RESEARCH PAPER

Enhancement Of Oral Bio-Availability Of Hydrophobic Drugs Through Lipid Formulations

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ABSTRACT

Poor aqueous solubility is one of the major challenges in oral drug delivery, as it significantly affects the dissolution, absorption, and bioavailability of many pharmaceutical compounds. A considerable number of newly developed drugs belong to Biopharmaceutical Classification System (BCS) Class II and IV categories, which exhibit low water solubility and poor absorption characteristics. To overcome these limitations, lipid-based formulations have gained considerable attention as an effective strategy for enhancing the oral bioavailability of poorly water-soluble drugs. These formulations improve drug solubilization in the gastrointestinal tract and facilitate enhanced drug absorption through lymphatic transport and improved membrane permeability.

Various lipid-based drug delivery systems, including self-emulsifying drug delivery systems (SEDDS), nanoemulsions, microemulsions, liposomes, and solid lipid nanoparticles, have demonstrated significant potential in improving dissolution and therapeutic efficacy. These systems form fine dispersions upon contact with gastrointestinal fluids, thereby increasing the surface area available for absorption. Furthermore, lipid excipients help maintain the drug in a solubilized state and may reduce first-pass hepatic metabolism. Recent advancements in formulation techniques and excipient technologies have further improved the stability, safety, and effectiveness of lipid-based delivery systems, making them a promising approach for modern pharmaceutical research and oral drug therapy.

Keywords: Bioavailability, Poorly Water-Soluble Drugs, Lipid-Based Formulations, SEDDS, Nanoemulsions, Drug Delivery Systems, Solubility Enhancement, Oral Drug Delivery.

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INTRODUCTION

A key pharmacologic component that affects how well a medication is absorbed and, in turn, how healing it is. Due to their poor aqueous dissolvability, a great deal of the recently created medications are lipophilic and have not made their way onto the marketing. It is especially important to distinguish between a substance's solubility and its ability to dissolve or liquefy, as the latter can also happen as a result of a chemical reaction. One of the biggest challenges facing researchers in formulation is the drug's solubility behavior. Most of the drugs that are in the developmental pipelines result from the Great Throughput Screening technique, which increases sub-atomic loading and consequently causes significant bioavailability problems. Problems with solubility affect most substances. Therefore, the requirement to build. As chemical research progresses, pharmaceuticals technology also rise. Medication procedures are definitely less expensive than chemical gets nearer, although also take a lot of time. Given that water makes up around 70% of the human body, a drug ought to dissolve easily while maintaining an adequate degree of bioavailable (Pinnamaneni S). 1.1 Gastrointestinal administration of drugs Techniques In the realm of pharmaceutical delivery technology, those who formulate continued to favor the route of digestion for drug administration. Due to the advantages offered to both the buyer and the producer, this type of medication is the one with the greatest recognition and optimal organizational structure among the other types. Despite its popularity, consumable courses have limited permeability due to first-pass metabolism.

These constraints get much more stringent when it comes to medications composed of proteins and polysaccharides. In order to create a solution for straightforward continuation, the drug in the dose structure is administered and disintegrates in surrounding gastrointestinal fluid. The ability to dissolve of the procedure is restricted. The medicinal product in the solution it contains crosses across the cell membranes within the digestive system. The ability to penetrate of the procedure is restricted. The medicine is then taken up by the bloodstream. To put it briefly, the level of permeability and dispersion of a medicine affects its consumption and, in turn, its absorption into the body. Medication the ability to dissolve, in addition to permeability, therefore a key component in drug dissolution and is necessary for drug transportation towards the interface point. Dependent according to the medicines's class, it may not dissolve well enough to deliver the medicinal product transport. The curative effectiveness of a medicine correlates to its bioavailability, which is directly correlated with the dissolution of its medicinal compounds. Tissue dissolvability threshold must be achieved to get the desired concentration of medicine in fundamental diffusion for pharmacological reaction to be demonstrated. Any drug's form of liquid is more rapidly and effectively absorbed by the body than its solid form. Solubility is an important characteristic for the bioavailability in the stomach of poorly soluble medicines. The bioavailability of substances is affected by the solvency obstacle, and as a consequence, its dissolvability enhancement is crucial. Drugs which tend to be difficult for dissolution are currently being rendered more easily absorbed by employing an abundance different cutting-edge technique (Devane J). The phrases utilized for expressing liquidity in pharmacopoeia are listed in Table 1.1. (IP 2014)

Table 1.1: The solubility of Measurements

Measurements	Solute part (g) in solvent part (ml)
Insoluble practically	1 in > 11,000
Extremely weakly soluble	1 in 1100–1 in 11,000
Partially soluble	1 in 110 to 1 in 1100
Soluble sparingly	1 in 31 to 1 in 105
Soluble	1 in 11 to 1 in
Disintegrates in water	1 in 1 to 1 in 11
Highly soluble	1 in < 1.2

1. 2 Biopharmaceutical Classification System

A basic paradigm for pharmacological characterisation was developed to facilitate the development of immediate release (IR) robust dosage by mouth configurations. This academic system classifies medications based on their ability to dissolve in water and permeability of the intestinal tract. The above categorizing scheme explains three aspects of the

creation of drugs. Three of the main parameters that affect oral medication reception from instant releasing hard mouth dose formulations are permeability in the gut, the ability to dissolve, and disintegration. During the course of the lifespan of a good and throughout the first phases of medication growth, this classification system can be used to manage changes to the product. The USFDA direction archive on Quick Delivery Strong Oral Dose Structures: Scale up and Post it was initially introduced in Endorsement Changes (Hao Zhang) during the administrative dynamical cycles. Zhang Hao. Class boundaries If a medicine at its greatest dose dissolves in fewer than 250 milliliters of water at a pH of 1 to 7.5, it is said to be extremely soluble. Human absorption of the medicine exceeds 90% as compared to an intravenous reference dose, suggesting that the substance is very permeability. A medicine is considered to dissolve fast if more than 85% of the name guarantee solubilizes in less than thirty minutes when using USP devices I or II in an amount of less than 900 ml of cushion setups.

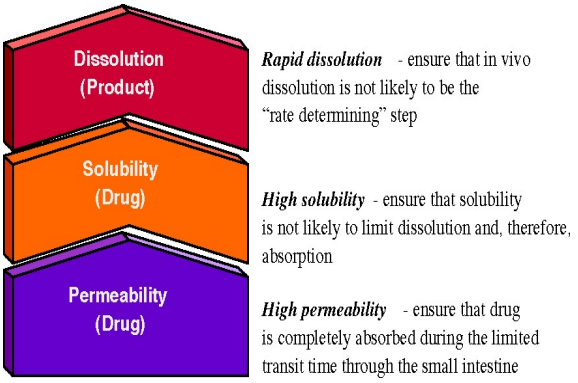


Figure 1.1: Objectives of BCS class boundaries

Classification:

Drugs are classified using the Biopharmaceutical classification system (BCS), which classify active pharmaceuticals for oral administration into four classes depending on their solubility and their permeability through the intestinal cell layer (Amidon GL). According to BCS, drug substances are classified in four classes as depicted in figure 1.2:
Class I: High Solubility – High Permeability Class II: Low Solubility – High Permeability Class III: High Solubility – Low Permeability Class IV: Low Solubility – Low Permeability

Figure 1.2: Biopharmaceutical classification system

Dissolution No = _Mean residence time
Mean Dissolution time

Absorption No = _Transit time
Absorption time

Due to their high solubility and permeability, Class I drugs have a high absorption and dissolution number. In the case of drugs like Verapamil and Propranolol, whose dissolution is extremely rapid, the rate at which the gastric emptying rate becomes the rate determining step is the rate at which the drug dissolves. Class II drugs have a high absorption number but a low dissolution number because of their low solubility and high permeability. As a rate-limiting step for absorption, in vivo drug dissolution is anticipated to occur at a very high dose number. When compared to class I drugs, the absorption of class II drugs typically occurs more slowly and over a longer period of time. Ketoconazole, Mefenamic acid, Nifedinpine, and ibuprofen are among the class I and class II medications that were most frequently observed for the in vitro-in vivo correlation (IVIVC). Due to their high solubility and low permeability, Class III drugs have a high dissolution number but a low absorption number.

Classification	High Permeability	High Solubility	Low Solubility
Class 1	Abacavir	Imipramine	Acetaminophen
	Amitryptyline	Ketorolac	Atropine
	Antipyrine	Ketoprofen	Amitryptyline
	Buspirone	Labetolol	Chloroquine
	Atropine	Levodopa	Buspirone
	Captopril	Lidocaine	Desipramine
	Caffeine	Meperidine	Prednisolone
	Chloroquine	Nifedipine	Captopril

	Desipramine	Promazine	Chloroquine
Class 2	Amiodarone	Quinidine	Dapsone
	Azithromycin	Talinolol	Digoxin
	Carvedilol	Warfarin	Ibuprofen
	Cisapride	Diazepam	Indinavir
	Danazol	Dapsone	Glipizide
	Itraconazole	Indinavir	Diazepam

Low Permeability	Class 3	Class 4
Acyclovir	Atenolol	Amphotericin B
Folinic acid	Atropine	Chlorthalidone
Amphotericin B	Bisoprolol	Colistin
Atenolol	Captopril	Furosemide
Lisinopril	Cefazolin	Mebendazole
Atropine	Cloxacillin	Neomycin
Bisoprolol	Dicloxacillin	Nadolol
Captopril	Famotidine	Pravastatin
Cefazolin	Metformin	Ranitidine
Cloxacillin	Ranitidine	Valsartan
Dicloxacillin	Valsartan	

The Process of Solubilization

Solubilization involves breaking inter-ionic or intermolecular bonds in the solute, making space among solvent molecules for the solute, and then allowing the solvent to interact with the solute's molecules or ions. Understanding the solubility of a substance is crucial in pharmaceutical studies. It is key to knowing how a drug will behave, helps with formulating drugs to meet delivery system requirements, and supports analyzing drugs in biological fluids for bioavailability studies and quality control.

Factors Influencing Solubility (Perrut M)

The bioavailability, dissolution, and absorption of a drug are closely linked to its solubility. Several factors affect solubility, including system temperature, pressure, the nature and composition of the solvent, and the solid's physical form. Understanding these factors is crucial for ensuring effective drug development and delivery.

Techniques of Solubility Enhancement (Amidon GL)

Several methods can enhance the solubility of drugs with poor solubility. Common strategies for improving solubility include:

Physical Modifications.

Particle Size Reduction**

Micronization: Reducing particle size to micron levels.

Sonocrystallization: Using ultrasonic waves to create smaller crystals.

Supercritical Fluid Processing: Employing supercritical fluids to modify particle size.

Spray Drying: Atomizing a solution to form fine particles through evaporation.

B. Modification of Crystal Habits

1 **Polymorphs:** Creating different crystalline forms of a drug.

Pseudo Polymorphs: Utilizing hydrates or solvates as alternative forms.

C. Drug Dispersion in Carriers

Eutectic Mixtures: Combining two or more components that form a lower melting point.

. **Solid Dispersions:** Distributing drugs in solid carriers to improve solubility.

3. **Solid Solutions:** Completely dissolving a drug in a carrier at a molecular level.

D. Complexation

Use of Complexing Agents: Enhancing solubility through chemical complexes.
E. Lipid-Based Drug Delivery Systems
Micro Emulsions: Stable dispersions of oil and water facilitated by surfactants.
Self Micro-Emulsifying Drug Delivery Systems (SMEDDS): Using a mix of oils and surfactants to form micro emulsions upon contact with aqueous media.
Chemical Modifications
Formation of Salts and Prodrugs: Converting a drug into its salt form or a prodrug to increase solubility.
Miscellaneous Approaches
Co-Solvency: Using solvents to enhance solubility.
Co-Crystallization: Creating crystalline complexes with other compounds.
Hydrotropy: Using hydrotropic agents to increase solubility in water.
Solubilizing Agents: Incorporating compounds that improve solubility.

LIPID BASED DRUG DELIVERY SYSTEM (Porter CJH)
Lipid solution, lipid emulsion, micro emulsion, dry emulsions are the example of recently developed lipid base delivery system. To get clarity on different systems and due to wide range of possible excipient combinations that may be used to form these lipid-based formulations, self emulsifying systems in particular a classification system have been established called as lipid formulation classification system (LFCS). T

Table 1.3: Classification of Lipid Based Drug Delivery System (Gershanik T)

Composition	Type I	Type II	Type III	Type IV
Oil	100%	35-75%	35-75%	< 25%
Glycerides (TG, DG, MG)	100%	35-75%	35-75%	< 25%
Surfactants				
HLB < 12	-	25-55%	-	-
HLB > 12	-	-	25-45%	25-60%
Hydrophilic Co-solvents	-	-	0-45%	25-55%
Particle size of dispersion (nm)	Coarse	105-245	105-245	45-95

The drug is solubilized in triglycerides, mixed glycerides, or an oil-in-water emulsion in Type I systems, and minimal emulsifiers are used to maintain stability. Low beginning fluid scattering require, absorption by pancreatic lipase/co-lipase in the GIT to create more amphiphilic lipid processing items in order to advance medication move into the colloidal watery stage. When a drug has good solubility and is potent or a highly hydrophobic molecule, Type I lipid formulations are the preferred choice. SEDDS are lipid formulations of type II. Self-emulsification is accomplished by surfactant fixation above 25% (w/w). At the interface of the oily and aqueous phases, the emulsification process involves the formation of an in situ crystalline, viscous liquid gel.

Figure 1.3 Possible Effect of Lipid Based Formulation on oral Drug Delivery System Table 1.4 Advantages and disadvantage of Lipid based drug delivery system (Legen L)

Formulation Type	Materials	Characteristics	Advantages	Disadvantages

Type I	Oils without surfactants (e.g., tri-, di-, and monoglycerides)	Non-dispersing; requires digestion	Generally recognized as safe (GRAS); simple; excellent compatibility with capsules	Limited solvent capacity; needs highly lipophilic drugs
Type II	Oils with water-insoluble surfactants	SEDDS formed without water-soluble components	Maintains solvent capacity upon dispersion	Turbid o/w dispersion (particle size 0.3–2.5 μm)
Type III	Oils, surfactants, and co-solvents (water-insoluble and water-soluble excipients)	SEDDS/SMEDDS formed with water-soluble components	Clear or nearly clear dispersion; drug absorption without digestion	Possible loss of solvent capacity upon dispersion; less digestible
Type IV	Water-soluble surfactants and co-solvents (no oils)	Formulation typically forms a micellar solution	Good solvent capacity for a range of drugs	Likely loss of solvent capacity upon dispersion; may not be suitable for digestion

S**Advantages of SMEDDS (Gang C):**

1. **Improved Oral Bioavailability:** Many poorly water-soluble drugs are absorbed at a rate that depends on their dissolution. SMEDDS improve bioavailability by presenting drugs in a solubilized and micro emulsified form, enhancing their transport through the intestinal membrane. This leads to better absorption, as seen with Halofantrine, which showed increased bioavailability compared to tablet formulations.

2. Ease of Manufacturing and Scale-Up: SMEDDS can be produced with simple and cost-effective equipment, making them attractive for large-scale manufacturing. This simplicity contributes to the interest in commercializing SMEDDS.

3. **Reduced Impact of Food:** The performance of a drug can vary based on food intake, leading to inconsistency in drug absorption. SMEDDS help achieve reproducible plasma profiles, reducing inter-subject and intra-subject variations in absorption, which enhances patient compliance. (Kawakami K.)

4. **Bypass Enzymatic Hydrolysis in the GIT:** SMEDDS can protect macromolecules like hormones and enzyme substrates from enzymatic hydrolysis. For example, Polysorbate, an emulsifier, can protect against cholinesterase degradation.

5. **Increased Drug Loading Capacity:** The use of surfactants and co-surfactants in SMEDDS allows for greater solubility of poorly water-soluble drugs, increasing the drug loading capacity compared to traditional lipid solutions.

Advantages of SMEDDS over Emulsions (Rajesh BV):

1. **Better Solubility and Stability:** SMEDDS improve the solubility of hydrophobic drugs and avoid the creaming that can occur with emulsions over time. Their thermodynamic stability allows for easier storage.
2. **Smaller Particle Size:** The smaller droplet size of SMEDDS, ranging from 2 to 100nm, offers more surface area for solubilization and absorption. This also leads to better intestinal penetration and bioavailability.
3. **Versatile Dosage Forms:** SMEDDS can be used in both solid and liquid dosage forms, allowing them to be encapsulated in soft and hard gelatin capsules.

Figure 1.4: Reasons for formulating drugs in liquid filled capsules

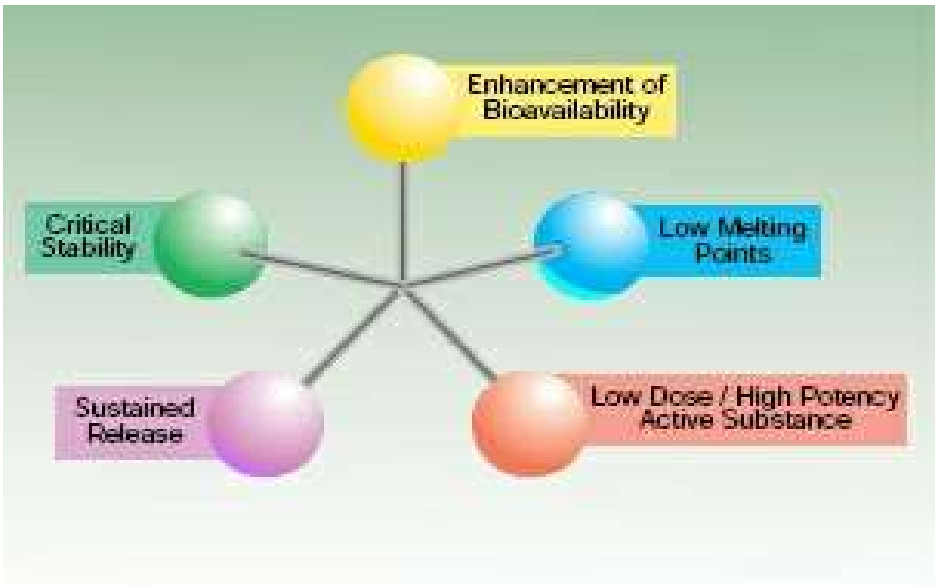


Table 1.6 List of vehicles compatible with hard gelatin capsules

Sr. No	Chemical Name	Brand Name
Lipophilic Liquid Vehicles (Oils)		
1	Arachis oil, Castor oil, Cottonseed oil, Corn oil, Olive oil, Sesame oil, Sunflower oil	
2	Medium-chain triglycerides	Akomed, Capmul, Miglyol, Crodamol
Semi-Solid Lipophilic Vehicles		
3	Hydrogenated arachis oil	Groundnut 38
4	Hydrogenated castor oil	Cutina HR
5	Hydrogenated cottonseed oil	Sterotex 80
6	Hydrogenated palm oil	Softisan 160
7	Hydrogenated soy oil	Akosol 408
8	Cetosteryl alcohol	Cetanol
9	Glyceryl behenate	Compritol 999 ATO
10	Glyceryl Palmitostearate	Pricirol ATO 10
Solubilizing Agents/Surfactants/Emulsifying Agents		
11	Polysorbate 80	Tween 85

12	Propylene glycol monocaprylate	Capryol 100
13	Poly Glycenated glycerol	Gelucire 50/13
14	Macrogol glycerol hydroxystearate	Cremophor RH 45
15	Polyoxyethylated oleic glycerides	Labrafil M 2130
16	PEG 4000 and above	Carbowax
17	Polyethylene-polypropylene glycol	Poloxamer 407
18	Glyceryl ricinoleate	Softigen 55
Excipients with Limited Compatibility in Hard Gelatin Capsules (at 100% level but compatible below 70%)		
19	Ethanol	
20	PEG 400/600, Glycerine, Propylene glycol	
21	Sorbitan mono oleate	Span 85
22	Diethylene glycol monoethyl ether	Transcutol HP

The liquid formulation may be filled in hard or soft gelatin capsules. A comparison between the two types of capsules is presented in Table 1.7

Table 1.7 Comparison between soft Gelatin and liquid filled hard gelatin capsules

Sr. No	Aspect	Soft Gelatin Capsule	Hard Gelatin Capsule
1	In-house development and manufacture	Complex and messy; difficult to fill in-house	Can be filled with conventional capsule machines
2	Small batch production	Challenging	Feasible
3	Scale-up	Requires large quantities; often outsourced	Simple and typically in-house; scale-up studies possible
4	Combination filling: Liquid and pellets	Not feasible	Possible
5	Partial filling	Not feasible	Possible
6	Permeability of shell to oxygen	High due to plasticizer and moisture	Low permeability; contains less plasticizer
7	Limitation on excipients for formulation	Can tolerate hygroscopic excipients	Avoid high concentrations of hygroscopic excipients
8	Risk of drug migration	High for drugs soluble in plasticizer	Low
9	Capsule dimensions	May vary	Can be predefined
10	Plasticizer in shell	Yes	Comparatively less
11	Sensitivity to heat and humidity	High due to plasticizer	Relatively lower

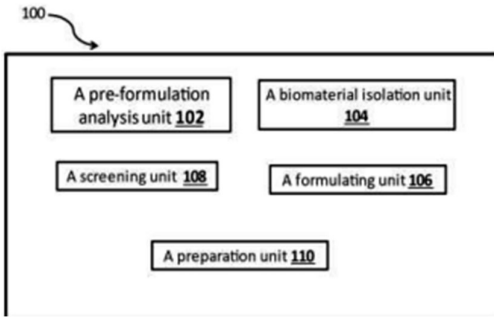


Figure 1demonstrates a block diagram of a method for creating a medication delivery system that is self-emulsifying.

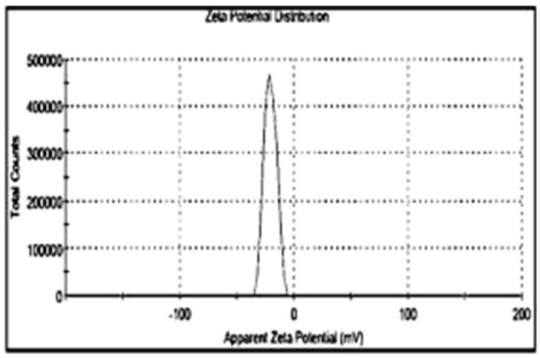
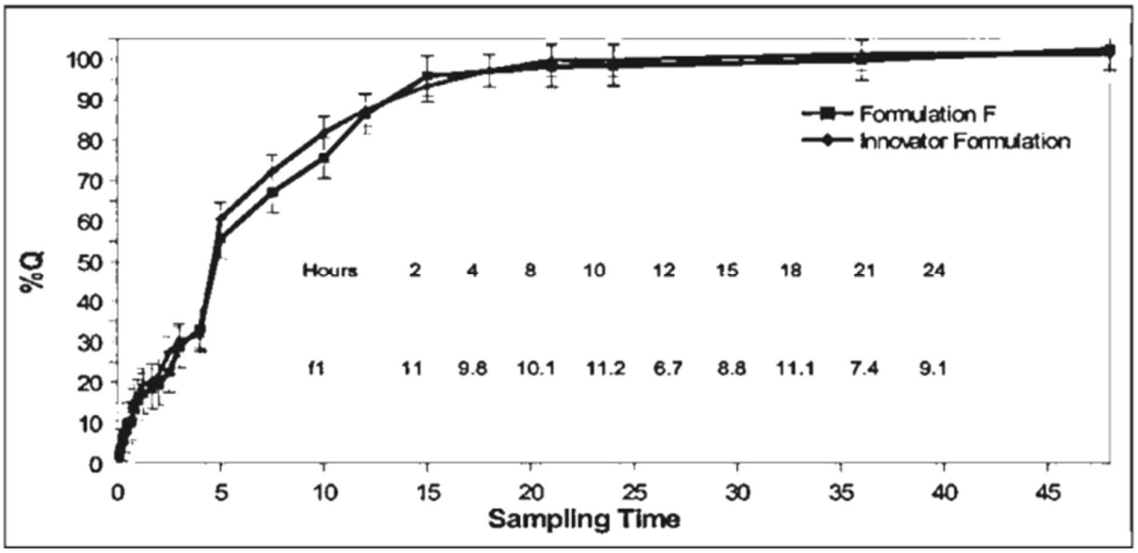


Figure 2 illustrates the zeta potential measurements of the nano emulsion

Formulation	Droplet Size	PDI
F1	11.8	0.115
F2	12.1	0.150
F3	12.9	0.185
F4	18.7	0.040
F5	19.1	0.200

Table 1. Illustrates a table representing the globules size and PDI data



METHODOLOGY AND RESULT

PREPARATION OF SOLID SELF MICROEMULSIFYING DELIVERY SYSTEM

Solid SMEDDS (S-SMEDDS)

To enhance drug stability and create a formulation that can function as both a solid and a liquid dosage form, Solid Self-Nano Emulsifying Drug Delivery Systems (S-SMEDDS) were developed from the optimized liquid SMEDDS of selected Class II drugs.

Methodology of S-SMEDDS

1. Adsorption to the Solid Carrier

The carrier materials were chosen based on their high surface area and capacity to adsorb the liquid SMEDDS. This method involves slowly adding the pre- concentrate SMEDD to the solid carriers while mixing continuously to ensure uniform adsorption. The pre-concentrate was added at a rate of 0.1ml while stirring. The resulting mixture, once evenly adsorbed, was air-dried and then filled into hard gelatin capsules. Various carriers were evaluated, including lactose, micro-crystalline cellulose, hydroxypropyl methyl cellulose, Aerosil, PVP K-30, and anhydrous dibasic calcium phosphate. The carrier with the best results was used to develop the solid SMEDDS for encapsulation.

2. Preparation of S-SMEDDS

The optimized liquid SMEDDS, containing drugs such as 200mg of Dexi buprofen and 10mg of Atorvastatin Calcium, was converted into solid SMEDDS by adding it to the chosen solid carrier in a controlled manner with continuous mixing. This process results in granules of the solid SMEDDS, which are then filled into hard gelatin capsules for ease of administration and increased stability.

Analytical Methods for S-SMEDDS

1. In-Vitro Dissolution

The dissolution testing was carried out using the same method described in the previous section for liquid SMEDDS. This test is crucial for understanding the release profile of the drug from the solid SMEDDS.

2. Scanning Electron Microscopy (SEM)

To observe the physical characteristics of the optimized formulations, a small amount of the sample was mounted on a stub and sputter-coated with gold particles. These samples were then examined under a scanning electron

microscope (SEM) at an accelerating voltage of 10 kV. Surface images were captured to analyze the texture and uniformity of the solid SMEDDS.

3. Differential Scanning Calorimetry (DSC)

Differential scanning calorimetry was used to determine the thermal properties of the S-SMEDDS. A Perkin-Elmer DSC-7 was employed, with 4-6 mg of product placed in perforated aluminum sealed pans. The samples were heated from 40°C to 200°C at a rate of 5°C/min in an inert nitrogen environment. This analysis helps determine the melting points and heat of fusion for the samples, providing insights into their thermal stability.

By adopting these methodologies, the conversion of liquid SMEDDS into solid SMEDDS can be achieved, offering a stable and versatile dosage form with dual functionality. This approach enhances drug stability, facilitates drug delivery, and allows for better handling and storage compared to traditional liquid formulations.

Table 6.1: Adsorbent selection

Formulation Code	Name of the Adsorbent	Amount of SMEDD Adsorbed	Amount of Adsorbent Required for Free-Flowing Powder
Dexibuprofen			
DS1	Aerosil 400	0.85ml	310 mg
DS2	Aerosil 250	0.85ml	330 mg
DS3	Dibasic Calcium Phosphate	0.85ml	410 mg
Atorvastatin Calcium			
AS1	Aerosil 400	0.65ml	165 mg
AS2	Aerosil 250	0.65ml	190 mg
AS3	Dibasic Calcium Phosphate	0.65ml	195 mg

Table 6.2: Powder Characteristics of S – SMEDDS

Formulation Code	Bulk Density (g/ml)	Tapped Density (g/ml)	Carr's Index (%)	Hausner's Ratio	Inference
DS1	0.450	0.530	15	1.19	Good
DS2	0.415	0.528	22	1.25	Passable
DS3	0.440	0.590	25	1.34	Passable
AS1	0.440	0.523	15	1.18	Good
AS2	0.425	0.537	21	1.23	Passable
AS3	0.418	0.573	27	1.36	Passable

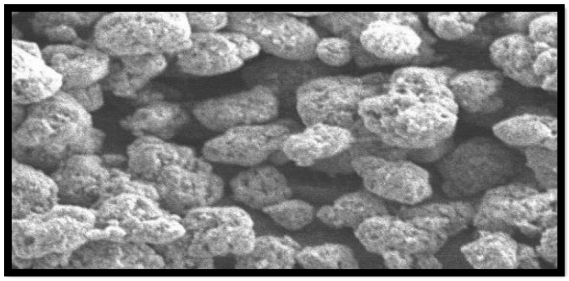


Fig 6.1: SEM Dexibuprofen S- SMEDDS of after adsorption DS

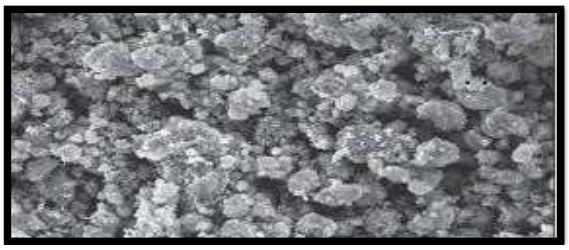


Fig 6.2: SEM Atorvastatin calcium S- SMEDDS of after adsorption AS1

Table 6.3: In-vitro drug release of Dexibuprofen S – SMEDDS

Time in mins	% Drug Release		
	DS1	DS2	DS3
0	0	0	0
15	22	30	15
30	35	50	25
45	50	63	45
60	65	89	56

Table 6.4: In-vitro drug release of Atorvastatin Calcium S- SMEDDS

Time in mins	% Drug Release		
	AS1	AS2	AS3
5	70	63	56
10	88.6	80.7	68
15	95.3	86.6	83.6
20	97.3	93	89
30	98.7	94	93

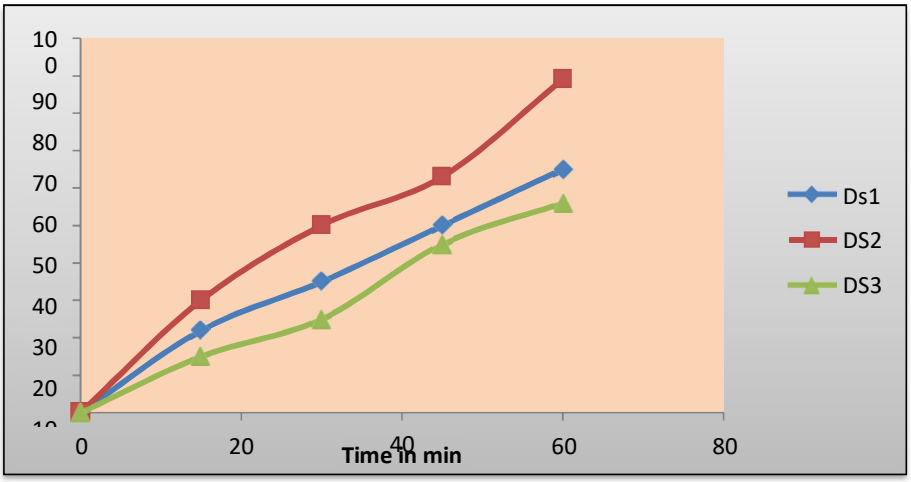


Fig: 6.3: In-vitro drug release from different S-SMEDDS of Dexibuprofen

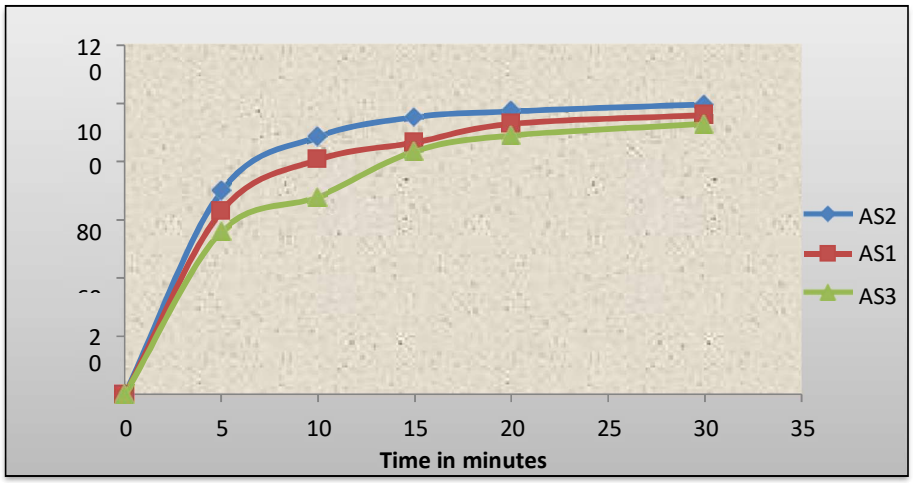


Fig: 6.4: In-vitro drug release from different S- SMEDDS of Atorvastatin Calcium

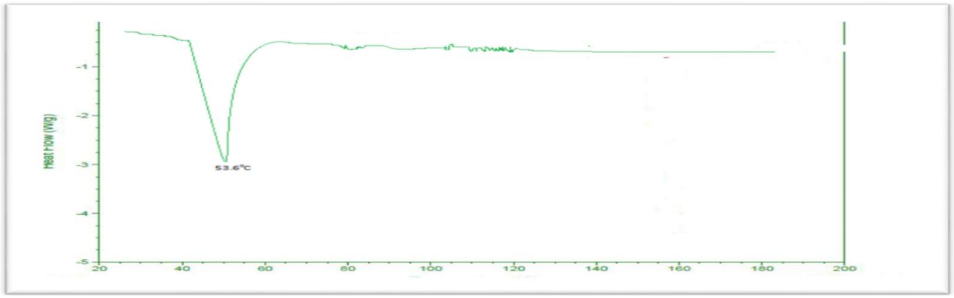
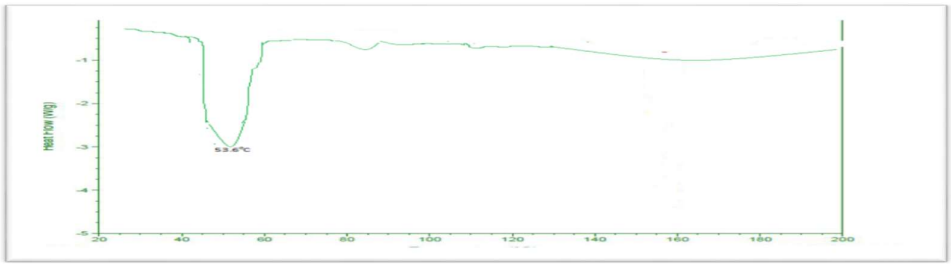


Fig 6.5: DSC Scan of Pure Dexibuprofen

Fig 6.6: DSC Scan of Dexibuprofen S – SMEDDS



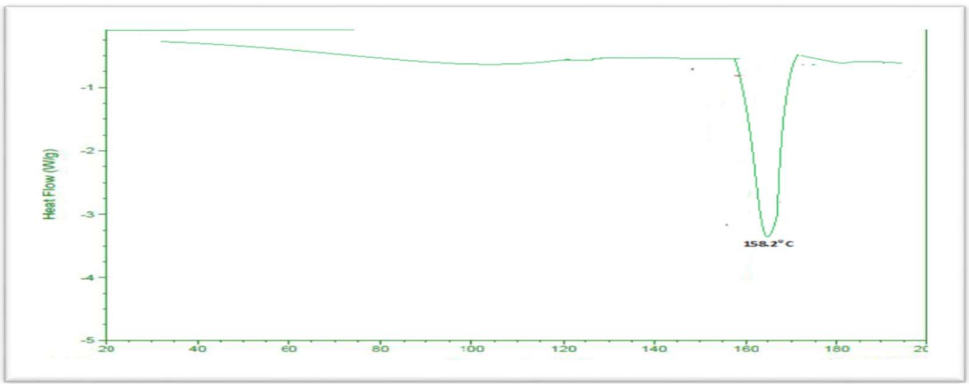


Fig 6.7: DSC Scan of the pure Atorvastatin Calcium

Fig: 6.8: DSC Scan of the Atorvastatin Calcium S- SMEDD

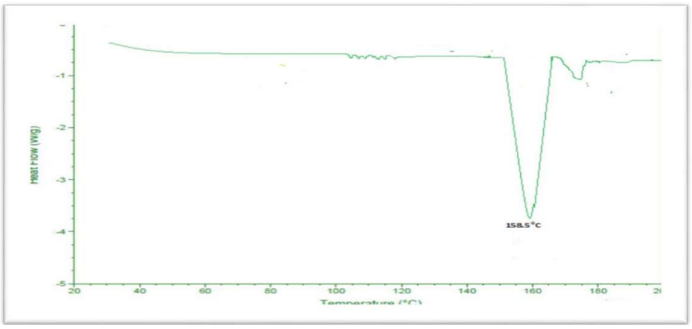


Table 6.5: Accelerated Stability Studies of S-SMEDDS

Parameters	Initial	1M	2M	3M
DS1				
Assay	100.8	98.6	97.2	95
AS1				
Assay	99.6	97	95.3	93.4

Table No 6.6: Real time Stability Studies of S-SMEDDS

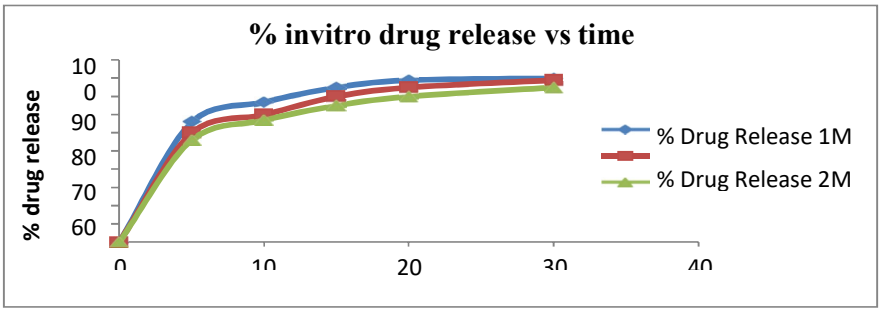
Parameters	Initial	1M	2M	3M
DS1				
Assay	100.8	99	97.8	97
AS1				
Assay	99.6	98.1	97.2	96

Table 6.7: In-vitro-dissolution after accelerated stability studies of Dexibuprofen S - SMEDDS

Time in mins	% Drug Release
	1M
0	0
15	28
30	43
45	59
60	82

Table 6.8: In-vitro-dissolution after real time stability studies of Dexibuprofen S - SMEDDS

Time in mins	% Drug Release
	1M
0	0
15	28
30	45
45	60
60	84



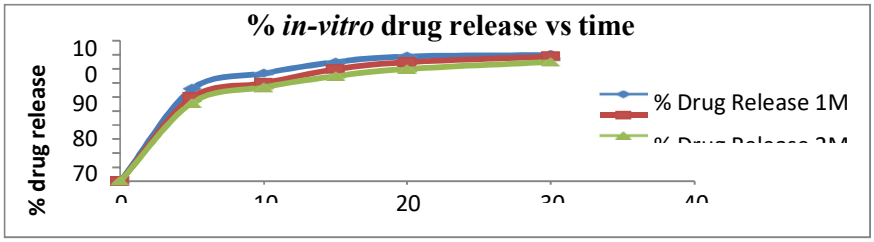


Figure 6.9: In-vitro-dissolution after accelerated stability studies of Dexibuprofen S - SMED

Table 6.9: In-vitro-dissolution after accelerated stability studies of Atorvastatin Calcium S - SMEDDS

Time in mins	% Drug Release		
	1M	2M	3M
0	0	0	0
5	66	60	56
10	77	70	67
15	85	80	75

20	89	85	80
30	90	89	85

Table 6.10: In-vitro-dissolution after real time stability studies of Atorvastatin Calcium S - SMEDD

Time in mins	% Drug Release		
	1M	2M	3M
0	0	0	0
5	67	65	60
10	82	85	80
15	87	89	83
20	90	91	88
30	95	93	94

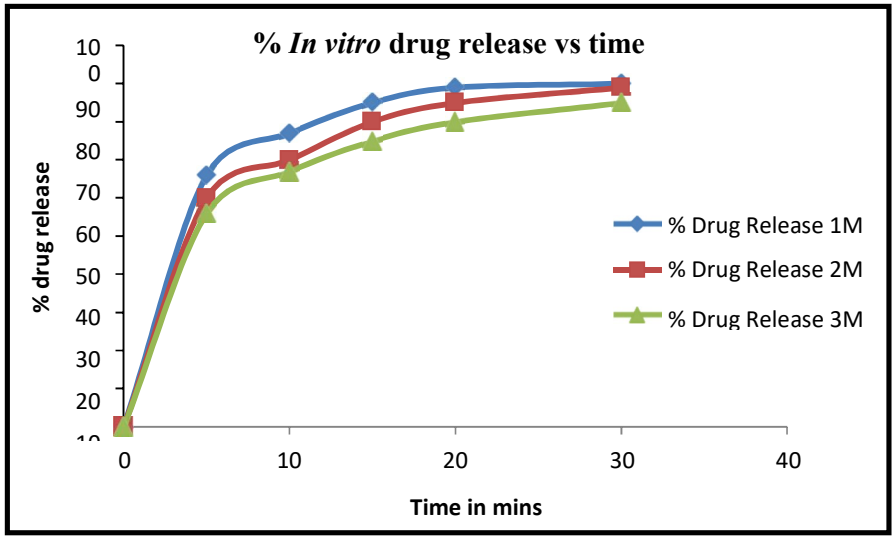


Figure 6.11: In-vitro-dissolution accelerated stability studies of Atorvastatin Calcium S - SMEDDS

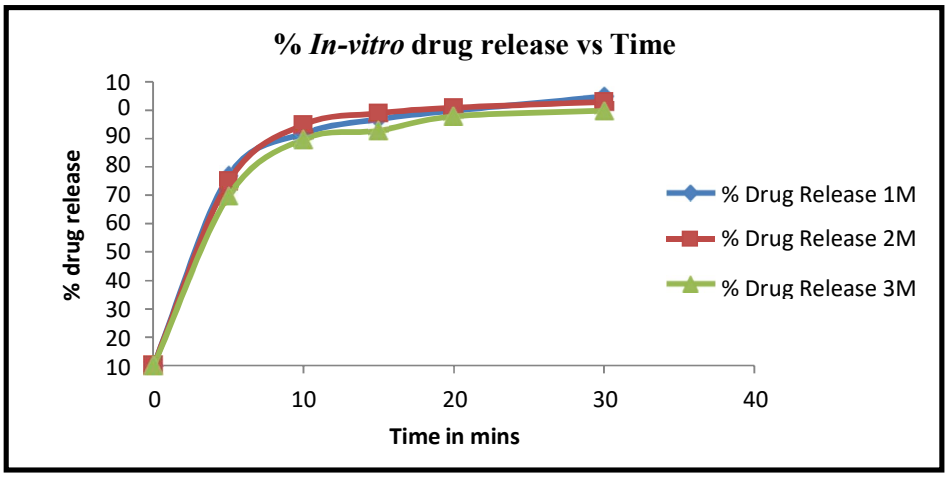


Figure 6.12: In-vitro-dissolution after real time stability studies of Atorvastatin Calcium S - SMEDDS

CONCLUSION

After accelerated `stability studies it is been observed that assay is decreased to 95% and 93% for Dexibuprofen and Atorvastatin Calcium, that for real time studies is 97% and 96% respectively. The In-vitro drug release is decreased to 75% and 85% for Dexibuprofen and Atorvastatin Calcium respectively for accelerated stability studies. Which shows the formulation is not stable at extreme temperature. Lipid-based formulations have emerged as a highly effective strategy for improving the bioavailability of poorly water-soluble drugs. These systems enhance drug solubilization, dissolution, and absorption by promoting efficient dispersion in the gastrointestinal tract and facilitating lymphatic transport. Various lipid-based delivery approaches such as self-emulsifying drug delivery systems, nanoemulsions, liposomes, and solid lipid nanoparticles have shown significant success in overcoming the limitations associated with poor aqueous solubility. In addition to improving oral absorption, these formulations may also reduce first-pass metabolism and enhance therapeutic efficacy. Recent advancements in lipid excipients and formulation technologies have further increased the stability, safety, and commercial applicability of these systems. Therefore, lipid-based drug delivery systems represent a promising and innovative approach in modern pharmaceutical development for enhancing the therapeutic performance of poorly water-soluble drugs and improving patient compliance and treatment outcomes

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