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# "ENHANCED ORAL BIOAVAILABILITY OF IBUPROFEN BY A NOVEL SOLID SELF EMULSIFYING DRUG DELIVERY SYSTEM"

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## ABSTRACT

Nonsteroidal anti-inflammatory drugs, or NSAIDs, like ibuprofen, are commonly used because of their analgesic and anti-inflammatory qualities. Unfortunately, its therapeutic efficacy and bioavailability are restricted by its poor aqueous solubility. In this work, we developed a solid self-emulsifying drug delivery system (S-SEDDS) to improve ibuprofen's oral bioavailability. Ibuprofen, lipid excipients, surfactants, and co-surfactants were used to prepare the S-SEDDS formulation. Particle size, zeta potential, and morphology were some of the physicochemical characteristics that were assessed for the optimised formulation. To assess the ibuprofen dissolution profile of the S-SEDDS formulation in comparison to a commercial ibuprofen formulation, in vitro dissolution studies were carried out. Moreover, oral bioavailability of ibuprofen from the S-SEDDS formulation in comparison to the commercial formulation was evaluated through in vivo pharmacokinetic studies conducted in rats. In comparison to the commercial formulation, the S-SEDDS formulation considerably increased the oral bioavailability and dissolving rate of ibuprofen, according to the studies. All things considered, our research indicates that solid self-emulsifying drug delivery systems are a viable means of increasing the oral bioavailability of poorly soluble medications, such as ibuprofen, which will increase their therapeutic efficacy and patient compliance.

**KEYWORDS:** Self Emulsifying Drug Delivery System, Ibuprofen, Bioavailability, Solubility.

## INTRODUCTION

Oral drug delivery has been suggested as one of the approaches for long-term medication administration. Nearly 40% of novel therapeutic candidates have poor water solubility. It is

oral administration of such lipophillic drugs. Significant inter- and intraindividual variability, insufficient dose proportionality, and inadequate oral bioavailability are frequently associated with it. This oral bioavailability improvement is being pursued to increase the clinical effectiveness of lipophilic medications. excessive subject variation both within and between subjects as well as an insufficient dosage.[1]

A number of medications, such as ibuprofen, have low water solubility, which reduces their oral bioavailability and thus clinical efficacy. Researchers have looked into novel formulations to improve drug solubility and absorption in response to this challenge, such as solid self-emulsifying drug delivery systems (S-SEDDS).

An effective method for increasing the oral bioavailability of poorly water-soluble medications like ibuprofen is called S-SEDDS. They are made up of oil phases, co-solvents, surfactants, and solid dosage forms containing lipophilic drugs. When S-SEDDS come into contact with gastrointestinal fluids, they quickly create microemulsions or fine oil-in-water emulsions that improve drug solubilization and dispersion.[2]

Ibuprofen is an anti-inflammatory, analgesic, and antipyretic nonsteroidal anti-inflammatory lipophilic drug (NSAID). We use ibuprofen to treat rheumatoid arthritis. mild discomfort, osteoarthritis, anddysmenorrhea. This stops the drug's first pass metabolism. supplies and workshops. Only a small amount of the medication is systemically available, and it has a first pass effect. Ibuprofen's hepato gastrointestinal first pass metabolism may be passed through via the Sedds, which could be advantageous.[3]

To sum up, the creation of solid self-emulsifying drug delivery systems is a viable approach to resolving issues related to the low oral bioavailability of medications such as ibuprofen. Through enhanced solubility, improved absorption, and better patient compliance, S-SEDDS hold significant potential for optimizing drug delivery and enhancing therapeutic efficacy.[4] A major development in pharmaceutical formulations targeted at enhancing the therapeutic efficacy of poorly water-soluble drugs is the enhanced oral bioavailability of ibuprofen made possible by the solid self-emulsifying drug delivery system (S-SEDDS). Due to its poor solubility in the gastrointestinal tract, ibuprofen, a common nonsteroidal anti-inflammatory drug (NSAID), frequently has limited bioavailability when taken orally. This limitation can lead to suboptimal therapeutic outcomes and the need for higher dosages, which in turn increases the risk of adverse effects.

The goal of solid self-emulsifying drug delivery systems is to improve the solubility and, in turn, the bioavailability of lipophilic drugs such as ibuprofen through novel formulations. When gastrointestinal fluids come into contact with S-SEDDS, a blend of oils, co-surfactants, and surfactants naturally creates fine oil-in-water emulsions. Through emulsification, the drug's surface area for dissolution is greatly increased, resulting in improved absorption through the intestinal mucosa.

Liquid SEDDS formulations have various practical issues, including stability, portability, and patient compliance, which are addressed by solidifying the liquid form. Combining the benefits of solid and self-emulsifying formulations, the liquid self-emulsifying system is transformed into a solid dosage form, usually by means of techniques like spray drying, freeze drying, or adsorbing the liquid onto solid carriers. This results in a stable, easy-to-handle, and effective delivery system that maximizes the bioavailability of ibuprofen.

In conclusion, a viable strategy for addressing the issues of poor solubility and restricted bioavailability for ibuprofen is the development of solid self-emulsifying drug delivery systems. This innovative formulation not only improves the therapeutic efficacy of ibuprofen but also enhances patient convenience and compliance, potentially leading to better clinical outcomes.

**OBJECTIVE**

1. To research and assess the efficacy and formulation of a new solid self-emulsifying drug delivery system (S-SEDDS) to increase ibuprofen's oral bioavailability.
2. The objectives of this work are to describe the S-SEDDS formulation, appraise its solubilization characteristics, analyse its in vitro performance with respect to emulsification effectiveness and dissolution rate, and explore its in vivo pharmacokinetic profile.
3. The aim of this study is to evaluate the potential of the S-SEDDS formulation to address the drawbacks of traditional ibuprofen formulations, including low solubility and bioavailability, and to offer insights into its viability as a promising drug delivery system for augmenting ibuprofen's therapeutic efficacy.

**Proposed Plan of Work**

1. **Literature Review**

   Review existing literature on S-SEDDS formulations, ibuprofen delivery systems, and bioavailability enhancement strategies.

2. **Selection of Excipients**

   Choose appropriate excipients, such as oils, surfactants, and co-solvents, by considering their solubility, stability, and safety characteristics**.**

3. **Formulation Optimization**

   Design and optimize the S-SEDDS formulation using techniques such as pseudoternary phase diagrams and response surface methodology to achieve desired properties.

4. **Physicochemical Characterization**

   Undertake characterization studies to comprehend the physical properties of the S-SEDDS formulation, such as particle size analysis, zeta potential measurement, morphology assessment, and thermal analysis (DSC, TGA).

5. **In vitro Assessment**

   Assess the S-SEDDS formulation's emulsification effectiveness and dissolution profile using accepted techniques.

6. **Stability Studies**

   Perform stability studies under various storage conditions (temperature, humidity) to assess the physical and chemical stability of the S-SEDDS formulation over time.

**Hypothesis**

1. **Improved Solubility**: Because the SEDDS formulation contains surfactants and co-solvents, it may make ibuprofen more soluble in gastrointestinal fluids, improving drug absorption and dissolution.

2. **Enhanced Stability**: The solid SEDDS formulation may protect ibuprofen from degradation in the gastrointestinal tract, thereby increasing its stability and preserving its therapeutic efficacy.

3. **Enhanced Absorption**: The formulation's ability to self-emulsify may help create microemulsions or fine emulsions when it comes into contact with gastrointestinal fluids, which would increase the surface area available for drug absorption and enhance its permeability through the intestinal epithelium.

4. **Lymphatic Uptake**: Because the SEDDS formulation's lipid-based ingredients avoid the liver's first-pass metabolism and increase systemic bioavailability, they may facilitate drug uptake into the lymphatic system.

5. **Prolonged Residence Time**: The solid SEDDS formulation may adhere to the gastrointestinal mucosa, prolonging the residence time of ibuprofen in the absorption site and enhancing its absorption kinetics.

6. **Reduced Variability**: The solid SEDDS formulation may exhibit reduced inter-individual variability in pharmacokinetics compared to conventional dosage forms, leading to more predictable and consistent drug absorption profiles.

7. **Improved Patient Compliance**: The solid SEDDS formulation may offer improved patient convenience and compliance due to its solid dosage form, which is easier to handle and administer compared to liquid formulations.

## METHODOLOGY

- **Materials**

Ibuprofen was provided by Dhamtec Pharma and Consultants (Taloja, Navi Mumbai), Oils like Coconut Oil, Soyabean Oil, Sunflower Oil, Castor Oil, Neem Oil were obtained by local market, surfactant like Tween 20, SLS were obtained by Balaji Chemicals. There was no need for additional purification because all other chemicals and solvents were r eagent grade.

- **Selection of oils and surfactants**

In this step we used to different types of oils then make screening of that oils it means take 1ml of oil then add drug 1mg and increase the drug until the drug is completely dissolve. Repeate the steps with different oils and check in which oil the drug is more soluble.

The same procedure repeated to screen the surfactant to choose the best surfactant. Take the surfactant and dissolve excess amount of drug and put the samples in orbital shaker for 3 days.

- **Building of the Ternary Phase**

The Building of the Ternary Phase by getting of oil, surfactant and water. The oil and surfactant take in different proportion for e.g take the oil 1ml and surfactant 9ml and water is drop wise until the turbidity occurs. similarly take 2,3,4,5 upto 9ml proportion and maintain the constant weight of oil and surfactant will be 1g.

1. Take a constant weight of 1gm.
2. Mix the proportion given in above information.
3. Add the water dropwise till the turbidity appears.
4. Combine the following three weights: oil (A), surfactant (B), water (C), and total weight (D).
5. Calculate the percentage of each component by following formulas

A/D×100.

B/D×100.

C/D×100.

- **Preparation Of Liquid SEDDS Formulation**

Liquid SEDDS formulation preparation Ibuprofen (20 percent w/v) in the formulation was dissolved at 250 degrees Celsius in a mixture of surfactant, oil, and cosurfactant to create the formulations. In order to obtain a clear solution, the final mixture was vortexed. 17.9% w/w ratio of drug was the final concentration in the liquid SEDDS. Earlier than self emulsification and particle size studies, the formulations were checked for indications of turbidity or phase separation.

- **Preparation of Solid SEDDS Formulation**

Magnetic stirring was used to suspend 500 mg of Aerosil 200 in 100 millilitres of ethanol. After that, 1 millilitre of liquid SEDDS was added while the mixture was continuously stirred at room temperature for 15 minutes in order to achieve a good suspension of Aerosil 200. A Buchi mini spray dryer B-190 apparatus (Buchi, Switzerland) was used to spray dry the suspension. The parameters were as follows: aspiration at 85%, inlet temperature of 60°C,

outlet temperature of 35°C, and feeding rate of 5 ml/min. 12.4% w/w ratio was the solid SEDDS's final drug content**.**

- **Characterization Of the Solid Self Emulsifying Drug Delivery System**

Solid SEDDS, or liquid solid self-emulsifying drug delivery system, was added in an amount of 150 mg to a volumetric flask containing 25 ml of distilled water. To make a fine emulsion, the flask was let to stand at room temperature for 12 hours while being gently shaken**.**

- **Total Drug Content**

Ensuring that every capsule in a batch contains the exact amount of medication and that there is little variation in the amount of drug substance contained in each capsule is the goal of the content uniformity test. In order to calculate the drug content percentage, A self-emulsifying capsule was placed inside a conical flask holding 100 millilitres of methanol, gently shaken with a mechanical shaking apparatus, and left overnight. A PC-based Double Beam UV Spectrophotometer was used to measure the absorbance of the resulting solution at 264 nm after it had been filtered through Whatmann filter paper and suitably diluted. Methanol was used as a blank.

**Disintegration Time**

Hard gelatin capsules containing a self-emulsifying, stable formulation containing 100 mg of ibuprofen were placed in a USP dissolution vessel with 900 ml of pH 6.8 phosphate buffer. The paddle of the device rotated at 100 revolutions per minute. It was noted how long it took for the capsule shell to break open and spill its contents into the dissolving media**.**

**In-Vitro dissolution test**

The dissolution profiles of the capsules containing the self-nanoemulsified formulations were determined by rotating 100 rpm in 900 ml of pH 6.8 phosphate buffer at 37±2°C using the USP Dissolution apparatus II. The investigation used five millilitre aliquots. 5 ml of fresh phosphate buffer was added in their place after the extracts were taken out of the dissolving medium at predetermined intervals. Studies on the dissolution of drugs in vitro.[5] The amount of ibuprofen released in the dissolution medium was measured with a UV Spectrophotometer that was calibrated to λmax 264 nm. The dissolution experiment was carried out three times in duplicate**.**

## RESULT AND DISCUSSION

### 1. Solubility Studies

When the oil, surfactants, cosurfactants, and medication were added to the aqueous phase of the self-emulsifying formulations, the result was a clear, monophasic liquid at room temperature, should have favourable solvent qualities to enable the drug to be presented in a solution.

Ibuprofen's solubility in phosphate buffer (pH 6.8), oil, methanol, and water was investigated. Oil, phosphate buffer pH 6.8, and organic solvents all showed that the medication was poorly soluble in water. fine. By examining the clarity of the oil/surfactant mixture, it was possible to determine whether the chosen oil was miscible in the surfactant and co-surfactant, or between 80 and 20 wt%, at a 2:1 volume ratio. An o/w emulsion can readily form in a system with a high HLB value, or more than 10, thanks to the combination of Tween 80 (HLB value of 15) and co-surfactant span 20 (HLB value of 8.6). The choice of castor oil as the solvent for dissolving the drug to create the oil phase was made due to its long chain fatty acid content, specifically oleic acid.

| **Vehicle** | **Solubility** |
|---|---|
| **Surfactant** | |
| Tween 20 | >1gm |
| Tween 60 | >1gm |
| **Oils** | |
| Castor oil | 15mg/ml |
| Coconut oil | 20mg/ml |
| Sunflower oil | 28mg/ml |
| Soyabean oil | 35mg/ml |
| **Co-Surfactant** | |
| Ethanol | 38mg/ml |
| Polyethylene glycol | 25mg/ml |

**Building of the Ternary Phase**

The Building of the Ternary Phase by getting of oil, surfactant and water. The oil and surfactant take in different proportion for e.g take the oil 1ml and surfactant 9ml and water is drop wise until the turbidity occurs. similarly take 2,3,4,5 upto 9ml proportion and maintain the constant weight of oil and surfactant will be 1g.

1. Take a constant weight of 1gm.
2. Mix the proportion given in above information.
3. Add the water dropwise till the turbidity appears.

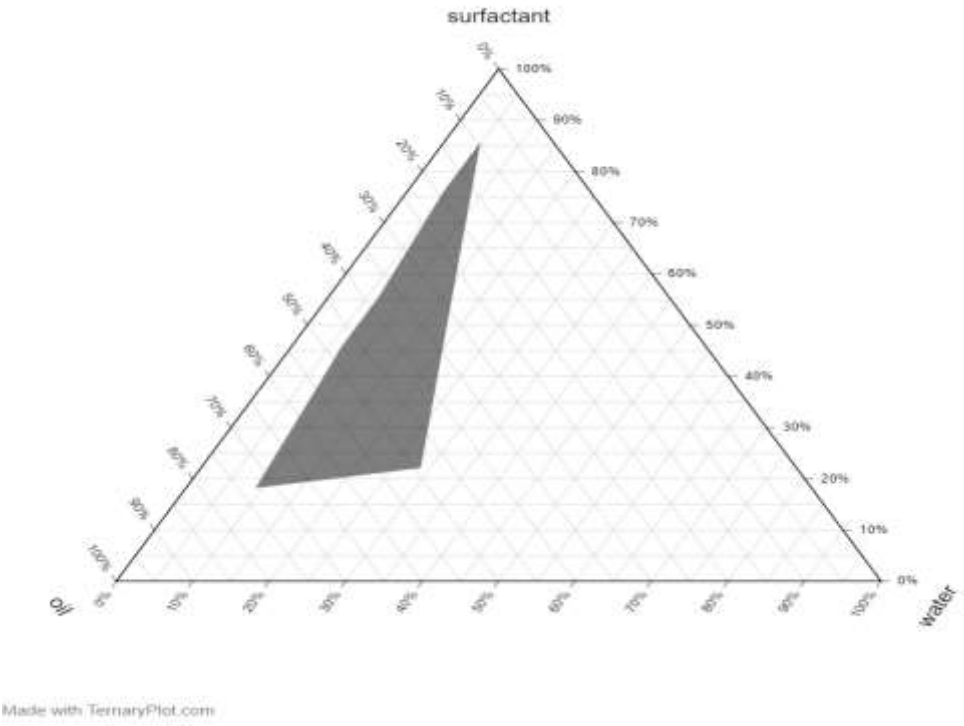
4. Combine the following three weights: oil (A), surfactant (B), water (C), and total weight (D).
5. Calculate the percentage of each component by following formulas.

A/D×100

B/D×100

C/D×100

| oil | Surfactant | water | oil % | surfactant% | water% |
|---|---|---|---|---|---|
| 1 | 9 | 0.5ml | 9.52% | 85.72% | 4.76% |
| 2 | 8 | 0.5ml | 19.04% | 76.20% | 4.76% |
| 3 | 7 | 0.6ml | 28.57% | 65.77% | 5.66% |
| 4 | 6 | 0.7ml | 38.09% | 55.37% | 6.54% |
| 5 | 5 | 0.7ml | 47.61% | 45.85% | 6.54% |
| 6 | 4 | 0.8ml | 55.55% | 37.05% | 7.40% |
| 7 | 3 | 0.9ml | 64.22% | 27.52% | 8.26% |
| 8 | 2 | 1.0ml | 72.72% | 18.19% | 9.09% |
| 9 | 1 | 1.3ml | 79.65% | 8.85% | 11.50% |




## Characterization and Evaluation

### Diluation Test

The basis for this test is the emulsion's external phase's solubility. Turbidity is created by mixing emulsion and water to create a W/O emulsion. Clear solution is produced when O/W emulsion is added to oil.

1. Water can be used to dilute W/O emulsion
2. It is possible to dilute O/W emulsion with oil.

- **Globule Size Detection**

1. Ensure the microscope is properly set up and calibrated.
2. Clean the microscope lenses, eyepiece, and objective lenses to ensure clear observation.
3. Place a calibrated eyepiece micrometer in the eyepiece of the microscope.
4. Shake the emulsion sample well to ensure uniform distribution of globules.
5. Using a dropper or pipette, place a small drop of the emulsion onto a clean glass slide.
6. If the emulsion is too concentrated, dilute it with distilled water to obtain a clear view of individual globules.
7. To prevent air bubbles, gently cover the drop with a cover slip.
8. On the cover slip, put a drop of immersion oil if you're using an oil immersion objective. A cover slip should be placed over the drop carefully to prevent air bubbles.
9. A drop of immersion oil should be placed on the cover slip if you are using an oil immersion objective.
10. Make sure the eyepiece micrometre is used to calibrate the microscope. This involves comparing the divisions on the eyepiece micrometer with a stage micrometer to establish the actual distance each division represents at a specific magnification.
11. Focus on a single field of view where the emulsion globules are visible.
12. Using the calibrated eyepiece micrometer, measure the diameter of several globules in the field of view.
13. Record the measurements for a statistically significant number of globules (e.g., 50-100 globules) to ensure accuracy.
14. Convert the micrometer readings to actual size using the calibration factor determined earlier.
15. For example, if one division on the eyepiece micrometer corresponds to 1 µm at the selected magnification, then a globule that spans 5 divisions is 5 µm in diameter.
16. Calculate the average globule size by summing the diameters of all measured globules and dividing by the number of globules measured.
17. Determine the size distribution by categorizing the globules into size ranges (e.g., 0-1 µm, 1-2 µm, etc.) and calculating the percentage of globules in each range.
18. Compute standard deviation and other statistical parameters to assess the uniformity of the globule sizes.

**Absolute drug Content**

The purpose of the content uniformity test is to guarantee that each capsule in a batch contains the precise amount of medication and that there is minimal variation in the amount of drug substance contained in each capsule. To determine the percentage of drug content, A conical flask containing 100 ml of methanol was filled with a self-emulsifying capsule, shaken gently with a mechanical shaking device, and left overnight. The resultant solution was filtered through Whatmann filter paper, appropriately diluted, and its absorbance was measured at 264 nm using a PC-based Double Beam UV Spectrophotometer with methanol serving as a blank.

| **Sr. No.** | **Batch** | **Weight Uniformity** (mg and SD) | **Content Uniformity** (mg and SD) |
|---|---|---|---|
| 1 | C1 | 660mg | 99.69mg |
| 2 | C2 | 662mg | 98.70mg |
| 3 | C3 | 664mg | 97.50mg |
| 4 | C4 | 665mg | 97.60mg |
| 5 | C5 | 670mg | 96.70mg |
| 6 | C6 | 675mg | 95.80mg |
| 7 | C7 | 673mg | 95.30mg |
| 8 | C8 | 677mg | 94.45mg |
| 9 | C9 | 678mg | 93.30mg |
| 10 | C10 | 676mg | 93.22mg |

**Disintegration Time**

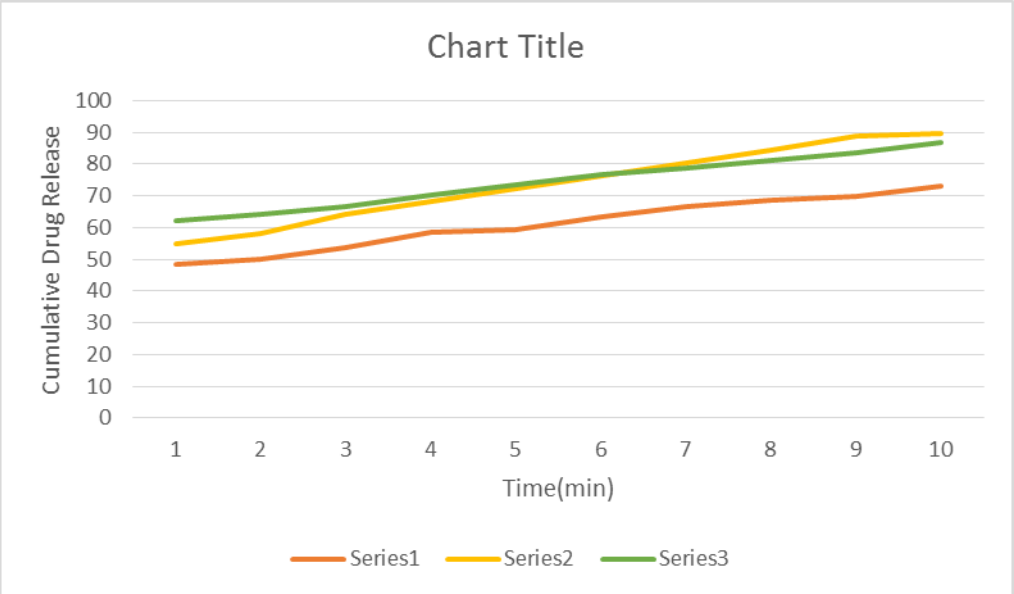
A stable, self-emulsifying formulation containing 100 mg of ibuprofen was placed into hard gelatin capsules and placed in a USP dissolution vessel with 900 ml of pH 6.8 phosphat buffer Rotation speed of the apparatus's paddle was 100 rpm. The amount of time that the capsule shell disintegrated, releasing its contents into the dissolving media, was recorded.

| **Batch** | **Time for Disintegrate** |
|---|---|
| T1 | 4.1 |
| T2 | 4.2 |
| T3 | 4.0 |
| T4 | 3.9 |
| T5 | 3.78 |
| T6 | 3.1 |
| T7 | 3.65 |
| T8 | 3.4 |
| T9 | 2.8 |
| T10 | 2.5 |

**In-Vitro dissolution test**

Utilising the USP Dissolution apparatus II at 37±2°C and 100 rpm of rotation in 900 ml of pH 6.8 phosphate buffer, the dissolution profiles of the capsules containing the self-nanoemulsified formulations were ascertained. Five millilitre aliquots were used in the investigation. extracted from the dissolving medium at predetermined intervals, and 5 ml of brand-new phosphate buffer was added in their place. Drug dissolution experiments conducted in vitro.[5] Using a UV Spectrophotometer set to λ max 264 nm, the amount of ibuprofen released in the dissolution medium was calculated. Three duplicates of the dissolution experiment were conducted.

| Sr. No | Time | Cumulative Drug Release% | | |
|---|---|---|---|---|
| | | C2 | C4 | C8 |
| 1 | 5 | 48.5 | 54.80 | 62.15 |
| 2 | 10 | 50.20 | 58.20 | 64.30 |
| 3 | 15 | 53.48 | 64.33 | 66.50 |
| 4 | 20 | 58.48 | 68.22 | 70.30 |
| 5 | 25 | 59.50 | 72.10 | 73.50 |
| 6 | 30 | 63.50 | 76.30 | 76.70 |
| 7 | 35 | 66.60 | 80.30 | 78.67 |
| 8 | 40 | 68.70 | 84.40 | 81.30 |
| 9 | 45 | 69.70 | 88.60 | 83.45 |
| 10 | 50 | 73.10 | 89.50 | 86.74 |




**CONCLUSION**

Solid Self-Emulsifying Drug Delivery Systems (S-SEDDS) present a significant advancement in enhancing the oral bioavailability of ibuprofen, a widely used non-steroidal

anti-inflammatory drug (NSAID) with poor water solubility. By leveraging a mixture of oils, surfactants, and co-surfactants, S-SEDDS facilitate the formation of fine oil-in-water emulsions upon contact with gastrointestinal fluids. This process significantly improves the solubility and absorption of ibuprofen, leading to enhanced bioavailability.

The solidification of SEDDS into a solid form offers several practical benefits, including improved stability, ease of handling, and better patient compliance compared to liquid formulations. Techniques such as spray drying, freeze drying, and adsorption onto solid carriers are employed to achieve this transformation. These methods ensure that the solid formulation retains the self-emulsifying properties essential for optimal drug delivery.

Key steps in formulating S-SEDDS for ibuprofen include the careful selection of ingredients, optimizing their ratios, and validating the emulsification efficiency. Characterization techniques such as particle size analysis, stability studies, and in vitro dissolution tests are crucial in confirming the effectiveness of the formulation. Additionally, in vivo bioavailability studies are essential to demonstrate the practical benefits of S-SEDDS in enhancing ibuprofen absorption.

**AKNOWLEDGEMENT**

The successful completion of this project on the enhanced oral bioavailability of ibuprofen using Solid Self-Emulsifying Drug Delivery Systems (S-SEDDS) has been a significant milestone, and it would not have been possible without the support, guidance, and contributions of several individuals and institutions.

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