level employed as excipients
Regulatory Status	GRAS listed (Generally regarded as safe). Included in parentral and non parentral medicines licensed in UK

2.2.4. Aerosil 200:

Table 11: Excipients profile Aerosil 200

Synonyms	Hydrophilic fumed silica
Empirical formula	SiO_2
Molecular weight	60.08
Decription	It is light, loose, bluish white coloured, odourless, tasteless, amorphous powder
Functional category	Adsorbent (inert solid carrier), Improvement of free flow and anti-cacking characteristics of powders
Solubility	Practically insoluble in organic solvents, water and acids, except Hydrofluoric acid; soluble in hot solutions of alkali hydroxides
Physico-chemical data	Properties — Typical Value Specific surface area (BET) — 1.06-1.12m^2/g Average primary particle size — 20-200 nm pH in 4% dispersion — 3.7 - 4.7 Moisture 2 hours at 105^0C — < 1.5 wt% SiO_2 content — >99.8 wt %
Regulatory status	CAS No. 112,945-52-5, 7631-86-9 Registered in TSCA (USA), AICS (Australia), DSL (Canada)
Safety	Colloidal silicon dioxide is widely used in oral and topical pharmaceutical products and is generally regarded as an essentially nontoxic and nonirritant excipient.
Packaging and storage	Aerosil 200 is suppliedin multiple layer 10kg bags. It is recommended to store the product in closed containers under dry conditions and to protect the material from volatile substances. Aerosil 200 should be used within 2 years after production.

2.2.5 Microcrystalline cellulose:

Table 12: Excipients profile microcrystalline cellulose

Synonyms	Cellulose gel
Empirical formula	$(C_6H_{10}O_5)n$
Molecular	36000
Description	White, odorless, tasteless
Functional category	Adsorbent (inert solid carrier), Improvement of free flow

	and anti-cacking characteristics of powders
Solubility	Practically insoluble in water, freely soluble in acetone, soluble in diethylene glycol, practically insoluble in ethanol and in methylene chloride. It dissolves in dilute solutions of alkali
Physico-chemical data	Properties — Typical Value Average particle size — 50-180 microns Moisture content — about 5 % Heavy metal — max 10 ppm Free acid content — max 3 %
Regulatory status	CAS No. 9004-36-4 GRAS listed. Included in the FDA Inactive Ingredients Database (inhalations; oral capsules powders, suspensions, syrups and tablets; topical and vaginal preparations). Included in non parentral medicines licensed in the UK. Included in the Canadian List of Acceptable Non medicinal Ingredients.
Safety	Microcrystalline cellulose is widely used in oral pharmaceutical formulations and food products and is generally regarded as aralatively nontoxic and nonirritant material
Packaging and storage	The bulk material should be stored in a well closed container in a cool, dry place.

2.2.6 Compritol 888 ATO:

Table 13: Excipients profile compritol 888 ATO

Synonyms	Glyceryl dibehenate EP,Glyceryl behenate NF
Empirical formula	$C_{69}H_{134}O_6$
Molecular weight	1010
Appearance	Amorphous powder
Melting Point	70^0C
HLB Value	2
Functional category	Viscosifying agent, sustained release & flowing ability for oral formulation, lubricating agent, binding agent
Solubility	Soluble in chloroform, methylene chloride, insoluble in ethanol
Physico-chemical data	Properties — Typical Value Density value — 0.94g/cm^3 Saponification Value — 145-165 mgKOH/g Acid Value — <=4.00 mgKOH/g Moisture content — < =1.00 %
Regulatory status	FCC,GRAS,GSFA,EP,USP-NF,FDAIIG,JPED/JP
Packaging and storage	The bulk material should be stored in a well closed container in a cool, dry place, avoiding contact with air.

2.2.7. Magnesium Stearate:

Table 14: Excipients profile Magnesium Stearate

Synonyms	Dibasic magnesium stearate; magnesium distearate; magnesia stearas; magnesium octadecanoate; octadecanoic acid, magnesium salt; stearic acid, magnesium salt; Synpro 90
Chemical Name	Octadecanoic acid magnesium salt

Empirical formula	C36H70MgO4
Molecular	591.24
Description	stearate is a very fine, light white, precipitated ormilled, impalpable powder of low bulk density, having a faint odorof stearic acid and a characteristic taste
Functional category	Tablet and capsule lubricant.
Solubility	Practically insoluble in ethanol, ethanol (95%), ether and water; slightly soluble in warm benzene and warm ethanol (95%).
Physico-chemical data	Properties Typical Value Density (true) 1.092 g/cm3 Flash point 250°C Specific surface area 1.6–14.8 m2/g pH 6.0-8.0 Water content max 8 %
Packaging and storage	The bulk material should be stored in a well closed container in a cool, dry place

2.2.8. Hydroxy Propyl Methyl Cellulose K4:

Table 15: Excipients profile Hydroxy Propyl Methyl Cellulose K4

Synonyms	HPMC, Methocel, Pharmacoat
Chemical Name	Cellulose hydroxypropyl methyl ether
Molecular weight :	10,000-15, 00, 000
Description	It is odorless and tasteless, white or creamy white colored fibrous or granular powder
Functional category	Coating agent, film former, rate controlling polymers for sustained release, stabilizing agent, suspending agent, tablet binder and viscosity-increasing agent .
Solubility	Soluble in cold water, insoluble in chloroform, ethanol and ether but soluble in mixtures of ethanol and dichloromethane and mixtures of methanol and chloromethane.
Physico-chemical data	Properties Typical Value Density (bulk) 0.341 g/cm3 Melting point 190-200°C Specific surface area 1.6–14.8 m2/g pH (1%w/w solution) 5.5-8.0 Viscosity (2%w/v solution) 3000-5600 (mPas)
Storage condition	The powder should be stored in a well-closed container in a cool and dry place.
Safety	It is generally regarded as nontoxic and nonirritant material, although excessive consumption may have a laxative effect.

2.2.9 Sodium Starch Glycolate:

Table 16: Excipients profile Sodium starch glycolate

Synonyms	Carboxymethyl starch, sodium salt; carboxymethylamylun natricum, Explosol
Chemical Name	Sodium carboxy methyl starch
Description	A white or almost white, fine, free-flowing powder, very hygroscopic,.
Functional category	Tablet & Capsule disintegrant.
Solubility	Practically insoluble in methylene chloride. It gives a translucent suspension in water.

Physico-chemical data	Properties	Typical Value
	Density (bulk)	0.756 g/cm^3
	Melting point	200°C
	Specific surface area	0.24 m^2/g
	pH (1%w/w solution)	5.5-7.5
	Viscosity (2%w/v solution)	200cP
Storage condition	The powder should be stored in a well-closed container in-order to protect it from wide variations of humidity and temperature which may cause cacking.	
Safety	It is widely used in oral pharmaceutical formulations and is generally regarded as nontoxic and nonirritant material.	

3. EXPERIMENTAL WORK:

3.1 Pre-formulation Studies:

3.1.1 Drug Identification.

Pre-formulation studies were done on the drug which included appearance, color and odor; observed value was compared with the reported value.

A. Melting Point:

Melting point of Ibuprofen was determined by melting point apparatus using capillary method. Observed value was compared with the reported value.

B. FT-IR Study:

IR absorption spectrum of drug was recorded by using Shimadzu FTIR spectrophotometer wherein 2-4 mg of drug sample was used. FT-IR spectrophotometer using potassium bromide (KBr) pellets. KBr pellets were prepared by gently mixing the sample with KBr (1:100).FT-IR spectrum of given drug sample was taken by placing drug sample holder. The sample was scanned from 4,000 to 400 cm-1.

C. Differential Scanning Calorimetry:

The thermal behavior of drug was examined by DSC, using Differential Scanning Calorimeter Mettler Toledo. Accurately weighed sample of drug (3 mg) was run at the scanning rate of 50°C/min over a temperature range of 50 to 300°C.

D. Ultra Violet (UV) Spectroscopy:

Standard Calibration curve of Ibuprofen in 0.1N Hcl (λmax):

Weighed accurately a quantity 10mg of Ibuprofen, shake with 10ml of methanol in 100ml of volumetric flask and diluted up to volume 90 ml with 0.1N Hcl to form primary stock solution. Dilute 0.2, 0.4, 0.6, 0.8, 1, 1.2, 1.4 ml of primary stock solution to form primary stock solution to 10.0ml with 0.1N HCl in each separate volumetric flask to form secondary stock solution of 2, 4, 6, 8, 10, 12, 14, µg/ml. Use secondary stock solution for suitable dilutions and measure for absorbance at 221 nm of the resulting solution against 0.1N Hcl as blank.

3.2 Screening of Excipients:[51]

Screening of excipients was made on the basis of solubility of Ibuprofen in different oils, Surfactants and Co-surfactants. On the basis of ease of emulsification and percent transparency of surfactants and co-surfactants.

3.2.1 Solubility determination of Ibuprofen in different oils, surfactants, & co-surfactants:

Procedure:

Solubility studies of Ibuprofen were conducted in different oils, surfactants and co-surfactants which are shown in table below:

A) Oils	Lemon Oil, Lemongrass Oil, Sesame oil, Arachis Oil, Capmul MCM
B) Surfactant	Tween 80, Tween 60, Span 80, Acconon, Kolliphore TPGS.
C) Co- Surfactant	Propylene Glycol, PEG 400, Lauroglycol 90,Labrasol,Labrafac PG.

The solubility of drug in various oils, surfactants and co-surfactants was determined by using **shake flask method**. An excess amount of drug was added to each vial containing 2 ml of the selected vehicle i.e. oil, surfactant & co-surfactant. After sealing, the mixture was vortexed using a cyclomixer for 10 min in order to facilitate proper mixing of drug with the vehicles. Mixtures were then shaken for 72 hrs in an orbital shaker maintained at 37 ± 1°C for equilibration. Equilibrated samples were centrifuged at 5,000 rpm for 15 min, followed by filtration through membrane filter (0.22 μm). Drug was quantified directly by using a UV-Vis spectrophotometer (Shimadzu-1700, japan) at λmax 221 nm.[55]

3.2.2 Emulsification Ability:

Emulsification ability of various surfactants was screened. Surfactant (300 mg) was added to of the selected oily phase (300 mg). The mixture was gently heated at 40–45 °C for 30 seconds to attain homogenization of components. The mixture, 50 mg, was weighed and diluted with doubly distilled water to 50 ml to obtain a fine emulsion. The ease of emulsion formation was scrutinized by counting the number of volumetric flask inversions to give a uniform emulsion and were observed visually for relative turbidity. The resulting emulsions were allowed to stand for 2 h and transmittance was observed at 638 nm. The surfactant forming a clear emulsion with fewer inversions and higher transmittance was selected. Various co-surfactants were screened for MEDDS formulation. Mixtures of 100 mg of co-surfactant, 200 mg of selected surfactant and 300 mg of selected oil phase were prepared and evaluated in the same manner as described in the above section on surfactant screening. [62,63]

3.2.3 Percent Transparency:

The screening of surfactant and co-surfactants was conducted on the basis of percent transparency. The percent transmittance was determined for surfactant and co-surfactants. The mixture, 50mg, was accurately weighed and diluted to 50ml with double distilled water to yield fine emulsion. The ease of formation of emulsions was noted by noting the number of flask inversions required to give uniform emulsion. The resulting emulsions were observed visually for the relative turbidity. The emulsions were allowed to stand for 2 hr and their transmittance was measured at 638 nm by UV-double beam spectrophotometer 1800 (Shimadzu)using distilled water as blank.[62,63]

3.2.4 Selection of Surfactant Mixture ($S_{mix.}$) Ratio:

On the basis of solubility and emulsification studies, mixtures of surfactant and co-surfactant (Smix) in different ratios (1:1, 1:2, 2:1) were prepared. All prepared mixtures were then subjected for ease emulsification, for that each mixture, 50mg, was accurately weighed and diluted to 50ml with double distilled water to yield fine emulsion. The ease of formation of emulsions was noted by noting the number of flask inversions required to give uniform emulsion. The resulting emulsions were observed visually for the relative turbidity. The emulsions were allowed to stand for 2 hrs and their transmittance was measured at 638 nm by UV- double beam spectrophotometer 1800 (Shimadzu) using distilled water as blank.[62,63]

3.3 Drug Excipient Compatibility Study:

The drug-excipients interaction study was carried out by using physical observation and Drug content. To study the compatibility of various formulation excipients with Ibuprofen, mixtures were prepared by mixing the drug with each formulation excipient separately in the ratio of 1:1 and characterized for its Appearance, Color, Odor and Drug content etc. at time intervals of 0 days,7 days,15 days and 30 days.

3.4 Construction of Pseudo-Ternary Phase Diagrams:

Three types ternary phase diagram were constructed to determine microemulsion region. The

total amount of oil and surfactant: Co-surfactant (1:1, 1:2, 2:1) should be 100%. In order to find out concentration range of components for the existing range of microemulsions, ternary phase diagrams were constructed using water titration method.

1. Mixtures of tween 80 and lauroglycol 90(Smix) in different ratios by mass (1:1, 1:2, 2:1) were prepared.
2.All the mixtures were mixed with oil(lemongrass oil) each separately in different ratios of 1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2 and 9:1 with a total volume of 2 ml. The prepared mixtures were vortexed and then titrated with water drop wise using a micro syringe under gentle agitation. After each addition, mixtures were observed visually (turbid or clear). Percent of components at which a clear mixture was formed was figured out by constructing a pseudo ternary phase diagram using the **TRIPLOT** software for fabrication of ternary plot. [52, 53, 54]

3.5 Formulation of SEDDS:

From the ternary phase diagram, the ratios of surfactant to co-surfactant were optimized. Then, by varying the ratio of oil to optimized ratio of surfactant to co-surfactant, different formulations were prepared with drug. Oil was added to the mixture of surfactant and co-surfactant in ratio in these formulations was then vortexed for 5–10 min with a vortex shaker until a clear solution was obtained. On the basis of pseudo ternary phase diagram five formulations was selected for further study, it was given in table 17. [35, 55, 56]

Table 17: Formulation Table

FC	Drug (mg)	Oil (mg)	Surfactant: Co-surfactant ratio (mg)		
			1:1	1:2	2:1
F1	200	400	600	-	-
F2	200	200	-	800	-
F3	200	600	-	-	400
F4	200	200	-	-	800
F5	200	400	-	-	600

3.6 Evaluation of Liquid SEDDS of Ibuprofen:

A. Phase Separation Study:

All liquid SEDDS formulation (0.05ml) was added to 100 ml volumetric flask and diluted with 0.1N Hcl up to the mark. After inverting the volumetric flask for 3-4 times, each mixture was stored for 2hr and phase separation was observed visually.[49,57]

B. Centrifugation Study:

All formulations were centrifuged at 3000 rpm for 15 min. and observed for phase separation, creaming and cracking. The formulations which showed maximum stability (no creaming, cracking, phase separation) were selected.[49,57]

C. Drug Content:

Prepared liquid SEDDS formulations F1 to F5 containing Ibuprofen equivalent to 200 mg added in the volumetric flask containing 100 ml of methanol and mixed it well with mechanical shaking and inverting volumetric flask 2 to 3 times. Then from this solution appropriate amount of solution was taken out and then diluted appropriately with methanol and drug content was determined using UV-spectrophotometer at λmax 221nm.[50,57.58]

D. % Transmittance:

For all formulations F1- F5, 1 ml of Liquid SMEDDS was diluted to 100 ml distilled water and observed for any turbidity and % transmittance was measured at 650 nm using UV–vis spectrophotometer (Shimadzu-1800, Japan) against distilled water as a blank.[64]

E. Globule Size Determination:

Globule size was determined for F1-F5 formulation. A 0.5 ml of the homogeneous mixture was measured and diluted up to 100 ml with distilled water in beaker of 100ml. Then beaker was placed on magnetic stirrer for 5 min. Then samples were taken for globule size determination. Globule size of the resulting dispersions was determined by Zeta Seizer Nano ZS (Malvern Instruments, Malvern, UK). .[47,56,59]

F. Determination of Self Emulsifying Time:

Self emulsification assessment is done through visual evaluation for formulation **F1- F5**, 100ml water and 0.1N Hcl solution was taken as medium which was stirred under magnetic stirrer with 100rpm at 37±0.5°C and pour 1ml of formulated SEDDS into the medium and the contents being mixed gently at 100rpm and determining the time required to form microemulsion upon dilution of SEDDS with water.[49,57,58]

G. Rheological Analysis:

For all formulations F1 to F5 were analysed in which (1 ml SEDDS) was subjected to viscosity determination. It was diluted 100 times with distilled water and then viscosity was measured using a Brookfield viscometer.[48,57]

H. In Vitro Dissolution Studies:

In 0.1 N Hcl-

In vitro dissolution of liquid SEDDS formulations F1-F5 was carried out by using dissolution test apparatus USP I (basket type). The liquid SEDDS 0.16 ml were filled into size '0' capsules. The dissolution fluid (900 ml) was maintained at 37ºC±0.5ºC. The speed of the stirrer was adjusted at a speed of 50rpm. An aliquote of 1 ml was withdrawn by means of a pipette at predetermined intervals for a period of 10 minutes and dilute upto 10 ml using 0.1N Hcl. Same quantity of fresh fluid equilibrated at 37ºC±0.5ºC was replaced to maintain apparent sink conditions inside the dissolution compartments. The aliquots were assayed spectrophotometrically at a maximum of 221 nm by using shimadzu UV-1800 spectrophotometer.[50,57]

❖ **Formulation Of Optimized Formulation :**

From above study the F5 formulation was selected as optimized formulation.

The formulation amount of Ibuprofen (200mg) was dissolved in the mixture of surfactant, co-surfactant and oil at 25˚C.The final mixture was vortexed until a clear solution (liquid SEDDS) was obtained**.**

Table 18: Formulation Table

FC	Drug (mg)	Oil (mg)	Surfactant: Co-surfactant ratio (mg)		
			1:1	1:2	2:1
F5	200	400	-	-	600

3.7 Evaluation of Optimized Formulation:

a) Zeta Potential Measurement:

From the globule size determination only F5 formulation was subjected to zeta potential determination. The zeta potential of F5 was determined by diluting the formulation with a ratio of 1:100 (v/v) with distilled water and mixed for 1min with cyclomixer using zeta sizer Delsa™ Nano (Beckman coulter, NX0088). Charge on emulsion droplets and their mean zeta potential values (±SD) were obtained.[55,59]

b) Polydispersity Index:

PDI measurement was carried out by dynamic light scattering with a Zetasizer Delsa™ Nano (NX0088). All samples were subjected to sonication prior to PDI determination.[55,59]

c) Differential Scanning Calorimetry (DSC):

The molecular state of the drug was evaluated by performing DSC analysis of pure drug and liquid formulation The DSC curves of the sample were obtained by a differential scanning calorimeter. The sample was placed in standard aluminium pans, and dry nitrogen was used as

effluent gas. All samples were scanned at a temperature ramp speed of 5 ℃/ min & the heat flow from 50-300℃.

d) In Vitro Drug Release Study:

Drug Release Study of optimized formulation F5 was compared with pure drug and marketed formulation.

Dissolution profiles of the optimized formulation was done by capsules filled with the self emulsified formulations using USP Dissolution apparatus I at 37±2°C and a rotation speed of 50 rpm in 900 ml 0.1 N HCL. During the study, 5ml aliquots were removed at predetermined time intervals from the dissolution medium and 5 ml of fresh 0.1 N HCL was replaced. The amount of ibuprofen released in the dissolution medium was determined by U.V Spectrophotometer at λ_{max} 221nm.The dissolution experiment was carried out in triplicate. [58]

3.8 SOLID SEDDS:

Conventional SEDDS are mostly prepared in a liquid form, which can produce some disadvantages such as low stability and portability, low drug loading and few choices of dosage forms. To address these problems, Solid SEDDS have been investigated, as alternative approach.

- **Adsorption of liquid SEDDS onto solid carrier:**

The optimized liquid SEDDS formulation **F5** was converted into free flowing powder by adsorption of liquid SEDDS onto Aerosil 200. S-SEDDS was prepared by mixing liquid SEDDS containing Ibuprofen with Aerosil 200. In brief liquid SEDDS was added drop wise over Aerosil 200 contained in broad petri plate. After each addition, mixture was homogenized using glass rod to ensure uniform distribution of formulation.

Resultant damp mass was passed through sieve no. 100 and dried using desiccator and stored until further use. For 0.16 ml of liquid SEDDS 200 mg of aerosil 200 was required.

- **Preliminary Study:**

Floating approach was achieved using two ingredients compritol and HPMC K4.Some preliminary trials were done by using these both ingredients with different concentrations and other ingredients were also added as it was finally converted to tablet dosage form.

Evaluation of powder blend was carried out after the addition of other ingredients required for the tablet compression.

Powder Blend Preparation Procedure:

Prepared solid SEFDDS containing Ibuprofen (200 mg) and other ingredients such as avicel ,magnesium stearate, sodium starch glycolate and talc were weighed accurately and mixed thoroughly.

Table 19: Preliminary Trials for the compritol concentration

Sr. No.	Ingredients	E1(mg)	E2 (mg)
1	Solid SEDDS	200	200
2	Compritol 888 ATO	150	250
3	Avicel	185	85
4	Sodium starch glycolate	5	5
5	Magnesium Stearate	3	3
6	Talc	7	7

- **Solid SEDDS consists 0.16 ml of liquid SEDDS and 200 mg of aerosil 200**

- **Blend Evaluation**
- **Flow Properties:**

1) Bulk Density:

Accurately weighed 5 gm sample of powder was placed into 100ml measuring cylinder. Volume occupied by the powder was noted without disturbing the cylinder and the bulk density was calculated using the equation,

$$Pb=\frac{M}{Vp}$$

Where,

ρ_b = bulk density,

M = weight of sample in grams,

V_p = final volumes of Powder in cm^3.

2) Tapped Density:

Accurately weighed 5 gm of powder sample was placed into 100 ml measuring cylinder. The cylinder was then subjected to a fixed number of taps (~100) until the powder bed has reached to the minimum. The final volume was recorded and the tap density was calculated by the following equation,

$$\boldsymbol{\rho t = \frac{M}{Vt}}$$

Where,

ρ_t = Tap density,

M = weight of powder in grams,

V_t = Tapped volume of Powder in cm^3

3) Angle of Repose (θ):

The maximum angle of possible between the surface of a pile of powder or granules and the horizontal plane. The granules were allowed to flow through the funnel fixed to a stand at a definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

$$\boldsymbol{\tan \theta = h/r}$$
$$\boldsymbol{\theta = \tan^{-1} (h/r)}$$

Where,

θ = angle of repose

h = height of the heap

r = radius of the heap

The relationship between Angle of repose and powder flow as follows

Table 20: The relationship between Angle of repose and powder flow

Sr. No.	Angle of repose	Powder flow
1	<25	Excellent
2	25-30	Good
3	30-40	Passable
4	>40	Very Poor

4) Compressibility Index:

The flow ability of powder can be evaluated by comparing the bulk density (Do) and tapped density (Df) of powder and the rate at which it packed down. Compressibility index is calculated by

Compressibility Index (%) = $\frac{Df-Do}{Df} \times 100$

Table 21: Flow properties corresponding to compressibility index

% compressibility	Flow Properties
<10	Excellent
11-15	Good
16-20	Fair
21-25	Passable
26-31	Poor

32-37	Very poor
>38	Extremely poor

5) Hausner's Ratio:

Hausner's ratio provides an indication of the degree of densification which could result from vibration of the feed hopper. A lower value of indicates better flow and vice versa.

Hausner's Ratio = Tapped density/Bulk density

Table 22: Specification of Hausner's Ratio

Hausner Ratio	Type of flow
Less than 1.25	Good flow (20% Car's index)
1.25-1.5	Moderate (33% Car's index)
Greater than 1.5	Poor flow

❖ **Preparation Of Tablet:**

The preparation process of tablet formulation (E1 & E2) includes above prepared powder blend passed through sieve no. 40 and compressed with 10 mm punch tablet machine (Labpress 12 station compression machine). The tablets were round with an average diameter of 10.0 ± 0.1mm and a thickness of 6.2 ± 0.2mm.

3.9 Evaluation of Tablets (S-SEFDDS):

1. Weight Variation Test:

Weight variation test was done by weighing 20 tablets individually, by using Sartorious balance (Model CP- 224 S). Calculating the average weight and comparing the individual tablet weight to the average weight. [59,60]

2. Tablet Thickness:

The thickness was measured by placing tablet between two arms of the Vernier caliper. 5 tablets were taken and their thickness was measured. [60,61]

3. Tablet Hardness:

The tablet hardness, which is the force required to break a tablet in a diametric compression force. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring.[59,60,61]

4. Friability:

The procedure was followed as per USP. 5 tablets were weighed and transferred to friabilator. It was then rotated for 4 min at 25 rpm. The tablets were removed and weighed again. Friability was calculated from the formula:[59,60]

$$\% \text{ Friability} = \frac{\text{Initial weight-Final weight}}{\text{Initial weight}} \times 100$$

5. Floating Test:

The time taken for the dosage form to emerge on the surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT).The in vitro floating test was determined by floating lag time. The tablets were placed in a 100 ml beaker containing 0.1N HCL. The time required for the tablet to rise to the surface and float was determined as floating lag time. The duration of time the dosage form constantly remained on the surface of the medium was determined as the total floating time.[61]

6. Percent Drug Content:

Drug content was estimated by extracting Ibuprofen from S-SEDDS. In brief S-SEDDS was dissolved in sufficient quantity of methanol. Solution was solicited for 10-15 min for extraction of the Ibuprofen in methanol and filtered. The absorbance of filtrate was read at 296 nm on UV- Visible Spectrophotometer (Shimadzu-1800, Japan).[64]

Dissolution Test for Tablets E1 & E2:

In vitro dissolution of tablet was carried out by using dissolution test apparatus USP II (paddle type). The dissolution fluid (900ml) was maintained at $37^{O}C \pm 0.5^{O}C$. The speed of the stirrer was adjusted at a speed 50rpm. An aliquot of 5 ml was withdrawn by means of pipette at predetermined intervals for a period of 0.5,1,2,3,4,5,6,7 and 8 hrs and make it up to 10 ml using 0.1N HCL. Same quantity of fresh fluid equilibrated at $37^{O}C \pm 0.5^{O}C$ was replaced to maintain apparent sink conditions inside the dissolution compartments. The aliquots were assayed by spectrophometrically at a maximum of 221 nm by using Shimadzu UV-1800 Spectrophotometer.[60,61]

From all above study E2 formulation was assessed further for other evaluation parameter such as FT-IR study, DSC, X-Ray diffraction and In vitro release study

- **Optimized Tablet E2 formulation**

Table 23: Formula for Optimized Tablet Preparation

Sr. No.	Ingredient	Quantity in mg/tablet
1	Solid-SEDDS	200
2	Compritol 888 ATO	250
3	Avicel	85
4	Sodium starch Glycolate	5
5	Magnesium stearate	3
6	Talc	7

3.10 Evaluation of Optimized E2 Formulation:

A. Interaction Study by FT-IR:

FTIR spectra of Ibuprofen (Drug), Aerosil 200 (Adsorbent), glyceryl behenate, talc avicel,sodium starch glycolate & magnesium stearate i.e. physical mixture of SEFDDS were recorded on Shimadzu FT-IR – 8400 spectrophotometer. Sample was placed in sample holder; The scanning was performed between $4000cm^{-1}$to $400cm^{-1}$ range.

B. Differential Scanning Calorimetry (DSC):

The molecular state of the drug in formulation was evaluated by performing DSC analysis of physical mixture of SEFDDS. The DSC curves of the samples were obtained by a differential scanning calorimeter. The sample (about 3.0 mg) was placed in standard aluminium pans, and dry nitrogen was used as effluent gas. All samples were scanned at a temperature ramp speed of $5^{O}C$/min and the heat flow from 50 to $300^{O}C$.

C. X-Ray Powder Diffraction:

The PXRD patterns of physical mixture of SEFDDS (includes ibuprofen, aerosil, glyceryl behenate, magnesium stearate, sodium starch glycolate and talc)was done using X-Ray diffractometer. The measuring conditions were as follows: CuKα radiation, nickel filtered; graphite monochromator; 45kV voltage; and 40mA current with X' celerator detector, All samples were run at 1^{O} (2θ) min^{-1} from 3^{O} to 45^{O} (2θ).

D. In Vitro Dissolution Study:

Drug release studies from solid SEFDDS were performed using USP dissolution apparatus II with 900 mL of 0.1 N Hcl as a medium at 37 ± 0.50C. The speed of the paddle was adjusted to 50 rpm. Ibuprofen loaded solid SEFDDS tablet (E2 and pure drug) were placed in a dissolution apparatus and at predetermined time intervals 0.5, 1, 2, 3, 4 5,6,7and 8 hrs; an aliquot (5 mL) of the sample was collected, filtered and analyzed for the content of Ibuprofen by UV Spectroscopy.

E. Stability Studies:

According to WHO guidelines, the stability studies were carried out on solid formulation i.e. Formulation E2.the formulation was stored at 40^{0} c ± 20 c/75% ±5% RH for 3 months (Climatic zone IV condition for accelerated testing) to assess their stability. After an intervals of 7, 15, 30, 60

and 90 days. Samples were withdrawn and tested for Appearance, Color, Odor, Drug content.

4. RESULT AND DISCUSSION:

4.1 Pre-formulation Studies:

4.1.1 Drug Identification:

Table 24: Pre-formulation Studies

Sr. No.	Parameter	Standard	Observed
1	Color	White	White
2	Odor	Odorless	Odorless
3	Appearance	Crystalline	Crystalline

Thus, from all the pre-formulation study it was observed that all physical properties of drugs complied with the standard specification.

A. Melting Point:

The average melting point of Ibuprofen was determined by capillary method and was found to be 77-78 ^{0} C, which is in good agreement with reported melting point.

B. FTIR Spectroscopy of Drug:

The IR spectrum of Ibuprofen was shown in fig no.7. The IR spectrum of Ibuprofen as in accordance with the reported peaks as given in below fig no.7 and table 25.

The basic peaks of Ibuprofen were observed at 2850-2970, 3010-3100, 1710, 2900, 1465 cm^{-1}.

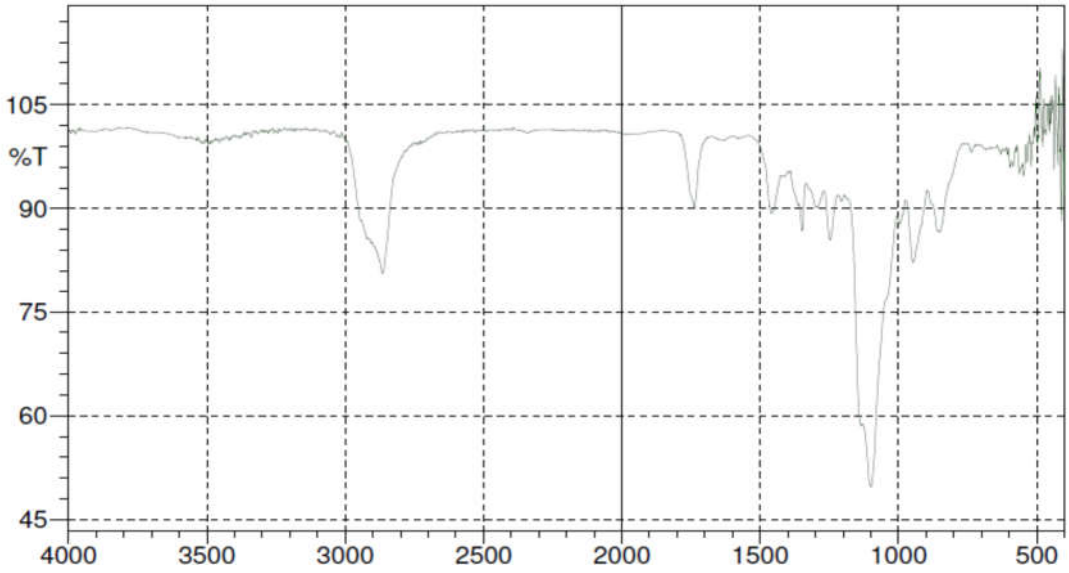


Figure No. 7: Infrared Spectrum of Ibuprofen

Table 25: FT-IR Study of Ibuprofen

Sr. No.	Functional group	Frequency,cm^{-1}
1	C-H Alkanes	2850-2970
2	C-H Aromatic ring	3010-3100
3	Carboxylic acid	1710
4	C-H Aldehyde	2900
5	-CH_2- bend	1465

C. Differential Scanning Calorimetry of Drug:

The DSC thermogram for plain ibuprofen was shown in fig no. 8.In DSC scan of ibuprofen sharp endothermic peak observed at 79.86^{0}C that is the characteristic peak of ibuprofen**.**

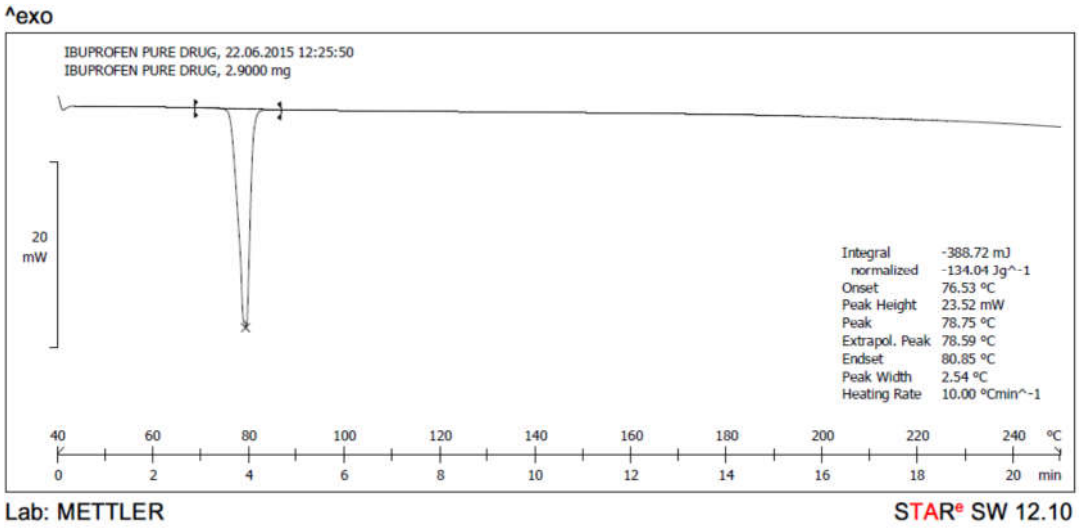


Figure No. 8: DSC Thermo Gram of Ibuprofen

D. Ultra Violet (UV) Spectroscopy:

The UV spectrum of Ibuprofen solution (10µg/ml) exhibited wavelength of absorbance maximum at 221 nm.

Standard Calibration Curve:

Standard calibration curve of Ibuprofen was drawn by plotting absorbance v/s concentration. The λmax of Ibuprofen in 0.1 N Hcl was found to be 221 nm. The absorbance values are tabulated in table 26. Standard calibration curve of Ibuprofen was found to be in the Beer's range between 2-14 µg/ml in shown fig no.9.

Table 26: Standard Calibration Curve

Sr. No.	Concentration (µg/ml)	Absorbance at 221 nm
1.	0	0.0000
2.	2	0.159
3.	4	0.255
4.	6	0.334
5.	8	0.456
6.	10	0.556
7.	12	0.678
8.	14	0.79

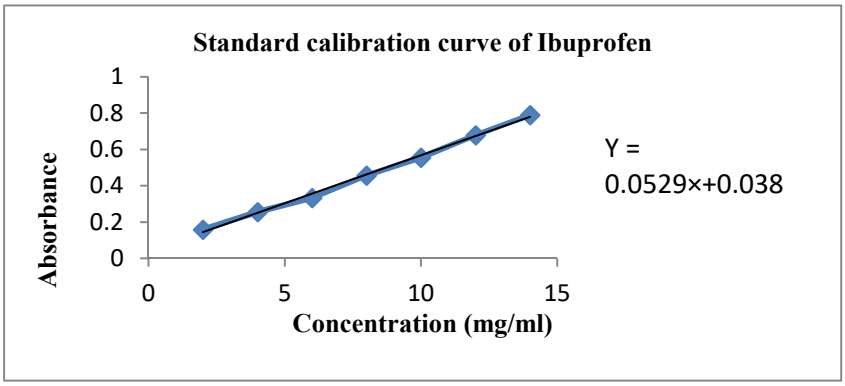


Figure No. 9: Calibration Curve of Ibuprofen in 0.1 N HCl

The standard calibration curve exhibited good coefficient of correlation as shown in table 27.

Table 27: Standard Calibration Curve Statistics

Sr. No.	Parameters	Observations
1	Absorbance Maximum	221 nm
2	Slope	0.0529
3	Intercept	0.0381
4	Correlation Coefficient (r^2)	0.9967

On the basis of melting point, UV spectrum, Infrared spectrum and DSC thermogram the procured sample of Ibuprofen was found to be of acceptable purity and quality. The sample was taken for further studies.

4.2 Screening of Excipients:

The screening of excipients is an important step in the formulation of self-emulsifying drug delivery systems (SEDDS). The formulation typically consists of oil, surfactant, co-surfactant, and drug, which should form a clear and stable solution when introduced into an aqueous medium. Selecting suitable oils with high solubilizing capacity is essential to achieve optimum drug loading and stability.

The self emulsifying formulations consisted of oil, surfactants, co-surfactants and drug should be a clear, monophasic liquid when it is introduced into aqueous medium and should have good solvent properties to present the drug in solution. So in the formulation of SEDDS the selection of suitable oil, Surfactant and co surfactant plays a key role to potentiate the solubility and drug loading. The components in formulation of self emulsifying formulation were selected to have maximum solubility of drug along with good miscibility with each other to produce a stable formulation.

4.2.1. Solubility Determination of Ibuprofen in Different Oils, Surfactants, & Co- Surfactants

A) Solubility Study of Ibuprofen in Different Oils:

Solubility studies were aimed at identifying suitable oil phase for the development of SEDDS for Ibuprofen. Identifying the suitable oil, having maximal solubilizing potential for drug under investigation is very important to achieve optimum drug loading. Solubility of Ibuprofen in various oily phases is presented in table 28.

Table 28: Solubility Study of Ibuprofen In Different Oils

Sr. No.	Oils	Solubility of Ibuprofen at 25 ^{0}C (mg/ml)
1	Lemongrass oil	1185.1
2	Lemon oil	695.21
3	Capmul MCM	583.86
4	Seasame oil	223
5	Arachis oil	151.25

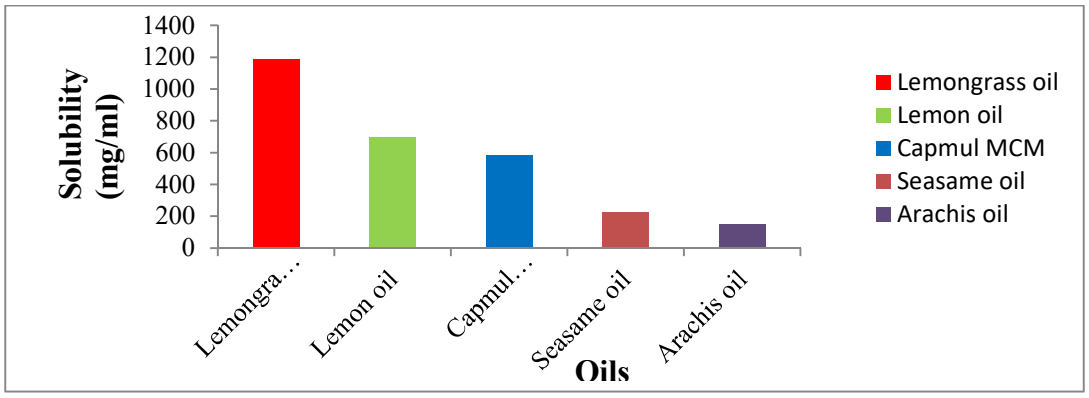


Figure No. 10: Solubility Study of Ibuprofen in Different Oils

Thus results revealed that the drug shows maximum solubility in Lemongrass oil i.e. 1185.1 mg /ml compared to other oils like in lemon oil, sesame oil, arachis oil, capmul MCM, etc. shown in fig no.10. Thus lemongrass oil was selected as oil phase in the formulation of SEDDS of Ibuprofen.

B) Solubility of Ibuprofen in Different Surfactants:

Solubility of Ibuprofen in various surfactant solutions was presented in table 29 respectively. Among vehicles tested tween 80 had shown maximum solubility of 295 mg/ml. It was type of nonionic surfactant generally consider safer than the ionic surfactants and are usually accepted for oral ingestion. They are also reported to provide better stability to emulsion over a wider range of pH and ionic strength. In addition, they can produce reversible changes in intestinal mucosal permeability, further facilitating absorption of drug.

Table 29: Solubility Of Ibuprofen In Different Surfactant

Sr. No.	Surfactant	Solubility of Ibuprofen at 25 ^{0}C (mg/ml)
1	Tween 80	295
2	Tween 60	235.4
3	Span 80	204
4	Acconon	198
5	TPGS	210

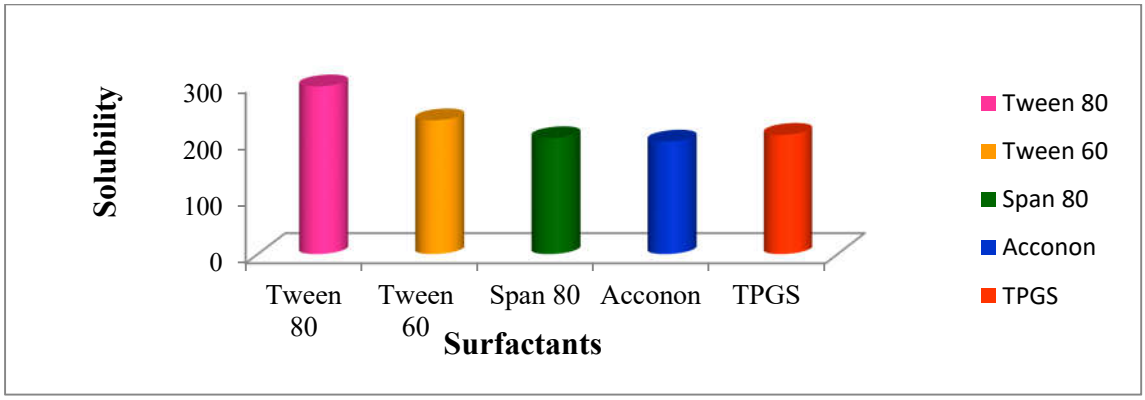


Figure No. 11: Solubility of Ibuprofen in Different Surfactant

C) Solubility Determination of Ibuprofen in Different Co-Surfactants:

Solubility of Ibuprofen in various co-surfactant solutions was presented in table 30 respectively. Among vehicles tested Lauroglycol 90 had shown maximum solubility of 499 mg/ml.

Table 30: Solubility of Ibuprofen in Different Co-Surfactant

Sr. No.	Co-surfactant	Solubility of Ibuprofen at 25 ^{0}C (mg/ml)
1	Propylene glycol	157.5
2	PEG 400	233.2
3	Lauroglycol 90	499
4	Labrasol	377
5	Labrafac PG	133

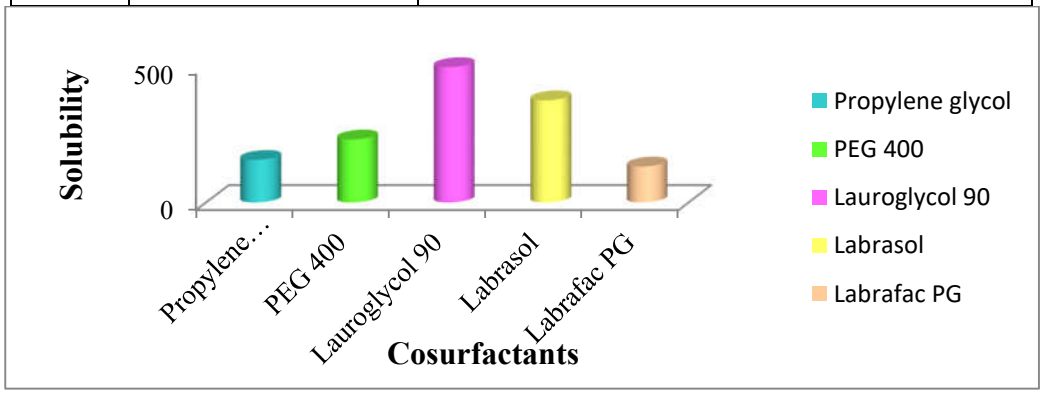


Figure No. 12: Solubility of Ibuprofen In Different Co-Surfactant

4.2.2 Emulsification Ability and Percent Transparency:

a) Surfactants:

Amongst various surfactants, selection was done on the basis of ease of emulsification and higher transmittance.

Table 31: Number of Volumetric Flask Inversions and Transmittance of Ibuprofen in Different Surfactants:

Sr. No.	Surfactant	Number of volumetric flask inversions	Transmittance at 638 nm
1	Tween 80	15	90.76 %
2	Tween 60	25	75.31 %
3	Span 80	45	56.34%
4	Acconon	31	68.84 %
5	TPGS	35	72.78%

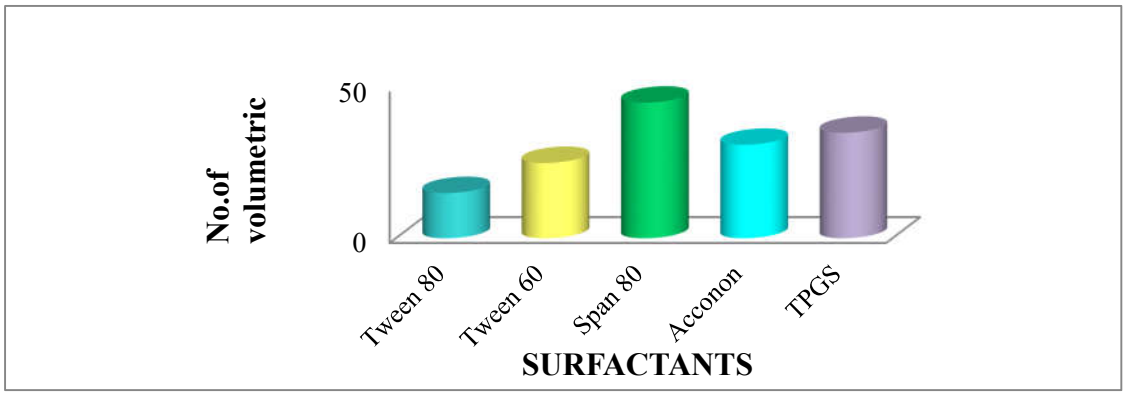


Figure No. 13: Ease of Emulsification of Various Surfactants

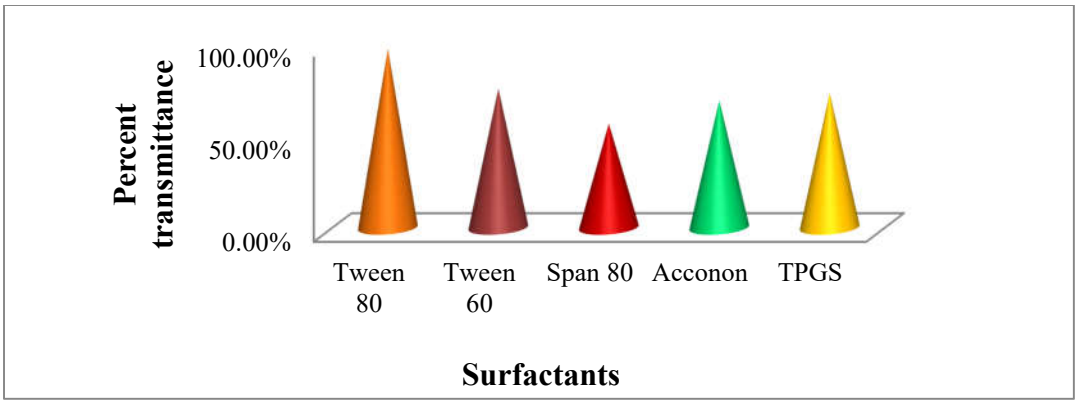


Figure No.14: Percentage Transmittance of Ibuprofen in Different Surfactants

The results revealed that Tween 80 showed 90.76 % transmittance and 15 inversions whereas other surfactants showed less transmittance and more inversions, respectively, hence Tween 80 was selected as a surfactant for further study.

b) Co-surfactant:

In case of the co-surfactants screened, Lauroglycol 90 showed 95.34 % transmittance and 15 inversions compared to other co-surfactants showed less transmittance and more inversions, respectively.

Table 32: Number of Volumetric Flask Inversions and Transmittance of Ibuprofen in Different Co-Surfactant

Sr. o.	Co-surfactant	Number of volumetric flask inversions	Transmittance at 638 nm
1	Propylene glycol	50	88.76 %
2	PEG 400	35	58.76 %
3	Lauroglycol 90	20	95.34%
4	Labrasol	68	71.84 %
5	Labrafac PG	47	80.54%

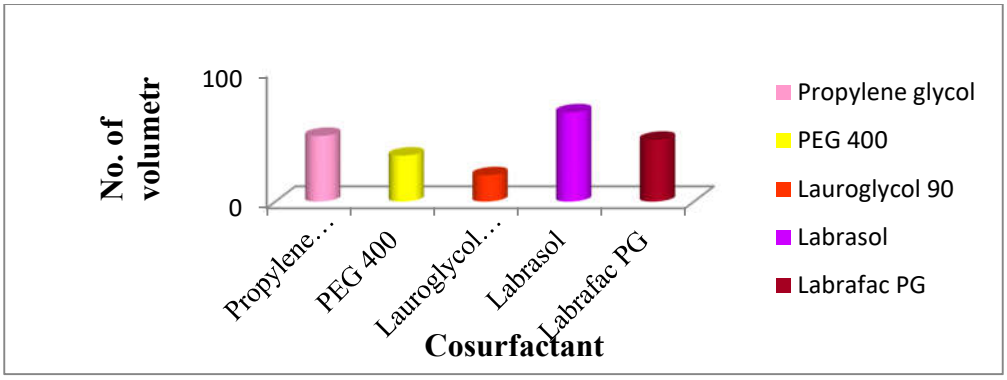


Figure No.15: Ease of Emulsification of Various Co-Surfactants

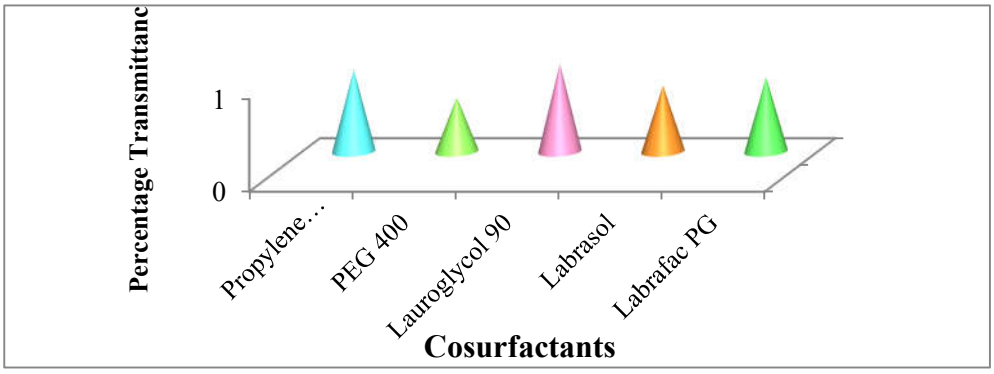


Figure No.16: Percentage Transmittance of Ibuprofen in Different Co-surfactants

4.2.4 Selection of Surfactant Mixture ($S_{mix.}$) Ratio:

On the basis of solubility and emulsification studies, mixtures of surfactant and co-surfactant (Smix) in different ratios (1:1, 1:2, 2:1, 1:3, 3:1) were prepared. All prepared mixtures were then subjected for ease emulsification and percent transmittance.

Table 33: Results for Emulsification Ability & % Transmittance of Surfactant Mixture ($S_{Mix.}$) Ratio:

Sr. No.	Surfactant Mixture Ratio ($S_{mix.}$)	Number of vol. flask inversions	Transmittance at 638 nm
1	1:1	30	79.65
2	1:2	35	86.33
3	2:1	25	91.52
4	1:3	40	70.56
5	3:1	45	65.32

Thus results revealed that, among various tested S_{mix}, ratio 1:1, 1:2, 2:1 shows minimum no. of volumetric flask inversion and better percent transmittance. Thus these three ratios were further subjected for depiction of microemulsion region by constructing ternary plots.

4.3 Drug-Excipients Compatibility Study:
All excipients (lemongrass oil lauroglycol 90,tween 80) and drug were mixed in vial in 1:1 ratio and observed for appearance, color, odor and drug content at interval of 0,7,9,15 and 30 days, and it was found that there was no changes in appearance, color , odor and drug content 95.70 %

4.4 Construction of Pseudo-Ternary Phase Diagrams:
For developing a suitable formulation of micro emulsions, the classical pseudo ternary phase diagram technique was followed by employing aqueous titration method. Briefly, oil was mixed with surfactant and co surfactant and titrated with water till a turbid emulsion was reached. Phase diagram was subsequently constructed from the data generated by plotting % of oil (lemongrass oil), water and total surfactant/co surfactant mixture (Smix):tween 80 and lauroglycol 90, at different ratios as three vertices of a triangle. The various Smix were tried such as; 1:1; 1:2 and 2:1. Among these ratios, Smix 2:1 fig. no.19. Was found to be the best combination with broader micro emulsion area and the emulsion formed was clear/ less turbid and was spontaneous in formation.

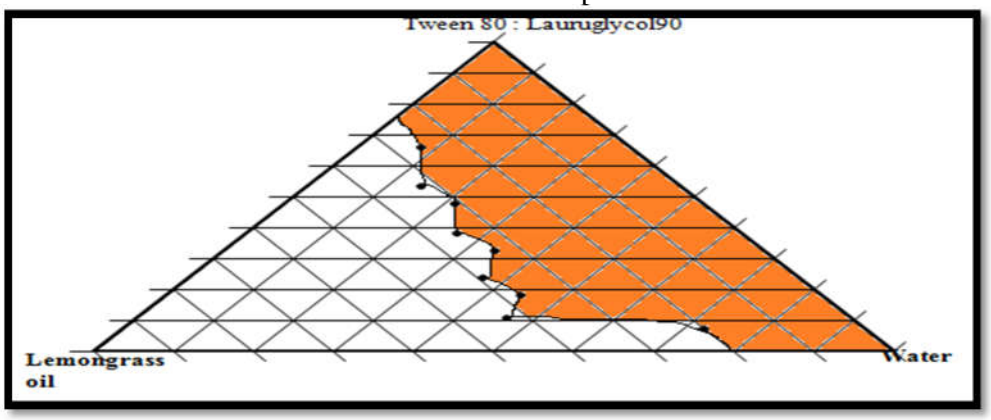


Figure No.17: Ternary Plot For ratio 1:1(Tween80: Lauroglycol 90)

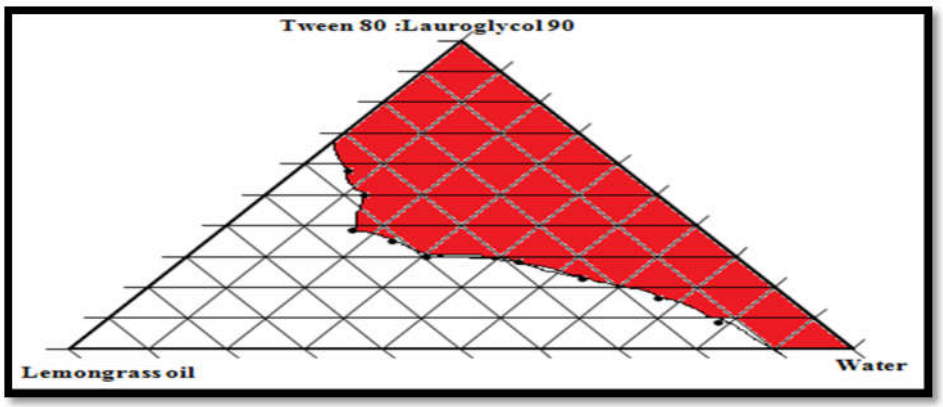


Figure No.18: Ternary Plot For ratio 1:2(Tween 80: Lauroglycol 90)

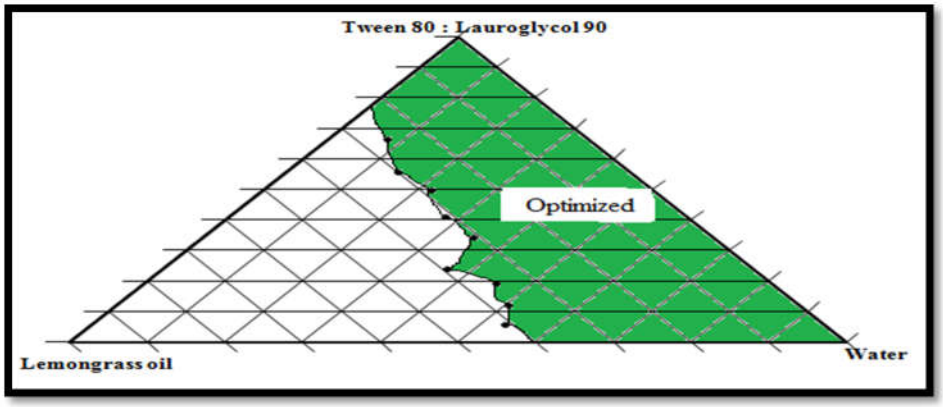


Figure No.19: Ternary Plot For ratio 2:1(Tween 80: Lauroglycol 90)

4.5 Selection of Formulations

Composition for Ibuprofen SEDDS formulations selected from pseudo ternary phase diagram prepared by water titration method shown in table 34

Table 34: Selected Formulations

FC	Drug (mg)	Oil (mg)	Surfactant: Co-surfactant ratio (mg)		
			1:1	1:2	2:1
F1	200	400	600	-	-
F2	200	200	-	800	-
F3	200	600	-	-	400
F4	200	200	-	-	800
F5	200	400	-	-	600

4.6 Evaluation of Self Emulsifying Drug Delivery System of Ibuprofen:

A. Phase Separation Study:

All formulations (F1- F5) were stable for two hours on 0.1 N HCl and distilled water. No phase separation occurred for all formulation (F1-F5). Hence all the formulations were subjected to further evaluation.

B. Centrifugation Study:

The formulations F1-F5 showed maximum stability (no creaming, cracking, phase separation) were observed.

C. Drug Content:

The % drug content for all formulations (F1-F5) was carried out in methanol. The % drug content increases as the surfactant concentration increases this may due to the solubilizing capacity of surfactants. The drug content uniformity in F1-F5 formulations was found to be 85.40, 91.38, 92.89, 89.95 and 96.67, hence result revealed that drug content was higher in F5 formulation indicating uniform drug dispersion in formulation compared to other i.e F1-F4.

D. % Transmittance:

Transmittance study revealed that as the concentration of surfactant increases the transmittance of resulting emulsion decreases. Percent transmittance of all formulation F1-F5 was found to be 74.97%, 76.35%, 85.15%, 81.26%, 94.33%. F5 formulation showed highest transmittance.

E. Globule Size Determination:

It has been reported that particle size distribution is one of the most important characteristics affecting the in vivo fate of emulsions. The globule size of the emulsion also determines the rate and extent of release. The smaller the globule size, larger the surface area provided for drug absorption. Globule size of F1-F5 formulation was 410 nm, 390 nm, 400 nm, 360 nm, 349 nm. The globule size of F5 formulation was lowest as compared with F1-F4, which was desirable, indicating that the system had narrow size.

G) Emulsification Time:

The emulsification rate is a useful index to appraise emulsification efficiency of a formulation. The selected formulations were subjected to assessment of emulsification time. The result divulged that F1-F5 emulsification time ≤ 1.9 min, ≤ 2 min, ≥ 1.5 min, ≥ 2 min and ≤ 1,5 min .Only F5 formulation showed minimum emulsification time of ≤ 1.5 min. and therefore F5 was found best and assessed for further evaluation.

H) Rheological Analysis:

Viscosity of the formulations F1-F5 was found to be 125.57 cP, 120.86 cP, 123.51 cP, 115.82 cP, 110.18 cP and F5 formulation showed less viscosity compared to other formulation.

I) In Vitro Dissolution Test:

Drug release from the SEDDS formulation (F5) was found significantly higher as compared with that of other formulations and also compared with pure drug. It could be suggested that the SEDDS formulation resulted in spontaneous formation of a microemulsion with a small droplet size, which permitted a faster rate of drug release into the aqueous phase, much faster than that of others. Thus this greater availability of dissolved Ibuprofen from the SEDDS formulation could lead to higher absorption and higher oral bioavailability. The maximum drug release was found to be 97.58 ± 0.6 from the F5 formulation and results were shown in table 35.

Table 35: In Vitro Drug Release of F1-F5 Formulations

TIME	F1	F2	F3	F4	F5
0	0	0	0	0	0
10	12.34	13.45	11.45	15.67	20.98
20	38.76	37.67	32.31	41.54	43.65
30	69.65	63.23	61.87	69.65	76.84
40	76.54	74.87	72.34	82.45	89.43
50	81.23	81.32	79.81	85.65	96.98
60	87.67	84.58	81.34	89.31	97.58

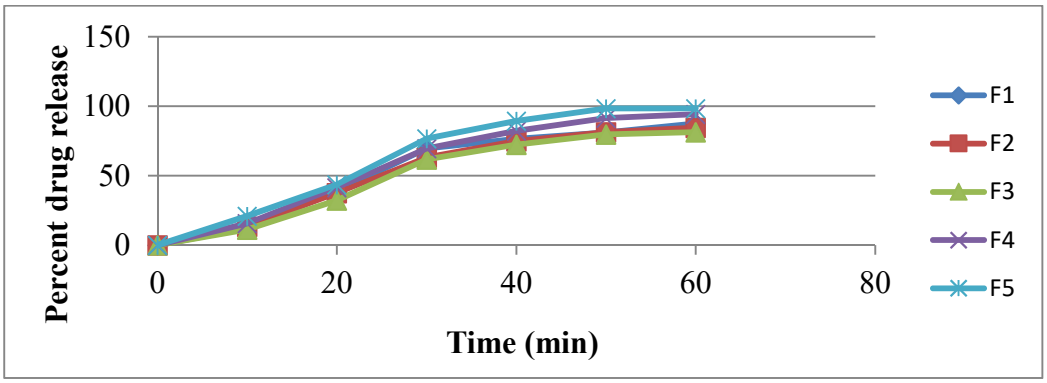


Figure No. 20: Graph of in Vitro Drug Release (F1-F5)

Table 36: Common Evaluation Parameters of F1 -F5 Liquid Formulation.

Parameter	F1	F2	F3	F4	F5
Phase separation	No	No	No	No	No
Centrifugation study	Stable	Stable	Stable	Stable	Stable
Drug content (%)	85.40	91.38	92.89	89.95	96.67
Percent Transmittance %)	74.97±0.12	76.35±0.13	85.15±0.15	81.26±0.02	94.33±0.12
Globule size (nm)	410	390	400	360	349
Emulsification time (min)	≤ 1.9	≤ 2	≥ 1.5	≥ 2	≤ 1.5
Rheological study (cP)	125.57	120.86	123.51	115.82	110.18
In Vitro drug release data at 60 min (%)	87.67	84.58	81.34	89.31	97.58

❖ From all above evaluation parameters of liquid formulations F1-F5 it was concluded that F5 formulation showed the best result in all parameters hence it assessed for further evaluation parameters such as zeta potential, PDI, DSC and In vitro drug release compared with pure drug and marketed formulation.

4.7 Evaluation Parameters of Selected F5 Formulation:

a) Globule Size Analysis of F5 Formulation was found to be 349 nm.

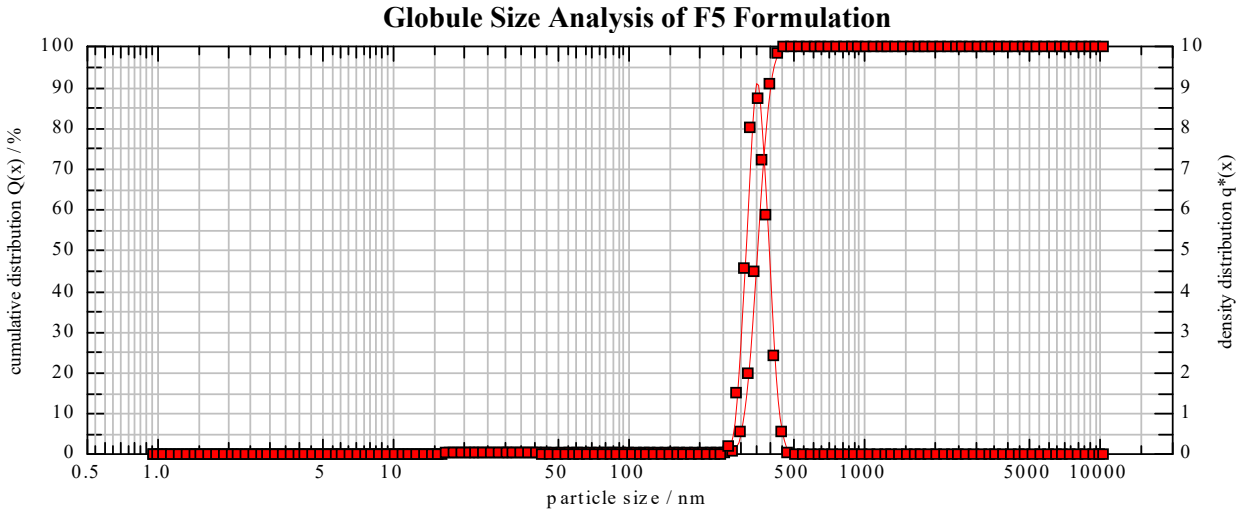


Figure No. 21: Globule Size Analysis

b) Zeta Potential Measurement:

Zeta potential of F5 formulation was found to -27.08 (mV) which was desirable for achieving the better result. It shows the physical stability of the system. The magnitude of the zeta potential gives an indication of the potential stability of the colloidal system.

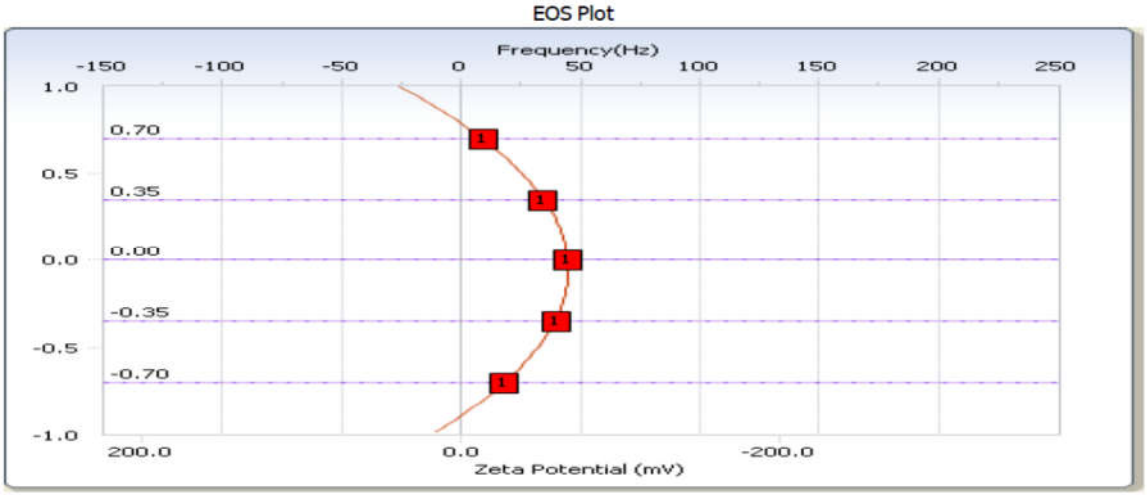


Figure No.22: Zeta Potential of F5 Formulation

Measurement Results:

Zeta Potential : -27.08 (mV)	Doppler shift : 18.14(Hz)
Mobility : -2.277e-004 (cm²/Vs)	Base Frequency : 127.2 (Hz)
Conductivity : -0.0015(mS/cm)	

c) Polydispersity Index (PDI):

Formulation F5 was showed lower droplet size than other formulation. Hence formulation F5 was selected for PDI study, showed in table 37. Formulations F5 followed the criteria of microemulsion

by having the PDI 0.21 respectively, indicating the uniformity of particles.

Table 37: Polydispersity Index of formulations F5

FC	X10	X50	X90	X90-X10	X90-X10/X50
F5	9.89	15.09	17.23	2.14	0.21638

d) DSC Analysis:

DSC curve of S-SEDDS-F5 was shown in fig.no.23**.** The physical mixtures were prepared by simply mixing the carriers and drug. Pure Ibuprofen showed a sharp endothermic peak at about 79^0C corresponding to its melting point and indicating its crystalline nature. Aerosil200 did not show any peak over the entire range of the tested temperatures. The melting point, which appeared in the drug peak, was shown with a reduced intensity in physical mixture .No obvious peak of the drug was found in the solid SEDDS–F5 indicating that the drug must be present molecularly dissolved state in solid SEDDS.

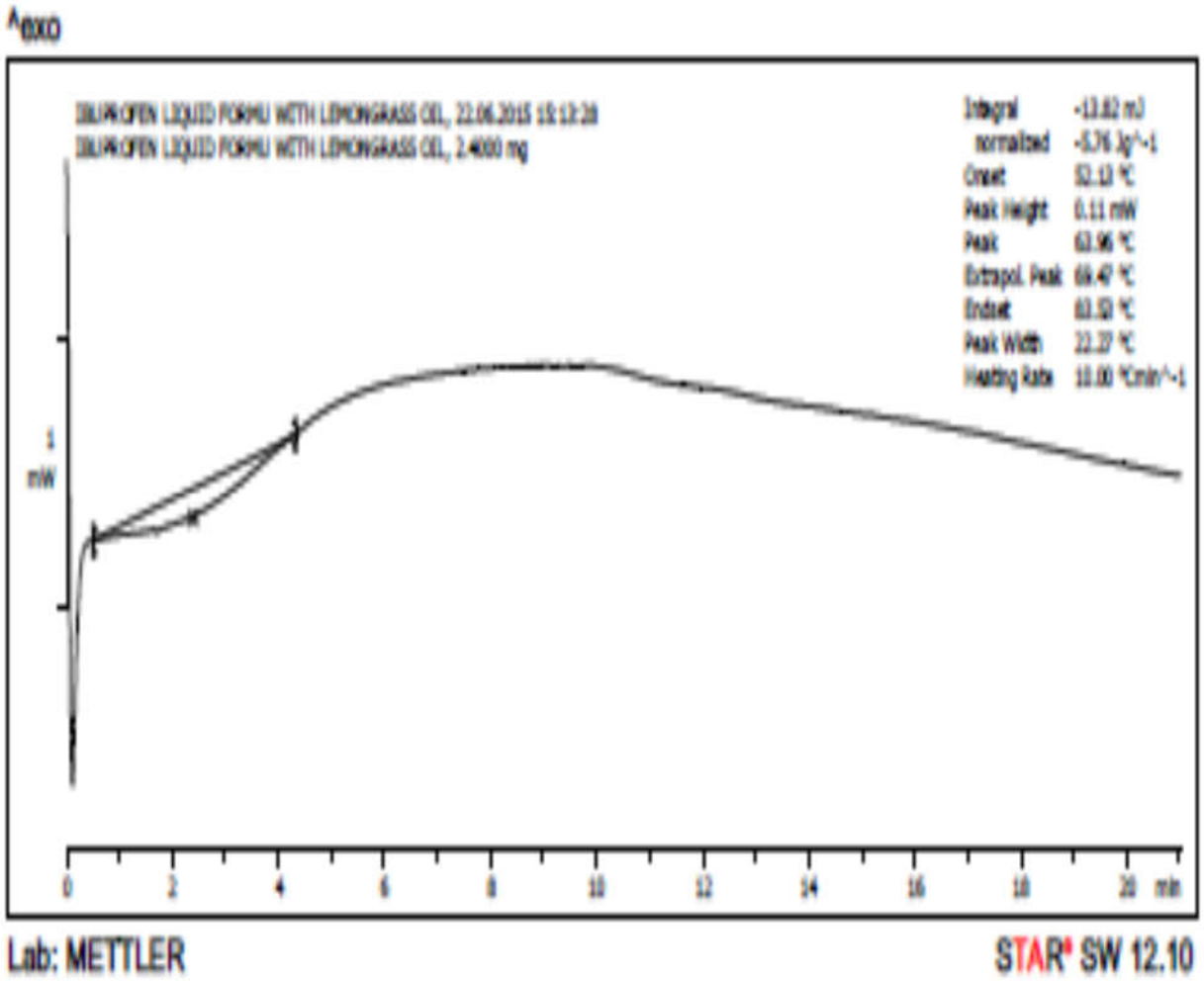


Figure No.23: DSC Thermogram of Selected F5 Formulation

d) In Vitro Release Study:

Dissolution profile of optimized formulation F5 was compared with pure drug and marketed formulation and absorbance was measured at 10 min time interval and, in 1 hour study 97.58 % drug was released for F5 formulation.

Table 38: In Vitro Drug Release study

Time (min)	F5	Marketed	Pure drug
0	0	0	0

10	20.98	15.2	4.93
20	43.65	23.55	6.2
30	76.84	27.67	8.21
40	89.43	33.23	9.45
50	96.98	41.43	10.25
60	97.58	53.57	14.32

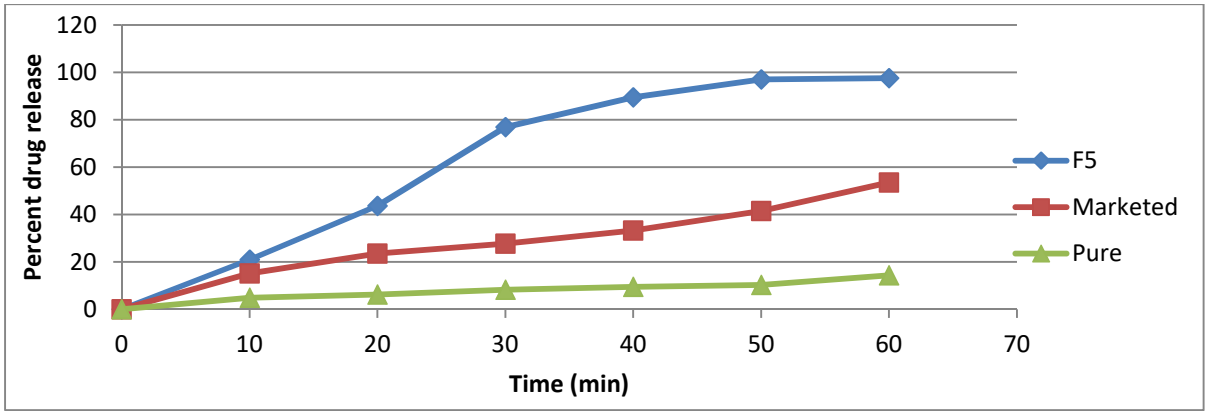


Figure No. 24: Graph of In Vitro Drug Release

4.8 SOLID SEDDS:

❖ **Adsorption of liquid SEDDS onto solid carrier:**

Liquid SEDDS was converted into solid formulation by adsorbing it on aerosol 200 for 200 mg of ibuprofen 0.16 ml of liquid SEDDS and 200 mg of aerosol was used

❖ **Preliminary trials:**

After the solidification of liquid SEDDS with aerosol 200, compritol and HPMC K4 was added for the floating purpose along with this other ingredients also added required for the tablet compression. This whole powder blend of HPMC K4 and compritol used and trial were carried out for the tablet and it was observed that hardness and friability of tablet of HPMC K4 was very poor and hence it was rejected and powder blend of compritol with two different formulations (E1 & E2) was assessed for the further study.

Table 39: Evaluation Parameters of Powder Blend of E1 & E2

Parameter	E1	E2
Tapped density	0.491±0.012	0.547±0.010
Bulk density	0.424±0.005	0.488±0.010
Carr's Index	13.64±0.95	15.02±0.78
Hausner's ratio	1.163±0.02	1.200±0.07
Angle of repose	23.20±1.04	28.35±1.02

4.9 Evaluation of Tablet:

A. Evaluation of powder blend of E1 & E2:

The above powder blend of formulation E1 and E2 was directly compressed into tablet and further assessed for their evaluation parameter.

Table 40: Evaluation of Powder Blend of E1-E2

Parameter	**E1**	**E2**
Weight variation	549.8±1.687	550.2±1.370
Tablet thickness	6.3 ± 0.2	6.2 ± 0.3
Tablet hardness	4.8±0.2	5.2±0.3
Friability	0.24	0.38

Floating time	7.5 hrs	8 hrs
Drug content	86.78	96.56

B. Dissolution Study of Formulation E1 and E2:

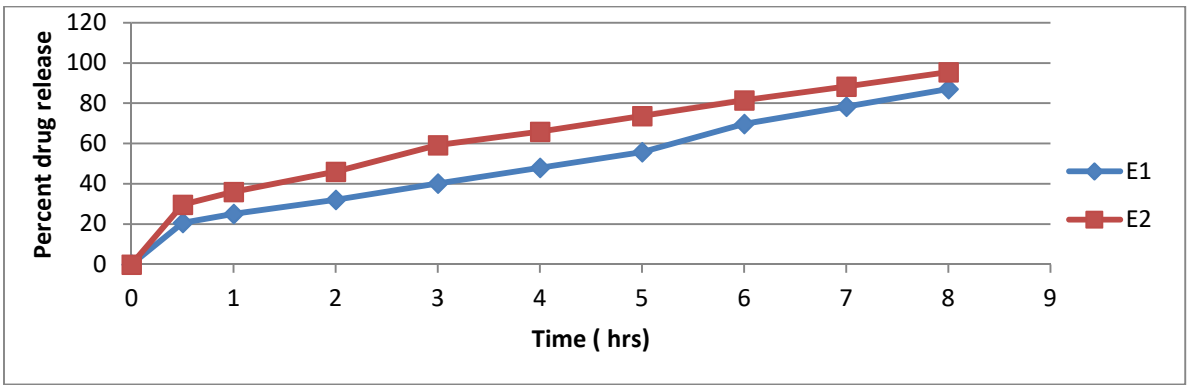
Dissolution Test for Tablets:

In vitro dissolution of formulation E1 and E2 was carried out by using dissolution test apparatus USP II (paddle type), using 0.1 N Hcl. The dissolution of tablet formulation E2 was showed maximum drug release (95.56%) in 0.1N Hcl for 8 hrs.

Table 41: In Vitro Drug Release of Formulation E1 and E2

Time (hrs)	E1	E2
0	0	0
0.5	20.58	29.68
1	25.05	36.10
2	31.97	45.97
3	40.15	59.28
4	47.96	65.90
5	55.72	73.76
6	69.73	81.54
7	78.34	88.29
8	87.06	95.56

Figure No.25: In Vitro Drug



Release of E1 and E2

From all above observation it was concluded that E2 formulation showed best result and it has grater floating efficiency than E1 hence it assessed for further evaluation parameter.

4.10 Evaluation Study of E2 Formulation:

a) **FT-IR Study:**

Fig no.26 illustrates the FT-IR spectra of solid SEFDDS. The pure drug Ibuprofen exhibit characteristic peaks at 2850- 2970 cm^{-1}(C-H alkanes), 3010 -3100 cm^{-1} (C-H aromatic ring), 1710 cm^{-1} (carboxylic acid), 2900 cm^{-1}(C-H aldehyde), 1465 cm^{-1} (CH_2 bend) .The peaks at 2850- 2970 cm^{-1}, 3010 -3100 cm^{-1} , 1710 cm^{-1}, 2900 $cm^{-1,}$ were disappeared and drop in intensity at 1710 cm^{-1} indicate physical interaction between the drug and formulation ingredients. However the absence of extra peaks suggests that there was no possible chemical interaction between the drug and formulation ingredients.

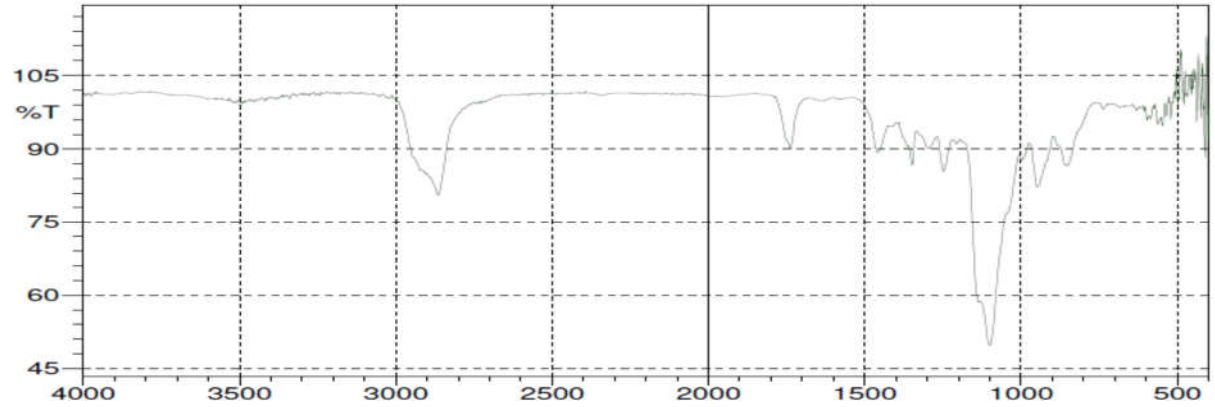


Figure No. 26: FTIR of Solid SEDDS Selected E2 Formulation

b) **DSC Study:**

Pure Ibuprofen showed a sharp endothermic peak at about 79 ^{0}C corresponding to its melting point and indicating its crystalline nature. Aerosil 200 did not show any peak over the entire range of the tested temperatures fig.no.28. The melting point, which appeared in the drug peak, was shown with a reduced intensity in Solid SEFDDS formulation fig.no.28. No obvious peak of the drug was found in the formulation indicating that the drug must be present molecularly dissolved state in solid SEFDDS.

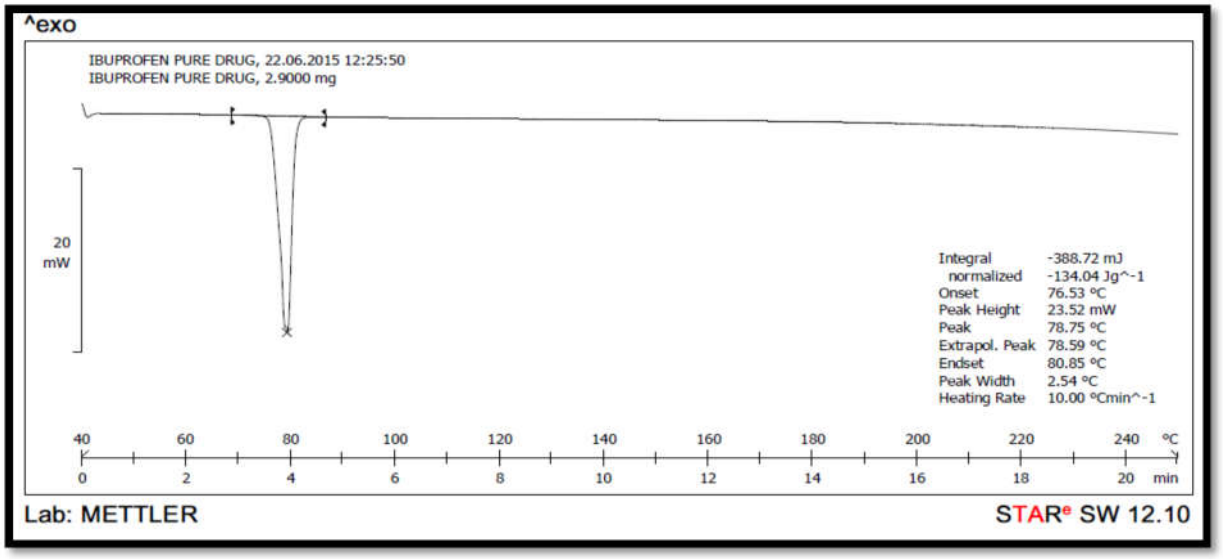


Figure No.27: DSC Thermogram of Ibuprofen

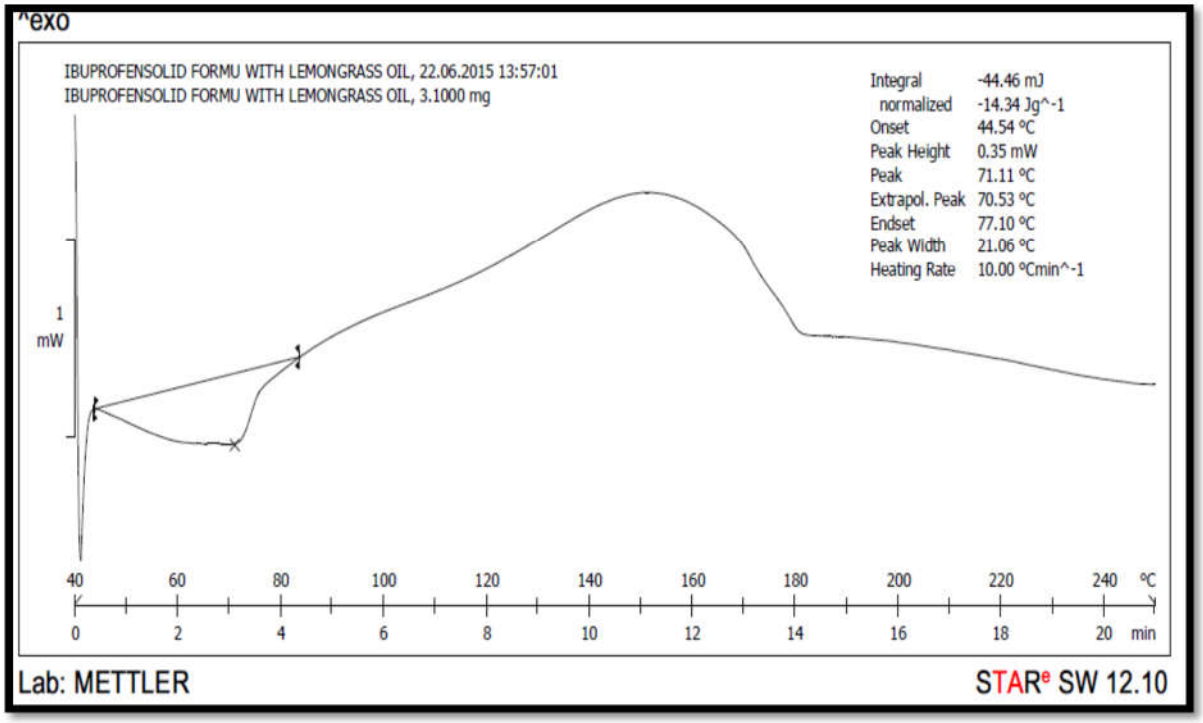


Figure No. 28: DSC Curve of Solid SEFDDS Formulation

c) X-Ray Powder Diffraction:

The powder X-ray diffractometry patterns of solid formulation was presented in fig. no.30. Ibuprofen had sharp peaks at the diffraction angles, showing a typical crystalline pattern fig. no.29.S-SEFDDS formulation showed peaks at diffraction angles, showing an amorphous pattern.

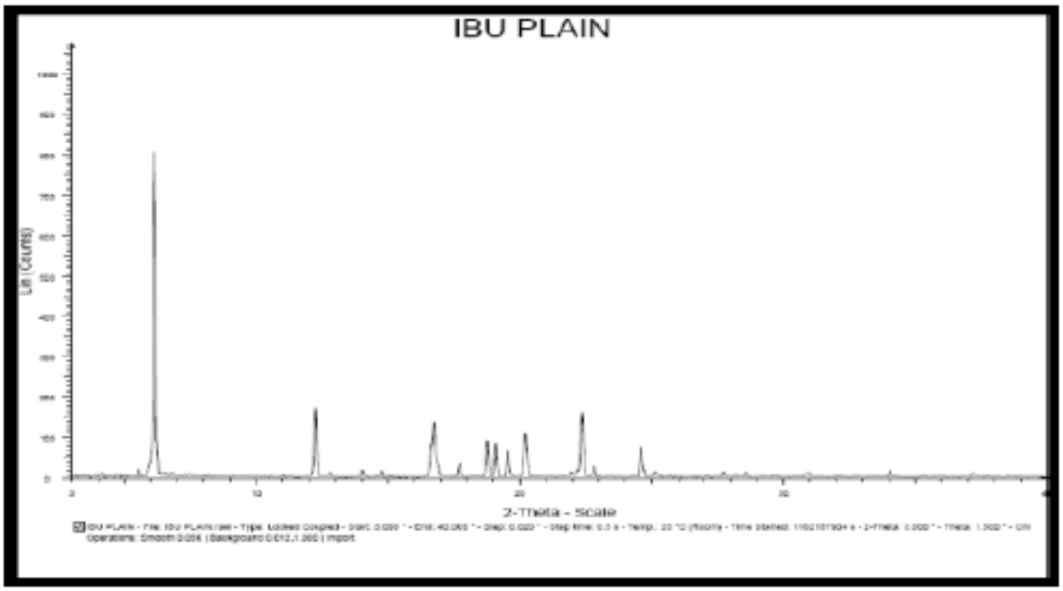


Figure No. 29: XRD Image of Ibuprofen

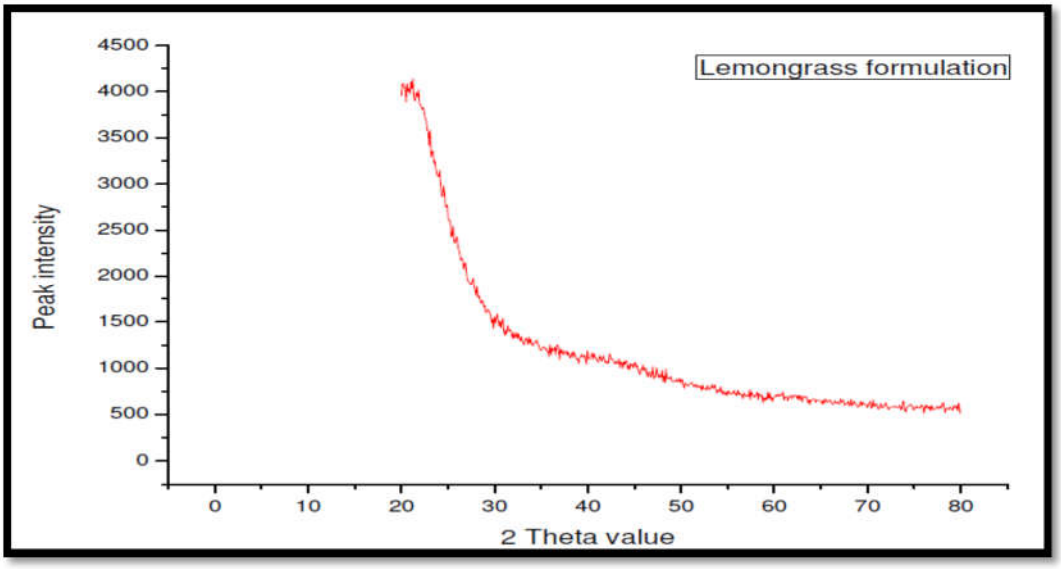


Figure No. 30: XRD Image of Solid SEFDDS

d) In Vitro Dissolution Study:

Drug release from the SEFDDS formulation E2 and pure drug was carried out for 8 hrs, and it provided a drug release of 95.56 % while pure drug dissolved slowly and only 40.89 % of the drug in solution at 8 hr. Therefore only the new developed Ibuprofen SEFDDS exhibits release of Ibuprofen of about 95 % over an 8 hr period.

Table 42: In Vitro Drug Release Of Formulation E2 And Pure

Time (hrs)	E2 (Percent drug release)	Pure drug (Percent drug release)
0	0	0
0.5	29.68	6.34
1	36.1	10.45
2	45.97	16.23
3	59.28	21.45
4	65.9	30.67
5	73.76	31.89
6	81.54	36.19
7	88.29	39.67
8	95.56	40.89

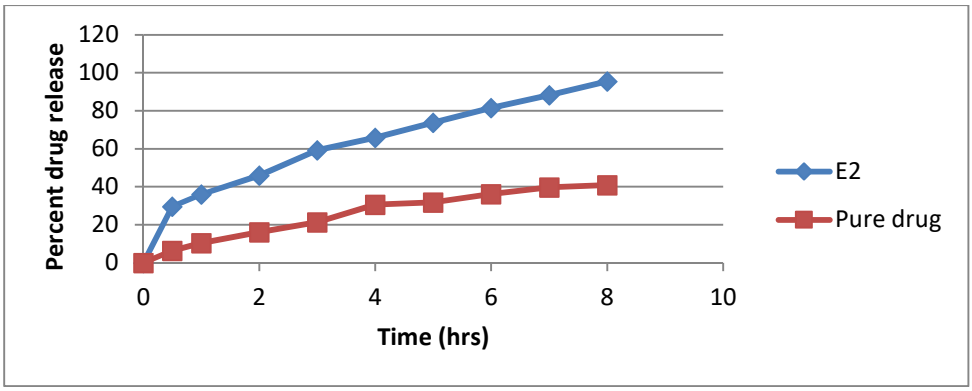


Figure No. 31: In Vitro Drug Release of E2 and Pure Drug

4.11 Stability Studies:

The E2 formulation was placed into the petriplate and kept in stability chamber at (40 ± 2oC, 75% ± 5% RH). Then sample was observed for any physical changes and evaluated for drug content.

Table 43: Stability test

Sr. No	Parameter	7 Days	15 Days	30 Days	60 Days	90 Days
1	Appearance	Round shaped with smooth texture	Round shaped with smooth texture	Round shaped with smooth texture	Round shaped with smooth texture	Round shaped with smooth texture
2	Colour	White	White	White	White	White
3	Odor	Lemongrass	Lemongrass	Lemongrass	Lemongrass	Lemongrass
4	Drug content (%)	96.87	96.74	96.79	96.45	96.20

5. SUMMARY AND CONCLUSION:

Ibuprofen is BCS Class II non steroidal anti inflammatory molecule has very low and variable bioavailability due to its extremely poor solubility in water .The objective of the study was to improve its solubility and dissolution rate of Ibuprofen by formulating Self Emulsifying Floating Drug Delivery System (SEFDDS).

In present study, SEDDS formulated with Lemongrass oil as the oil phase, Tween 80 as surfactant and Lauroglycol 90 as a co-surfactant on the basis of solubility studies. Pseudo ternary phase diagram was constructed for three ratios of surfactant and co-surfactant ratios 1:1, 1:2, 2:1 from this five formulation were selected. Prepared formulations were subjected for evaluation parameters such as phase separation study, centrifugation study, % drug content, transmittance study, globule size determination, emulsification time, rheological analysis, in vitro dissolution study etc. From all these evaluation parameters F5 formulation was selected as optimized formulation which shows no phase separation, stable, 96.67% drug content, 94.33% percent transmittance, 349 nm globule size, ≤ 1.5 min emulsification time, 110.18 cP viscosity and 97.58 % drug release.

Optimized liquid formulation (F5) also subjected to PDI, DSC, In vitro drug release studies and result shows 0.21 PDI indicating uniform distribution of emulsion, DSC showed the molecularly dissolved state of drug as there was no sharp peak in the graph and drug release was 97.58 % Optimized liquid SEDDS was converted to S-SEFDDS by using adsorbent Aerosol 200. Floating approach was achieved using compritol888ATO. With compritol88ATO we tried two different concentrations and it was formulated into tablet dosage form E1 & E2. Powder blend of E2 formulation showed good results hence tablet of the same formulation was prepared and therefore E2 was assessed for further evaluation parameter FT-IR, DSC, X-Ray Diffraction study and In vitro drug release study. Result of E2 formulation of FT-IR was shown that no drug and excipients interaction, for the DSC there was a sharp peak as drug was in dissolved state and X-Ray study revealed that crystalline nature of drug and In vitro drug release 95.56 % in 8 hrs. So E2 formulation selected as optimized formulation. From the entire study it was concluded that, SEFDDS of Ibuprofen showed an increase in both the solubility and dissolution rate and also gastric residence time of drug.

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