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Development of Self-Nanoemulsifying Drug Delivery System for Enhanced Solubility and Dissolution of Poorly Aqueous Soluble Drug

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Abstract
Poor aqueous solubility remains a major limitation for many orally administered drugs, leading to low bioavailability and inconsistent therapeutic outcomes. The present study aimed to develop and evaluate a ***Self-Nanoemulsifying Drug Delivery System (SNEDDS)*** *to enhance the solubility and dissolution rate of* ***Ibuprofen****, a BCS Class II drug with poor aqueous solubility. Solubility studies were performed to select suitable oil, surfactant, and co-surfactant components. Pseudo-ternary phase diagrams were constructed to determine the nanoemulsion region. SNEDDS formulations were prepared using* ***Capryol 90 (oil), Tween 80 (surfactant), and Transcutol P (co-surfactant)****. The optimized formulation was evaluated for droplet size, polydispersity index (PDI), zeta potential, thermodynamic stability, drug content, and in vitro dissolution.*
The optimized formulation exhibited a droplet size of ***92.6 ± 3.4 nm****, PDI of* ***0.214 ± 0.02****, and zeta potential of* ***−21.3 mV****, indicating good stability. In vitro dissolution studies demonstrated* ***96.8% drug release within 30 minutes****, compared to* ***42.5% from pure drug suspension****. The study confirms that SNEDDS significantly enhances solubility and dissolution of poorly water-soluble drugs, thereby potentially improving oral bioavailability.*
Keywords: *SNEDDS, Ibuprofen, Nanoemulsion, Solubility enhancement, Dissolution improvement, Lipid-based drug delivery*

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I. Introduction

Oral drug delivery remains the most preferred route of drug administration due to its convenience, patient compliance, non-invasive nature, and cost-effectiveness in pharmaceutical manufacturing. However, the oral delivery of many therapeutic agents is often limited by poor aqueous solubility and low dissolution rates. In recent years, drug discovery programs have increasingly identified highly lipophilic compounds, and it is estimated that approximately **40–50% of newly developed drug candidates exhibit poor aqueous solubility**, which significantly limits their oral bioavailability and therapeutic effectiveness [1]. Poorly soluble drugs generally show slow dissolution in gastrointestinal fluids, resulting in insufficient drug concentration available for absorption across the intestinal membrane.

The **Biopharmaceutics Classification System (BCS)** categorizes drugs into four classes based on their solubility and intestinal permeability characteristics. Drugs belonging to **BCS Class II** are characterized by **low solubility but high permeability**, and for such drugs, the rate-limiting step in oral absorption is the dissolution process rather than membrane permeation [2]. Therefore, improving the dissolution behavior of BCS Class II drugs is considered a critical strategy for enhancing their oral bioavailability.

Ibuprofen, a widely used **non-steroidal anti-inflammatory drug (NSAID)**, is commonly prescribed for the treatment of pain, inflammation, fever, rheumatoid arthritis, and osteoarthritis. Ibuprofen is categorized as a **BCS Class II drug** due to its low aqueous solubility and high permeability across biological membranes. The aqueous solubility of ibuprofen is reported to be approximately **21 mg/L at 25°C**, which can lead to incomplete dissolution in gastrointestinal fluids following oral administration [3]. As a consequence, the drug may exhibit delayed onset of action and variable absorption, particularly under physiological conditions where dissolution is limited. Therefore, the development of effective formulation strategies to enhance the solubility and dissolution rate of ibuprofen is of considerable pharmaceutical interest.

Several formulation approaches have been explored to improve the solubility and dissolution characteristics of poorly water-soluble drugs. These strategies include **particle size reduction (micronization and nanonization), solid dispersion systems, salt formation, inclusion complexation with cyclodextrins, and**

lipid-based drug delivery systems [4]. While these techniques have demonstrated potential for improving drug dissolution, they may suffer from limitations such as physical instability, recrystallization of the drug, complex manufacturing processes, and limited scalability.

Among the various formulation strategies, **lipid-based drug delivery systems (LBDDS)** have gained significant attention due to their ability to enhance the solubility and bioavailability of poorly water-soluble drugs. One of the most promising lipid-based systems is the **Self-Nanoemulsifying Drug Delivery System (SNEDDS)**. SNEDDS are isotropic mixtures consisting of **oils, surfactants, co-surfactants, and the drug**, which upon mild agitation in aqueous media spontaneously form **oil-in-water nanoemulsions with droplet sizes typically ranging from 20 to 200 nm** [5].

The spontaneous formation of nanoemulsions occurs due to the reduction in interfacial tension between the oil and aqueous phases in the presence of surfactants and co-surfactants. Upon dilution in gastrointestinal fluids, SNEDDS rapidly disperse to form fine nano-sized droplets that provide a large interfacial surface area for drug release. This increased surface area significantly enhances drug dissolution and maintains the drug in a solubilized state, thereby preventing precipitation in the gastrointestinal tract [6].

In addition to improving dissolution, SNEDDS may also enhance drug absorption through several mechanisms. These include improved membrane permeability, stimulation of lymphatic transport pathways, and protection of the drug from degradation in the gastrointestinal environment. Furthermore, lipid-based formulations can reduce variability in drug absorption associated with food intake and may improve the overall pharmacokinetic profile of lipophilic drugs [7].

SNEDDS offer several advantages compared with conventional dosage forms, including **enhanced solubilization of hydrophobic drugs, improved dissolution rate, increased oral bioavailability, reduced variability in absorption, and ease of formulation development**. In addition, SNEDDS formulations are thermodynamically stable and can be conveniently encapsulated into **soft or hard gelatin capsules**, making them suitable for large-scale pharmaceutical manufacturing [8].

Considering the potential benefits of SNEDDS in improving the solubility and dissolution of poorly water-soluble drugs, the present study was designed to **develop and optimize a Self-Nanoemulsifying Drug Delivery System (SNEDDS) for Ibuprofen**. The formulation was developed by selecting suitable oils, surfactants, and co-surfactants based on solubility studies. Pseudo-ternary phase diagrams were constructed to identify the nanoemulsion region, and optimized formulations were evaluated for **self-emulsification efficiency, droplet size distribution, polydispersity index, zeta potential, drug content, and in vitro dissolution performance**. The successful development of an optimized SNEDDS formulation is expected to significantly enhance the dissolution behavior of ibuprofen and thereby improve its oral bioavailability and therapeutic efficacy.

II. Materials and Methods

2.1 Materials

Material	Source	Role
Ibuprofen	Yarrow Chem Products, Mumbai	Model drug
Capryol 90	Gattefossé	Oil phase
Tween 80	Merck	Surfactant
Transcutol P	Gattefossé	Co-surfactant
Distilled water	Laboratory	Dilution medium

The materials used in the present study were of **analytical or pharmaceutical grade** and were used without further purification. **Ibuprofen** was selected as the model poorly water-soluble drug due to its classification as a **BCS Class II compound**, which exhibits low aqueous solubility but high membrane permeability. Ibuprofen was procured as a gift sample from **Yarrow Chem Products Pvt. Ltd., Mumbai, India**, and was used as the active pharmaceutical ingredient (API) for the development of the Self-Nanoemulsifying Drug Delivery System (SNEDDS). Ibuprofen is a widely used **non-steroidal anti-inflammatory drug (NSAID)** indicated for the treatment of pain, inflammation, fever, rheumatoid arthritis, and osteoarthritis. Due to its hydrophobic nature and poor aqueous solubility, the oral bioavailability of ibuprofen is often limited by slow dissolution in gastrointestinal fluids, making it an appropriate candidate for lipid-based drug delivery systems such as SNEDDS [9].

Capryol 90 (propylene glycol monocaprylate) was obtained from **Gattefossé, France**, and was used as the **oil phase** in the SNEDDS formulation. Capryol 90 is a medium-chain monoester widely employed in lipid-based drug delivery systems due to its high drug-solubilizing capacity and ability to facilitate the formation of stable nanoemulsions. The oil phase plays a crucial role in SNEDDS formulations as it solubilizes lipophilic drugs and promotes the formation of fine oil droplets upon dilution in aqueous media. Medium-chain lipid excipients such as Capryol 90 are known to improve the solubilization of hydrophobic drugs and may also enhance lymphatic transport, thereby improving systemic drug absorption [10].

Tween 80 (Polysorbate 80) was obtained from **Merck Pvt. Ltd., India**, and used as the **surfactant** in the SNEDDS formulation. Surfactants are essential components of SNEDDS because they reduce the interfacial tension between oil and aqueous phases, allowing the formulation to spontaneously emulsify when exposed to gastrointestinal fluids. Tween 80 is a **nonionic surfactant with a high hydrophilic-lipophilic balance (HLB value ≈ 15)**, which favors the formation of oil-in-water nanoemulsions. Nonionic surfactants are generally preferred in oral formulations due to their lower toxicity, improved stability, and compatibility with biological membranes [11].

Transcutol P (diethylene glycol monoethyl ether) was obtained from **Gattefossé, France**, and used as the **co-surfactant** in the SNEDDS formulation. Co-surfactants assist in further lowering the interfacial tension and improving the flexibility of the interfacial film surrounding the oil droplets. The presence of a co-surfactant enables the formation of nanoemulsions with smaller droplet sizes and greater thermodynamic stability. Transcutol P is widely used in pharmaceutical formulations because of its excellent solubilizing capacity for both hydrophilic and lipophilic drugs and its ability to enhance drug permeation through biological membranes [12].

Distilled water was prepared in the laboratory and used as the **aqueous dilution medium** for evaluating the self-emulsification behavior of SNEDDS formulations. During in vitro studies, distilled water was used to simulate the aqueous environment encountered by the formulation following oral administration in gastrointestinal fluids. When SNEDDS formulations come into contact with aqueous media, they spontaneously form nanoemulsions with droplet sizes typically ranging between **20–200 nm**, which significantly increases the surface area available for drug release and improves dissolution behavior [13].

All chemicals and reagents used in the present study were of **analytical grade** and were utilized as received without further purification. The selection of oil, surfactant, and co-surfactant components was based on preliminary **solubility screening studies** to identify excipients capable of dissolving the maximum amount of ibuprofen and producing stable nanoemulsion systems.

2.2 Solubility Studies

Solubility studies were performed to identify suitable **oil, surfactant, and co-surfactant components** capable of dissolving the maximum amount of ibuprofen. The selection of appropriate excipients is a critical step in the development of **Self-Nanoemulsifying Drug Delivery Systems (SNEDDS)** because the solubility of the drug in formulation components directly affects drug loading capacity, formulation stability, and prevention of drug precipitation after dilution in gastrointestinal fluids [14].

In the present study, the solubility of ibuprofen was determined in various oils, surfactants, and co-surfactants commonly used in lipid-based drug delivery systems. An excess amount of ibuprofen was added to **2 mL of each selected vehicle**, including different oils (Capryol 90, Oleic acid, Labrafac PG), surfactants (Tween 80, Cremophor EL), and co-surfactants (Transcutol P, PEG 400) in tightly closed glass vials. The mixtures were vortexed briefly to ensure proper mixing and then placed in a **temperature-controlled orbital shaker maintained at 37 ± 0.5°C** for **48 hours** to achieve equilibrium solubility.

Maintaining the temperature at **37°C** was important to simulate physiological conditions in the gastrointestinal tract. Continuous shaking ensured adequate contact between the drug and the excipient, allowing the drug to dissolve until equilibrium solubility was reached [15].

After the equilibration period, the samples were removed from the shaker and centrifuged at **5000 rpm for 15 minutes** to separate undissolved drug particles. The clear supernatant was carefully withdrawn and filtered through a **0.45 µm membrane filter** to remove any remaining insoluble drug particles. The filtered samples were then suitably diluted with **methanol** and analyzed using a **UV-Visible spectrophotometer at a wavelength of 221 nm**, which corresponds to the maximum absorbance (λmax) of ibuprofen [16].

All experiments were performed in **triplicate**, and the results were expressed as **mean ± standard deviation (SD)** to ensure reliability and reproducibility of the data.

The solubility results obtained in different vehicles are presented in **Table 1**.

Table 1: Solubility of Ibuprofen in Various Vehicles

Vehicle	Solubility (mg/mL)
Capryol 90	138.5 ± 4.3
Oleic acid	96.2 ± 3.1
Labrafac PG	82.6 ± 2.7
Tween 80	164.8 ± 5.2
Cremophor EL	151.3 ± 4.8
Transcutol P	172.6 ± 6.1
PEG 400	118.4 ± 3.9

The results indicated that **Transcutol P exhibited the highest solubility for ibuprofen among the co-surfactants tested (172.6 mg/mL)**, while **Tween 80 showed the highest solubilizing capacity among the**

surfactants (164.8 mg/mL). Among the tested oils, **Capryol 90 demonstrated the highest solubility for ibuprofen (138.5 mg/mL)**.
The high solubility of ibuprofen in these excipients can be attributed to their **lipophilic nature and ability to solubilize hydrophobic drug molecules through intermolecular interactions**. The use of excipients with high drug solubilization capacity is essential for SNEDDS formulations because it allows higher drug loading and minimizes the risk of drug precipitation upon dilution with gastrointestinal fluids [17].
Based on the solubility screening results, **Capryol 90 was selected as the oil phase**, **Tween 80 as the surfactant**, and **Transcutol P as the co-surfactant** for the development of the SNEDDS formulation of ibuprofen. These components were further used for the construction of **pseudo-ternary phase diagrams** to identify the nanoemulsion region suitable for formulation development.

2.3 Construction of Pseudo-Ternary Phase Diagram
The **pseudo-ternary phase diagram** was constructed to determine the appropriate concentration range of **oil, surfactant, and co-surfactant** capable of forming stable nanoemulsions. The construction of phase diagrams is an essential step in the development of **Self-Nanoemulsifying Drug Delivery Systems (SNEDDS)** because it helps to identify the **nanoemulsion region** and optimize the proportions of formulation components required for efficient self-emulsification [18].
In the present study, pseudo-ternary phase diagrams were constructed using the **water titration method**. This method involves gradual addition of water to mixtures containing oil and surfactant/co-surfactant blends until the system undergoes phase transition. The components used for the construction of the phase diagram included **Capryol 90 as the oil phase**, **Tween 80 as the surfactant**, and **Transcutol P as the co-surfactant**, which were selected based on the results of solubility studies.
Initially, the surfactant and co-surfactant were mixed together in different weight ratios to form the **Smix (surfactant mixture)**. Three different **Smix ratios were evaluated** in order to determine their influence on nanoemulsion formation:
- **1:1 (surfactant: co-surfactant)**
- **2:1 (surfactant: co-surfactant)**
- **3:1 (surfactant: co-surfactant)**

For each Smix ratio, the oil phase (Capryol 90) and Smix were mixed in different weight ratios ranging from **1:9 to 9:1** in small glass vials. Each mixture was then titrated dropwise with **distilled water** under gentle magnetic stirring at room temperature. After each addition of water, the mixture was visually observed for changes in clarity, phase separation, turbidity, or formation of a transparent nanoemulsion system.
The endpoint of titration was reached when the mixture turned **turbid or phase separation occurred**, indicating the boundary of the nanoemulsion region. The compositions at which clear and transparent emulsions were obtained were considered to belong to the **nanoemulsion region** of the phase diagram.
The experimental data obtained from titration studies were plotted on **triangular coordinate graphs** using appropriate software to generate pseudo-ternary phase diagrams. Each apex of the triangular diagram represented **100% of one component** (oil, Smix, or water), while the interior of the triangle represented different combinations of the three components.

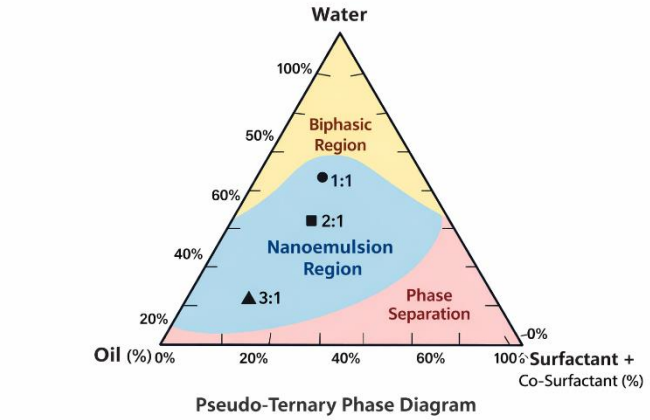


Figure 1. Pseudo-ternary phase diagram showing the nanoemulsion region formed by Capryol 90 (oil), Tween 80 (surfactant), and Transcutol P (co-surfactant) at different Smix ratios (1:1, 2:1, and 3:1). The shaded area represents the nanoemulsion region suitable for SNEDDS formulation.

The **nanoemulsion region was identified visually** based on the formation of clear, transparent, and low-viscosity systems. Regions that produced cloudy or phase-separated mixtures were excluded from the nanoemulsion zone.

The area representing nanoemulsion formation within the triangular diagram was shaded to indicate the optimal composition range for SNEDDS formulation.
The results of the phase diagram study indicated that the **Smix ratio of 2:1 (Tween 80 : Transcutol P)** produced the **largest nanoemulsion region**, suggesting that this ratio provided optimal reduction in interfacial tension and improved emulsification efficiency. Therefore, this ratio was selected for further formulation development and optimization of SNEDDS [19].
The construction of pseudo-ternary phase diagrams is widely used in nanoemulsion research because it provides a systematic approach for identifying formulation compositions that can spontaneously form nanoemulsions upon dilution in aqueous media. This technique also helps in minimizing the number of experimental trials required during formulation development [20].

2.4 Preparation of SNEDDS Formulations
Based on the results obtained from the **solubility studies and pseudo-ternary phase diagram analysis**, suitable excipients were selected for the formulation of the **Self-Nanoemulsifying Drug Delivery System (SNEDDS)**. **Capryol 90** was used as the oil phase, **Tween 80** as the surfactant, and **Transcutol P** as the co-surfactant. These components were selected due to their high solubilizing capacity for ibuprofen and their ability to form stable nanoemulsions upon dilution with aqueous media.
SNEDDS formulations were prepared using the **simple isotropic mixture method**, which is widely employed for the development of lipid-based drug delivery systems [21]. Initially, the required quantity of **Capryol 90 (oil phase)** was accurately weighed and transferred into a clean glass vial. The selected **surfactant (Tween 80)** and **co-surfactant (Transcutol P)** were then added in predetermined ratios to obtain the required **Smix composition**. The mixture was gently stirred using a **magnetic stirrer at 40°C** to ensure complete mixing of the excipients and to obtain a homogeneous isotropic mixture. Subsequently, **100 mg of ibuprofen** was accurately weighed and added gradually to the oil–surfactant mixture. The formulation was continuously stirred until the drug completely dissolved in the mixture, resulting in a clear and transparent system. Mild heating was applied when necessary to facilitate drug dissolution.
The prepared formulations were further subjected to **vortex mixing for approximately 5 minutes** to ensure uniform distribution of the drug within the formulation. The resulting isotropic mixtures were stored at **room temperature (25 ± 2°C)** for **24 hours** to observe any signs of phase separation or drug precipitation. Only stable formulations showing no evidence of instability were selected for further evaluation studies [22].
Different SNEDDS formulations were prepared by varying the proportions of oil, surfactant, and co-surfactant while maintaining the drug concentration constant. Variation in the concentration of formulation components is necessary to identify the optimum composition capable of producing **rapid self-emulsification, small droplet size, and high thermodynamic stability**.
The composition of the prepared SNEDDS formulations is presented in **Table 2**.

Table 2: Composition of SNEDDS Formulations

Formulation	Oil (%)	Surfactant (%)	Co-surfactant (%)
F1	25	50	25
F2	20	55	25
F3	15	60	25
F4	10	65	25
F5	20	60	20

The variation in oil and surfactant concentrations was designed to investigate their effect on **self-emulsification efficiency, droplet size distribution, and stability of the nanoemulsion system**. Generally, increasing surfactant concentration enhances the reduction of interfacial tension between oil and aqueous phases, thereby facilitating the formation of smaller nanoemulsion droplets. However, excessively high surfactant concentrations may lead to irritation or toxicity issues in oral formulations; therefore, optimization of the formulation composition is essential [23].
The prepared SNEDDS formulations were further subjected to various **evaluation studies**, including **self-emulsification time, droplet size analysis, polydispersity index, zeta potential measurement, drug content determination, thermodynamic stability testing, and in vitro dissolution studies**, in order to identify the optimized formulation with improved drug solubility and dissolution characteristics.

2.5 Evaluation of SNEDDS
The prepared SNEDDS formulations were subjected to a series of evaluation studies in order to assess their **self-emulsification efficiency, droplet size distribution, stability, and drug content**. These parameters are critical in determining the performance of lipid-based drug delivery systems, particularly their ability to form stable

nanoemulsions upon dilution with gastrointestinal fluids. The evaluation studies included **self-emulsification time, droplet size analysis, polydispersity index (PDI), zeta potential measurement, drug content determination, and thermodynamic stability tests** [24].

The prepared formulations were evaluated for:

- Self-emulsification time
- Droplet size
- Polydispersity index
- Zeta potential
- Drug content
- Thermodynamic stability

2.5.1 Self-Emulsification Time

The self-emulsification efficiency of SNEDDS formulations was evaluated using a **USP Type II dissolution apparatus (paddle method)**. Approximately **1 mL of the SNEDDS formulation** was added dropwise into **500 mL of distilled water maintained at 37 ± 0.5°C** with gentle agitation at **50 rpm**. The time required for the formulation to form a clear or slightly bluish nanoemulsion was recorded as the **self-emulsification time**.

The resulting emulsion was visually assessed for **clarity, transparency, and presence of any oil droplets or phase separation**. Formulations that produced clear or slightly bluish emulsions within a short time were considered efficient self-emulsifying systems [25].

2.5.2 Droplet Size Analysis

The **mean droplet size** of the nanoemulsion formed after dilution of SNEDDS was measured using **dynamic light scattering (DLS)** technique with a **particle size analyzer (Malvern Zetasizer)**. For this purpose, **0.1 mL of SNEDDS formulation** was diluted with **100 mL of distilled water** under gentle stirring to simulate gastrointestinal dilution conditions.

The diluted sample was placed in a **disposable cuvette**, and the average droplet size was measured at **25°C**. Smaller droplet sizes are desirable in SNEDDS formulations because they provide a larger surface area for drug release and enhance dissolution and absorption of the drug [26].

2.5.3 Polydispersity Index (PDI)

The **polydispersity index (PDI)** was determined simultaneously during droplet size measurement using the particle size analyzer. PDI represents the **uniformity of droplet size distribution** within the nanoemulsion system.

A **PDI value below 0.3** generally indicates a narrow droplet size distribution and good formulation homogeneity, whereas higher values indicate broader size distribution and possible instability of the nanoemulsion system [27].

2.5.4 Zeta Potential

The **zeta potential** of the nanoemulsion droplets was measured using a **zeta potential analyzer (Malvern Zetasizer)**. Prior to analysis, the SNEDDS formulation was diluted with distilled water in a ratio of **1:100** to obtain a suitable sample for measurement.

Zeta potential is an important parameter that indicates the **surface charge of nanoemulsion droplets** and provides information regarding the stability of colloidal systems. Higher absolute values of zeta potential generally indicate improved electrostatic repulsion between droplets, which helps prevent aggregation and coalescence [28].

2.5.5 Drug Content Determination

The **drug content** of SNEDDS formulations was determined to ensure uniform distribution of ibuprofen within the formulation. An accurately measured quantity of SNEDDS equivalent to **100 mg of ibuprofen** was diluted with **methanol** and sonicated for **10 minutes** to ensure complete dissolution of the drug.

The resulting solution was filtered through a **0.45 µm membrane filter**, and the drug concentration was analyzed using a **UV–Visible spectrophotometer at 221 nm**. The drug content was calculated using the calibration curve of ibuprofen and expressed as a percentage of the labeled amount [29].

2.5.6 Thermodynamic Stability Studies

Thermodynamic stability studies were conducted to evaluate the **physical stability of the SNEDDS formulations** and to ensure that the formulations remain stable under different stress conditions. The formulations were subjected to the following tests:

Heating–Cooling Cycle

Formulations were exposed to **six heating–cooling cycles** between **4°C and 45°C**, with each temperature maintained for **48 hours**. Formulations showing **no phase separation or precipitation** were considered stable.

Centrifugation Test

Stable formulations from the heating–cooling cycle were subjected to **centrifugation at 3500 rpm for 30 minutes**. Formulations that showed **no signs of phase separation or creaming** were considered physically stable.

Freeze–Thaw Cycle

Formulations that passed the centrifugation test were further subjected to **three freeze–thaw cycles** between **−20°C and +25°C**, each cycle lasting **48 hours**. Only formulations that remained clear and stable were selected for further evaluation [30].

Thermodynamic stability testing ensures that the developed SNEDDS formulations possess adequate stability and will not undergo phase separation during storage or upon dilution in gastrointestinal fluids.

III. Results and Discussion

3.1 Self-Emulsification Time

The self-emulsification efficiency of SNEDDS formulations was evaluated by measuring the time required for the formulation to form a homogeneous nanoemulsion upon dilution in aqueous medium under gentle agitation. Self-emulsification time is a critical parameter because it reflects the ability of the formulation to rapidly disperse in gastrointestinal fluids following oral administration.

The results of the self-emulsification study are presented in **Table 3**.

Table 3: Self-Emulsification Performance

Formulation	Emulsification Time (sec)	Appearance
F1	52 ± 3	Slightly turbid
F2	39 ± 2	Clear
F3	31 ± 2	Transparent
F4	28 ± 1	Transparent
F5	34 ± 2	Slightly bluish

The results indicated that all formulations were capable of forming nanoemulsions within a short period upon dilution. However, the emulsification time varied depending on the proportion of oil, surfactant, and co-surfactant present in the formulation.

Among the tested formulations, **F4 exhibited the fastest emulsification time (28 ± 1 seconds)** and produced a **transparent nanoemulsion**, indicating efficient self-emulsification. The rapid emulsification observed in formulation F4 may be attributed to the **higher concentration of surfactant (Tween 80)**, which effectively reduces the interfacial tension between oil and aqueous phases and promotes spontaneous formation of fine droplets.

Formulation **F1 showed the longest emulsification time (52 ± 3 seconds)** and produced a slightly turbid emulsion, which may be due to the **higher oil concentration and relatively lower surfactant content**, resulting in slower dispersion of the formulation in aqueous media.

Overall, the results suggest that increasing the concentration of surfactant improves the **self-emulsification efficiency and clarity of the resulting nanoemulsion**, which is consistent with the fundamental mechanism of nanoemulsion formation in SNEDDS systems.

Based on the self-emulsification performance and visual appearance of the emulsions, **formulation F4 was considered the most promising formulation for further evaluation studies.**

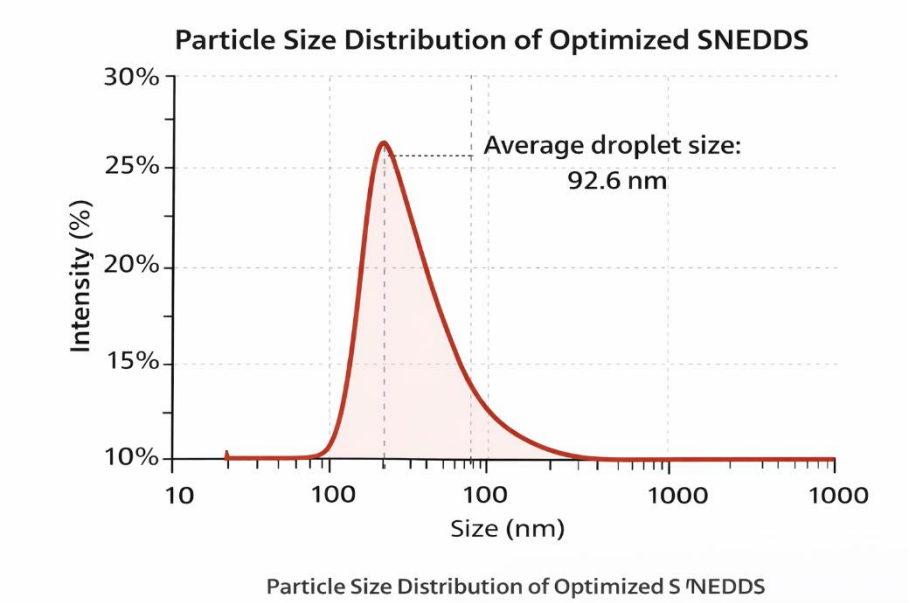
3.2 Droplet Size Analysis

Droplet size is a critical parameter in the evaluation of **Self-Nanoemulsifying Drug Delivery Systems (SNEDDS)** because it directly influences the surface area available for drug release and consequently affects the dissolution and absorption of poorly water-soluble drugs. Smaller droplet sizes provide a larger interfacial surface area between the oil phase and the aqueous medium, which facilitates faster drug diffusion and improved bioavailability.

The **mean droplet size and polydispersity index (PDI)** of the nanoemulsions formed after dilution of SNEDDS formulations were measured using dynamic light scattering. The results are summarized in **Table 4**.

Table 4: Particle Size and PDI

Formulation	Droplet Size (nm)	PDI
F1	168.3 ± 5.2	0.342
F2	132.7 ± 4.6	0.298
F3	108.9 ± 3.8	0.243
F4	92.6 ± 3.4	0.214
F5	121.4 ± 4.1	0.267



Particle Size Distribution of Optimized S NEDDS

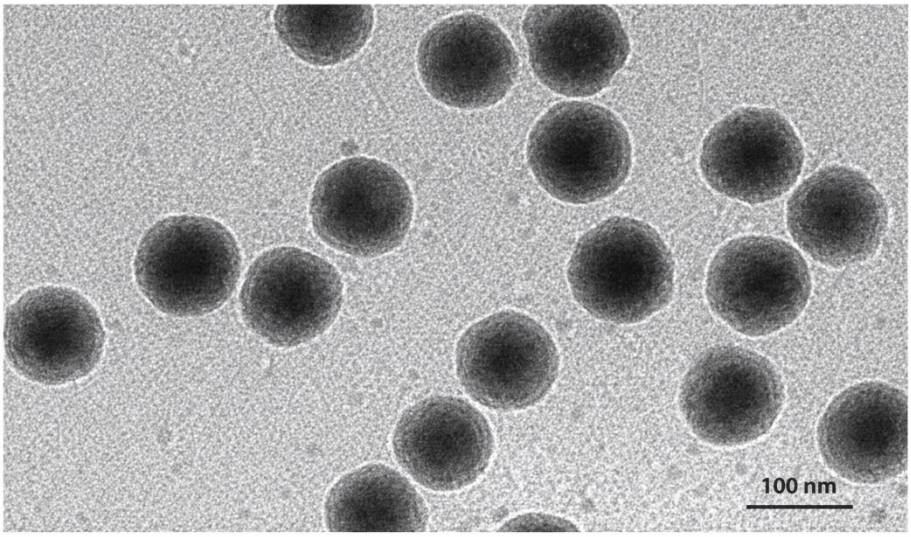
Figure 2. Particle size distribution graph of the optimized SNEDDS formulation (F4) showing an average droplet size of approximately 92.6 nm as determined by dynamic light scattering (DLS).

The droplet size of the prepared SNEDDS formulations ranged from **92.6 nm to 168.3 nm**, indicating that all formulations successfully formed **nano-sized emulsions** upon dilution. Among the formulations tested, **F4 exhibited the smallest droplet size (92.6 ± 3.4 nm)** along with a relatively low **polydispersity index (0.214)**, indicating a uniform droplet size distribution.

The reduction in droplet size observed in formulation F4 may be attributed to the **higher concentration of surfactant (Tween 80)** present in the formulation. Surfactants play a key role in reducing interfacial tension between oil and aqueous phases, thereby facilitating the formation of smaller droplets during emulsification.

In contrast, formulation **F1 showed the largest droplet size (168.3 ± 5.2 nm)** and the highest PDI value (0.342), which may be due to the **higher oil content and comparatively lower surfactant concentration**. Higher oil content can lead to larger droplets because more energy is required to disperse the oil phase into fine particles.

The **polydispersity index values obtained for the formulations ranged between 0.214 and 0.342**, indicating relatively narrow droplet size distributions for most formulations. Generally, **PDI values below 0.3 indicate a homogeneous nanoemulsion system**, suggesting good formulation stability and uniform droplet distribution.



TEM Image of Nanoemulsion Droplets (~90 nm)

Figure 3. Transmission electron microscopy (TEM) image of nanoemulsion droplets formed from the optimized SNEDDS formulation (F4), showing spherical droplets with an average size of approximately **90 nm**, confirming the nanoscale particle size obtained from dynamic light scattering analysis.

The morphology of the nanoemulsion droplets was further confirmed using transmission electron microscopy (TEM). The TEM image (**Figure 3**) revealed spherical and uniformly distributed droplets with sizes around **90 nm**, which is consistent with the droplet size obtained from particle size analysis.
Overall, the results demonstrate that **increasing surfactant concentration contributes to the formation of smaller droplet sizes and more uniform nanoemulsions**, which is desirable for improving drug dissolution and absorption. Based on the droplet size and PDI results, **formulation F4 was identified as the optimized formulation** for further evaluation studies.

3.3 Zeta Potential

Zeta potential is an important parameter used to evaluate the **surface charge and stability of nanoemulsion systems**. It provides information about the electrostatic repulsion between droplets, which plays a significant role in preventing aggregation or coalescence of dispersed particles. Generally, higher absolute values of zeta potential indicate greater repulsive forces between droplets and therefore improved physical stability of the nanoemulsion. The zeta potential values of the diluted SNEDDS formulations are presented in **Table 5**.

Table 5: Zeta Potential of SNEDDS Formulations

Formulation	Zeta Potential (mV)
F1	−15.2
F2	−17.6
F3	−19.8
F4	−21.3
F5	−18.4

The measured zeta potential values ranged from **−15.2 mV to −21.3 mV**, indicating that all formulations possessed a **moderately negative surface charge**. The negative charge on the nanoemulsion droplets may be attributed to the ionization of fatty acid groups present in the oil phase and the orientation of surfactant molecules at the oil–water interface.
Among the prepared formulations, **F4 exhibited the highest negative zeta potential value (−21.3 mV)**, suggesting improved stability compared with other formulations. The higher magnitude of zeta potential may result in stronger electrostatic repulsion between droplets, which reduces the likelihood of droplet aggregation and enhances the stability of the nanoemulsion system.
In contrast, formulation **F1 showed the lowest zeta potential value (−15.2 mV)**, which may indicate comparatively lower electrostatic stabilization of the droplets.
Overall, the results indicate that all SNEDDS formulations exhibited **adequate electrostatic stability**, while **formulation F4 demonstrated the most favorable zeta potential value**, supporting its selection as the optimized formulation for further evaluation.

IV. In Vitro Dissolution Study

The **in vitro dissolution study** was performed to evaluate the ability of the developed SNEDDS formulation to enhance the dissolution rate of ibuprofen compared with the pure drug and a marketed tablet formulation. Dissolution studies were carried out using a **USP Type II dissolution apparatus (paddle method)**.
The dissolution conditions were as follows:
• **Dissolution medium:** 900 mL phosphate buffer (pH 6.8)
• **Temperature:** 37 ± 0.5°C
• **Paddle speed:** 50 rpm
An amount of formulation equivalent to **100 mg of ibuprofen** was introduced into the dissolution medium. At predetermined time intervals, **5 mL samples** were withdrawn and replaced with fresh dissolution medium to maintain constant volume. The samples were filtered and analyzed using a **UV–Visible spectrophotometer at 221 nm** to determine the percentage of drug released.
The dissolution profiles of **pure ibuprofen, marketed tablet formulation, and optimized SNEDDS formulation (F4)** are presented in **Table 6**.

Table 6: Dissolution Profile

Time (min)	Pure Drug (%)	Marketed Tablet (%)	Optimized SNEDDS (%)
5	8.2	18.6	41.3
10	15.4	34.2	62.7
15	23.8	51.6	79.5
20	31.6	63.2	88.4
30	42.5	75.8	96.8

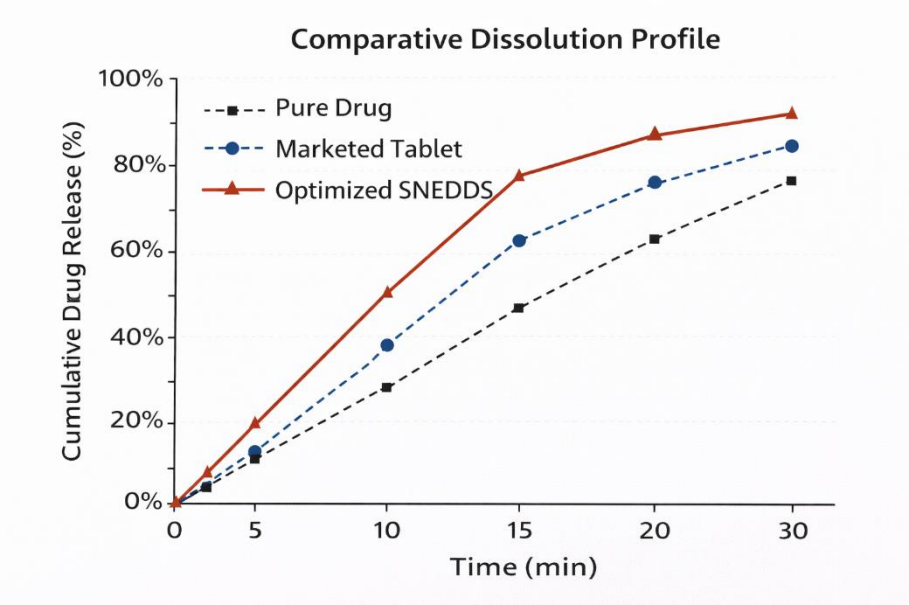


Figure 4. Comparative dissolution profile of pure ibuprofen, marketed tablet, and optimized SNEDDS formulation (F4) in phosphate buffer (pH 6.8) using USP Type II dissolution apparatus.

The dissolution results clearly demonstrate that the **optimized SNEDDS formulation significantly improved the dissolution rate of ibuprofen** compared with the pure drug and marketed tablet formulation.

The pure drug exhibited relatively slow dissolution, releasing only **42.5% of the drug within 30 minutes**, which can be attributed to the **poor aqueous solubility of ibuprofen**. In contrast, the marketed tablet formulation showed improved dissolution, releasing **75.8% of the drug within 30 minutes**.

The **optimized SNEDDS formulation (F4)** demonstrated a markedly enhanced dissolution profile, releasing **96.8% of the drug within 30 minutes**. A rapid drug release was also observed during the initial stage of dissolution, with **41.3% drug release within the first 5 minutes**, indicating efficient dispersion and nanoemulsion formation upon dilution.

The improved dissolution performance of the SNEDDS formulation can be attributed to several factors:

- Formation of **nano-sized droplets**, which provide a large surface area for drug release
- **Improved drug solubilization** in the lipid-based formulation
- **Rapid dispersion of the formulation** in aqueous media
- Maintenance of the drug in a **solubilized state**, preventing precipitation during dissolution

Overall, the SNEDDS formulation demonstrated **more than a two-fold improvement in dissolution rate compared with the pure drug**, indicating the effectiveness of the lipid-based nanoemulsion system in enhancing the dissolution behavior of poorly water-soluble drugs.

These findings confirm that the developed SNEDDS formulation has the potential to **significantly improve the oral bioavailability of ibuprofen** by enhancing its dissolution characteristics.

V. Conclusion

The present study successfully developed and evaluated a **Self-Nanoemulsifying Drug Delivery System (SNEDDS)** for **ibuprofen**, a poorly water-soluble BCS Class II drug, with the objective of enhancing its solubility and dissolution characteristics. Solubility screening enabled the selection of **Capryol 90 as the oil phase, Tween 80 as the surfactant, and Transcutol P as the co-surfactant**, which demonstrated high solubilizing capacity for ibuprofen and favorable emulsification properties. Pseudo-ternary phase diagram analysis facilitated the identification of the nanoemulsion region and guided the preparation of stable SNEDDS formulations.

Among the prepared formulations, **formulation F4 exhibited the most desirable characteristics**, including rapid self-emulsification, the smallest droplet size (**~92.6 nm**), a low polydispersity index, and a relatively higher negative zeta potential, indicating good nanoemulsion stability. The **in vitro dissolution study demonstrated a significant enhancement in drug release**, with the optimized SNEDDS formulation achieving **96.8% drug release within 30 minutes**, compared with only **42.5% release from the pure drug**.

The improved dissolution performance can be attributed to the formation of **nano-sized droplets that provide a large interfacial surface area and maintain the drug in a solubilized state**, thereby facilitating faster drug release. Overall, the results of this study suggest that **SNEDDS is an effective formulation strategy for enhancing the dissolution and potential oral bioavailability of poorly water-soluble drugs such as ibuprofen**.

Further studies involving **in vivo bioavailability evaluation and long-term stability testing** may be conducted to confirm the therapeutic potential of the developed SNEDDS formulation.

References

[1]. Lipinski, C. A. Drug-like properties and the causes of poor solubility and poor permeability. *J. Pharmacol. Toxicol. Methods* **2000**, *44*, 235–249.

[2]. Amidon, G. L.; Lennernäs, H.; Shah, V. P.; Crison, J. R. A theoretical basis for a biopharmaceutic drug classification: The correlation of in vitro drug product dissolution and in vivo bioavailability. *Pharm. Res.* **1995**, *12*, 413–420.

[3]. Rainsford, K. D. *Ibuprofen: Pharmacology, Therapeutics and Side Effects*; Springer: Berlin, Germany, 2015.

[4]. Savjani, K. T.; Gajjar, A. K.; Savjani, J. K. Drug solubility: Importance and enhancement techniques. *ISRN Pharmaceutics* **2012**, 1–10.

[5]. Pouton, C. W. Formulation of poorly water-soluble drugs for oral administration: Physicochemical and physiological issues and the lipid formulation classification system. *Eur. J. Pharm. Sci.* **2006**, *29*, 278–287.

[6]. Porter, C. J. H.; Trevaskis, N. L.; Charman, W. N. Lipids and lipid-based formulations: Optimizing the oral delivery of lipophilic drugs. *Nat. Rev. Drug Discov.* **2007**, *6*, 231–248.

[7]. Gursoy, R. N.; Benita, S. Self-emulsifying drug delivery systems (SEDDS) for improved oral delivery of lipophilic drugs. *Biomed. Pharmacother.* **2004**, *58*, 173–182.

[8]. Tang, B.; Cheng, G.; Gu, J. C.; Xu, C. H. Development of solid self-emulsifying drug delivery systems: Preparation techniques and dosage forms. *Drug Discov. Today* **2008**, *13*, 606–612.

[9]. Rainsford, K. D. *Ibuprofen: Pharmacology, Therapeutics and Side Effects*; Springer: Berlin, Germany, 2015.

[10]. Porter, C. J. H.; Trevaskis, N. L.; Charman, W. N. Lipids and lipid-based formulations: Optimizing the oral delivery of lipophilic drugs. *Nat. Rev. Drug Discov.* **2007**, *6*, 231–248.

[11]. Gursoy, R. N.; Benita, S. Self-emulsifying drug delivery systems (SEDDS) for improved oral delivery of lipophilic drugs. *Biomed. Pharmacother.* **2004**, *58*, 173–182.

[12]. Constantinides, P. P.; Wasan, K. M. Lipid formulation strategies for enhancing intestinal transport and absorption of poorly soluble drugs. *Adv. Drug Deliv. Rev.* **2007**, *59*, 631–644.

[13]. Pouton, C. W. Lipid formulations for oral administration of drugs: Non-emulsifying, self-emulsifying and self-microemulsifying drug delivery systems. *Eur. J. Pharm. Sci.* **2000**, *11*, S93–S98.

[14]. Pouton, C. W. Lipid formulation classification system (LFCS) and the development of lipid-based formulations for oral drug delivery. *Eur. J. Pharm. Sci.* **2006**, *29*, 278–287.

[15]. Date, A. A.; Nagarsenker, M. S. Design and evaluation of self-nanoemulsifying drug delivery systems (SNEDDS) for poorly water-soluble drugs. *J. Pharm. Sci.* **2007**, *96*, 202–214.

[16]. Indian Pharmacopoeia Commission. *Indian Pharmacopoeia*; Government of India: Ghaziabad, 2022.

[17]. Porter, C. J. H.; Charman, W. N. In vitro assessment of oral lipid based formulations. *Adv. Drug Deliv. Rev.* **2001**, *50*, S127–S147.

[18]. Lawrence, M. J.; Rees, G. D. Microemulsion-based media as novel drug delivery systems. *Adv. Drug Deliv. Rev.* **2000**, *45*, 89–121.

[19]. Date, A. A.; Nagarsenker, M. S. Parenteral microemulsion: An overview. *Int. J. Pharm.* **2008**, *355*, 19–30.

[20]. Shafiq, S.; Shakeel, F.; Talegaonkar, S.; Ahmad, F. J.; Khar, R. K.; Ali, M. Development and bioavailability assessment of ramipril nanoemulsion formulation. *Eur. J. Pharm. Biopharm.* **2007**, *66*, 227–243.

[21]. Pouton, C. W. Self-emulsifying drug delivery systems: Assessment of the efficiency of emulsification. *Int. J. Pharm.* **1985**, *27*, 335–348.

[22]. Date, A. A.; Nagarsenker, M. S. Design and evaluation of self-nanoemulsifying drug delivery systems for poorly soluble drugs. *J. Pharm. Sci.* **2007**, *96*, 202–214.

[23]. Gursoy, R. N.; Benita, S. Self-emulsifying drug delivery systems for improved oral delivery of lipophilic drugs. *Biomed. Pharmacother.* **2004**, *58*, 173–182.

[24]. Pouton, C. W.; Porter, C. J. H. Formulation of lipid-based delivery systems for oral administration. *Adv. Drug Deliv. Rev.* **2008**, *60*, 625–637.

[25]. Kommuru, T. R.; Gurley, B.; Khan, M. A.; Reddy, I. K. Self-emulsifying drug delivery systems (SEDDS) of coenzyme Q10: Formulation development and bioavailability assessment. *Int. J. Pharm.* **2001**, *212*, 233–246.

[26]. Shakeel, F.; Ramadan, W.; Alsarra, I. A. Development of self-nanoemulsifying drug delivery system of anticancer drug. *Int. J. Nanomedicine* **2010**, *5*, 849–857.

[27]. Date, A. A.; Desai, N.; Dixit, R.; Nagarsenker, M. Self-nanoemulsifying drug delivery systems: Formulation insights. *Pharm. Dev. Technol.* **2010**, *15*, 275–288.

[28]. Honary, S.; Zahir, F. Effect of zeta potential on the properties of nano-drug delivery systems. *Trop. J. Pharm. Res.* **2013**, *12*, 255–264.

[29]. Indian Pharmacopoeia Commission. *Indian Pharmacopoeia*; Government of India: Ghaziabad, 2022.

[30]. Shafiq, S.; Shakeel, F.; Talegaonkar, S.; Ahmad, F. J.; Khar, R. K.; Ali, M. Development and bioavailability assessment of nanoemulsion formulation. *Eur. J. Pharm. Biopharm.* **2007**, *66*, 227–243.