EVALUATION OF CASTOR OIL BASED SELF EMULSIFYING DRUG DELIVERY SYSTEMS (SEDDS) FOR DICLOFENAC POTASSIUM

BY

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CERTIFICATION

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DEDICATION

This work is dedicated to God Almighty, my Father in Heaven, the one who has been with me from the moment I was born up until I gained admission into University Of Benin, and helped me throughout my journey in Pharmacy school.

TO GOD BE THE GLORY.

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ABSTRACT

Background: Self emulsifying drug delivery systems (SEDDS) offer a means of enhancing the bioavailability and therapeutic efficacy of drugs with poor water solubility ; Evaluation a self emulsifying drug delivery system of diclofenac potassium using Castor oil as the lipid phase.

Method: Six batches of SEDDS labelled SD1, SD2, SD3, SD4, SD5, and SD6 were prepared by incorporating diclofenac potassium in SEDDS bases of Castor oil and Tween 80 at varying component ratios. The resulting formulations were evaluated for their self-emulsification performance upon dilution with water by visual inspection and classified according to standard emulsion grading criteria (Grade A, B, or C). They were evaluated for their self-emulsification performance, thermodynamic stability and Absorbance values.

Result: The emulsification performance demonstrated significant variability across the batches, with formulation SD1 successfully forming a highly stable Grade A emulsion, indicating rapid and fine self-microemulsification. Conversely, formulations SD2 and SD3 yielded a satisfactory Grade B emulsion, whereas formulations SD4, SD5 and SD6 resulted in a milky Grade C emulsion, signifying poor emulsification performance. Formulations SD1 - SD3 showed good stability, while SD4 – SD6 showed poor stability. The batches had absorbance values which ranged from 0.583 ± 0.154 to 0.719 ± 0.190 showing considerable drug entrapment.

Conclusion: The optimal performance of SD1 demonstrates that diclofenac potassium can be effectively formulated into a stable SEDDS using castor oil, offering a practical approach for improved in vitro dissolution and enhanced potential for clinical absorption.

Keywords: Diclofenac potassium, SEDDS, Self-emulsifying, Castor oil, Tween 80, Dissolution enhancement, Bioavailability.

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CHAPTER ONE

1.1. Introduction

1.1.1 Overview of diclofenac potassium

Diclofenac potassium is a common NSAIDs. It is a fast-acting, water-soluble salt version of the medication. It is mostly used to treat fever, inflammation, and pain brought on by a number of illnesses, such as migraines, musculoskeletal diseases, physical trauma, and postoperative pain (Azzopardi, 2007). For circumstances that call for a quick commencement of action, its potassium salt form is especially appropriate (Wallace *et al.,* 2006).

Examples of diclofenac potassium brands in the market are Cataflam® 50 mg and Voltaren® 50 mg, Pregnancare supplement, etc.

1.2.1. Chemical and physical properties of diclofenac potassium

i. Chemical name: 2-[(2,6-dichlorophenyl) amino] benzene acetic acid monopotassium salt.
ii. Molecular formula: $C_{14}H_{10}C_{l2}KNO_2$.
iii. Molecular weight: ~334.2 g/mol.
iv. Solubility: Highly water-soluble due to the potassium salt.
v. Formulations: Available as oral tablets, capsules, and soluble powders.
vi. Wavelength of maximum absorbance in phosphate buffer: 276nm (Peretz *et al.,* 2004).

The structure of diclofenac potassium is shown below.

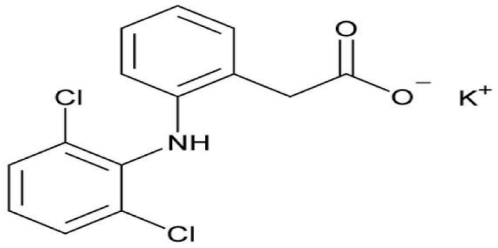


Figure 1.1: Chemical structure of diclofenac potassium (PubChem.org, 2025).

1.2. Mechanism of action of diclofenac potassium

It functions by inhibiting the enzymes known as cyclooxygenase (COX) specifically COX-1 and COX-2, lowering prostaglandin production which is a mediator of fever, inflammation, and discomfort. Diclofenac potassium reduces inflammation, discomfort, and high body temperature by focusing on these routes (Sinatra, 2009).

Uses of diclofenac potassium

- Severe pain: Pain following surgery, such as orthopedic or dental procedures, cramping during menstruation, or dysmenorrhea.
- Prolonged inflammatory disorders such as osteoarthritis, spondylitis ankylosing.
- Migraines: Because of its quick absorption, it works particularly well for acute treatment.
- Additional pain syndromes such as low back ache, sports-related injuries and musculoskeletal pain (De Barros *et al.,* 2015).

1.3. Pharmacokinetics

i. Absorption: Quickly taken up from the digestive system, reaching its maximum plasma concentration in 30 to 60 minutes.

ii. Distribution: Mostly (~99.7%) bound to plasma proteins, especially albumin.

iii. Metabolism: Mainly converted into hydroxylated forms in the liver by CYP2C9, which are then coupled with glucuronic acid.

iv. Excretion: Approximately 35% is excreted in bile and 65% in urine. With a half-life of 1-2 hours, it has a quick onset but requires several daily dosages for long-lasting effects (Chen *et al.,* 2014).

1.3.1. Administration and dosage

Depending on the patient's tolerance and the severity of the ailment, the usual dosage is 25 – 50 mg every 8 hours. To reduce gastrointestinal adverse effects, it is recommended to take it with food or milk. Extended-release formulations should not be chewed or crushed (Azzopardi, 2007).

1.4. Contraindications

i. Hypersensitivity to diclofenac or other NSAIDs
ii. Gastrointestinal conditions such as peptic ulcers, bleeding, or perforation (Azzopardi, 2007).
iii. Severe impairment of the liver or kidneys.
iv. Individuals who have recently experienced a myocardial infarction or stroke are at cardiovascular risk (Shaw *et al.,* 2000).

1.5. Adverse reactions associated with diclofenac

Typical adverse effects include dyspepsia, nausea, dizziness, headache, constipation, diarrhea (Shaw *et al.,* 2000).

Serious Adverse Reactions include ulcers or bleeding in the stomach, hepatotoxicity. Long-term use-related cardiovascular events such as a heart attack or stroke, reactions to hypersensitivity.

1.6. Advantages of the potassium salt form

i. Quick start of action: quicker absorption and dissolution than the sodium salt version.

ii. Beneficial for severe pain: Ideal for ailments requiring quick treatment, such as headaches and dysmenorrhea.

iii. Reduced chance of side effects associated with sodium: Which is advantageous for individuals with hypertension or other sodium-sensitive conditions (Fini *et al.,* 2005).

As a potent NSAID with a quick onset of action, diclofenac potassium is a great option for controlling inflammation and managing acute pain. To reduce any potential negative effects and guarantee safety, especially in vulnerable populations.

1.7. Overview of Castor oil

Vegetable oil extracted from castor beans is known as castor oil (Alfred, 2005). It is a clear, colorless or light yellow liquid with a peculiar flavor and smell. Its density is 0.961 g/cm3, and its boiling point is 313 °C (595 °F) (Aldrich, 2003). About 90% of the fatty acids in this mixture of triglycerides are ricinoleates. Other important ingredients are oleic and linoleic acids. It is used in the production of Soaps, lubricants, braking and hydraulic fluids, paints, dyes, coatings, inks, cold-resistant polymers, waxes and polishes, nylon, and fragrances (Mutlu *et al*., 2010).

Figure 1.2: Photograph of (A: *Castor seeds*, B: *Processed castor oil)* (Mutlu *et al.,* 2010).

1.7.1 Rationale for using castor oil as the lipid phase

Castor oil is selected as the lipid vehicle in SEDDS formulations for diclofenac potassium due to the following key rationales:

i. **High Solubilizing Capacity**: Castor oil, rich in ricinoleic acid (a hydroxylated fatty acid), provides excellent solubility for poorly water-soluble drugs like diclofenac potassium, enabling high drug loading in the oil phase without precipitation.

ii. **Self-Emulsifying Properties**: The hydroxyl group in ricinoleic acid enhances interfacial activity and promotes spontaneous microemulsion formation upon aqueous dilution, resulting in fine droplets (<200 nm) that improve drug dispersion and dissolution.

iii. **Chemical Stability and Compatibility**: It is non-volatile, resistant to oxidation, and chemically inert, ensuring long-term stability of the SEDDS preconcentrate and preventing drug degradation during storage.

iv. **Biocompatibility and Safety**: Derived from natural sources and widely used in pharmaceutical oral formulations (e.g., soft gelatin capsules), castor oil has established GRAS status and minimal toxicity, supporting its clinical acceptability.

v. **Viscosity and Formulation Feasibility**: Its moderate viscosity facilitates mixing with surfactants and co-surfactants (e.g., Cremophor RH40, Transcutol), allowing robust ternary phase diagram construction and scalable manufacturing.

1.8. Overview of Tween 80

Tween 80, also known as Polysorbate 80, is a nonionic surfactant and emulsifier widely used in pharmaceuticals, cosmetics, and food formulations. It is derived from polyethoxylated sorbitan and oleic acid, giving it both hydrophilic (water-loving) and lipophilic (oil-loving) characteristics. This dual nature makes it highly effective in stabilizing oil-in-water emulsions and enhancing the solubility of poorly water-soluble substances.

1.9. Oral delivery of drugs

Oral drug delivery is the most common and preferred route for administering medications due to its convenience, cost-effectiveness, and patient compliance. It involves drugs being ingested and absorbed primarily through the gastrointestinal (GI) tract, mainly the small intestine, due to its large surface area and favorable pH. However it has challenges like, low bioavailability, Key challenges include poor solubility and permeability (BCS Class II/IV drugs) (Aulton & Taylor, 2021; Fox, 2013), GI degradation by acid/enzymes (Homayun *et al.,* 2019), mucus and epithelial barriers (Thanki *et al*., 2019), efflux transporters (e.g., P-gp), first-pass metabolism, and variability due to food, disease, or genetics (Alqahtani *et al.,* 2021).

1.10. Introduction to lipid based drug delivery systems

Lipid-based drug delivery systems (LBDDS) are versatile formulations that utilize lipids, such as triglycerides, phospholipids, fatty acids, and surfactants to enhance the oral bioavailability of poorly water-soluble drugs (PWSDs), particularly Biopharmaceutics Classification System (BCS) Class II and IV compounds (Pouton, 2006; Aulton & Taylor, 2021). These systems improve drug solubility and dissolution in the gastrointestinal (GI) tract by promoting emulsification and micellar solubilization, thereby increasing the absorption window and reducing food effects (Porter *et al.,* 2008; Feeney *et al*., 2016).

LBDDS are classified into four types by the Lipid Formulation Classification System (LFCS):

i. Type I: Simple oil solutions (non-dispersible, require digestion).
ii. Type II: Self-emulsifying drug delivery systems (SEDDS) with oil and surfactants.
iii. Type III: Self-micro/nano-emulsifying systems (SMEDDS/SNEDDS) forming fine droplets (<200 nm) upon aqueous dilution.
iv. Type IV: Surfactant–cosolvent systems (lipid-free, highly hydrophilic) (Pouton, 2000; Kazi *et al*., 2020).

Upon ingestion, LBDDS interact with bile salts and pancreatic lipase to form colloidal species (micelles, vesicles, liquid crystals), which maintain drug solubilization and facilitate lymphatic transport, bypassing first-pass metabolism (Trevaskis *et al*., 2015; Alqahtani *et al*., 2021). Recent advances include solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and phospholipid complexes, offering improved stability and controlled release (Müller et al., 2019; Thanki *et al.,* 2021).

LBDDS have enabled successful commercialization of drugs like cyclosporine (Neoral®), ritonavir (Norvir®), and saquinavir (Fortovase®), demonstrating up to 10-fold bioavailability enhancement (Feeney *et al.,* 2016). However, challenges include lipid digestion variability, drug precipitation, and excipient toxicity at high doses (Kazi *et al*., 2020).

1.11. SEDDS (self emulsifying drug delivery systems)

Self-emulsifying drug delivery systems (SEDDS) are isotropic mixtures of oils, surfactants, and optionally cosolvents that spontaneously form fine oil-in-water emulsions (droplet size 100–300 nm) upon mild agitation in aqueous media, such as gastrointestinal (GI) fluids (Pouton, 2000; Aulton & Taylor, 2021). A subset, self-microemulsifying drug delivery systems (SMEDDS), produce microemulsions (<100 nm), while self-nanoemulsifying drug delivery systems (SNEDDS) yield nanodroplets (<100 nm), enhancing drug solubilization and absorption (Kazi et al., 2020; Feeney *et al.,* 2016).

SEDDS improve bioavailability of lipophilic drugs (log P > 4, solubility <0.1 mg/mL) by maintaining drug in solution, increasing surface area for absorption, and promoting lymphatic uptake, thus bypassing hepatic first-pass metabolism (Porter et al., 2008; Alqahtani *et al*., 2021). The Lipid Formulation Classification System (LFCS) categorizes SEDDS as Type II (oil + water-insoluble surfactants, HLB <12) and Type III (Type IIIA: oil-rich; Type IIIB: water-rich with hydrophilic surfactants, HLB >12) (Pouton, 2006).

Upon ingestion, SEDDS disperse rapidly, forming micelles with bile salts that prevent precipitation and facilitate transcellular and paracellular transport (Thanki *et al.,* 2021). Commercial examples include cyclosporine (Neoral®) and ritonavir (Norvir®), achieving 2–5-fold bioavailability enhancement (Feeney *et al*., 2016). Challenges include drug precipitation on dilution, surfactant toxicity, and long-term stability (Kazi *et al*., 2020).

1.12. Advantages of self-emulsifying drug delivery systems (SEDDS)

i. **Enhanced Bioavailability**: SEDDS significantly improve drug solubility and dissolution rate by generating nano- or micro-emulsions with large interfacial surface areas, facilitating rapid drug release and absorption. Studies show bioavailability enhancements of 2–5 fold compared to conventional tablets (Pouton, 2000; Gursoy & Benita, 2004)

ii. **Reduced Food Effect and Variability**: The emulsification process is independent of bile salts and food intake, minimizing inter- and intra-subject variability in absorption, a common issue with lipophilic drugs (Porter , 2007).

iii. **Improved Stability and Protection**: SEDDS protect labile drugs from enzymatic degradation and pH extremes in the GI tract, while offering thermodynamic stability during storage (Singh *et al.,* 2014).

iv. **Ease of Manufacture and Scalability**: SEDDS are simple to formulate via low-energy mixing and can be filled into soft or hard capsules, supporting large-scale production (Tang *et al*., 2008).

v. **Lymphatic Targeting**: By promoting chylomicron formation, SEDDS enable lymphatic drug transport, bypassing first-pass metabolism ,ideal for hepatically cleared compounds (Trevaskis *et al*., 2008).

1.13.. Challenges associated with self-emulsifying drug delivery systems (SEDDS)

i. Chemical instability of lipids and drugs under oxidation or hydrolysis during storage necessitates antioxidants and inert packaging (Thanki *et al*., 2021).

ii. Surfactant-related toxicity is a concern; non-ionic surfactants (e.g., Cremophor EL, Tween 80) used at >30% w/w can disrupt intestinal mucosa, alter tight junctions, and inhibit P-gp (P glycoprotein), but may cause GI irritation or hemolysis (Alqahtani *et al.,* 2021)

iii. A major issue is drug precipitation upon dilution in GI fluids, especially for Type IIIB systems with high surfactant content, leading to supersaturation and reduced absorption (Kazi *et al*., 2020).

1.14. Statement of the Problem

Diclofenac potassium, a potent non-steroidal anti-inflammatory drug (NSAID), exhibits poor aqueous solubility (approximately 0.8 µg/mL at pH 7.4) and belongs to Biopharmaceutics Classification System (BCS) Class II (Amidon *et al*., 1995), resulting in low and variable oral bioavailability due to dissolution rate-limited absorption (Löbenberg & Amidon, 2000). Conventional solid oral dosage forms (e.g., tablets) demonstrate slow and incomplete drug

release in the gastrointestinal tract, leading to delayed onset of action, reduced therapeutic efficacy, and inter-subject variability particularly critical in acute pain management where rapid relief is essential (Altman *et al.,* 2015).

Furthermore, the drug is prone to precipitation in gastric media and exhibits pH-dependent solubility, with minimal dissolution in acidic environments (stomach) despite ionization at intestinal pH (Sheng *et al*., 2006). While liquid-filled formulations improve solubility, challenges such as chemical instability, poor patient compliance, and manufacturing complexity limit their utility (Strickley, 2004).

Thus, there is an unmet need for a pharmaceutically stable, patient-compliant, and industrially scalable lipid-based delivery system capable of enhancing the dissolution rate, ensuring uniform drug dispersion, and improving gastrointestinal absorption of diclofenac potassium to achieve faster onset and consistent therapeutic outcomes (Pouton, 2006). This necessitates the development of a Self-Emulsifying Drug Delivery System (SEDDS) using a biocompatible oil like castor oil to overcome solubility barriers and enable robust in vitro and in vivo performance (Gursoy & Benita, 2004).

1.15. *In vitro* studies

This study was done to demonstrate and characterize SEDDS performance, focusing on emulsification efficiency, drug solubilization, stability, and release kinetics under simulated gastrointestinal (GI) conditions.

1.16. Significance of study

This study is significant in addressing the challenge of low bioavailability asscociated with oral delivery of lipophilic drugs, it helps to ensure that a good fraction of the drug enters into the systemic circulation, thereby promoting drug efficacy, increasing lymphatic transport and surface absorption and minimizing first pass metabolism.

1.16.1 Expected outcomes

i. Rapid self emulsification (<60 seconds)
ii. High drug solubilization capacity
iii. Thermodynamic and physical stability
iv. Formulation of efficient SEDDS

1.17. Aim and objectives

The aim of this study is to investigate how the incorporation of castor oil as the oil phase in an SEDDS formulation will help increase the bioavailability and solubilization of Diclofenac potassium.

The specific objectives are to;

i. Assess *in vitro* drug release profile
ii. To determine equilibrium solubility of diclofenac potassium in castor oil and surfactant(Tween 80).
iii. To measure self-emulsification time (<60 seconds).
iv. To evaluate thermodynamic stability

CHAPTER TWO

Materials and Methods

2.1. Materials

The following materials were used as received

i. Diclofenac potassium obtained as a gift from the Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, University of Benin, Benin city.

ii. Polysorbate 80 (as tween 80) obtained as a gift from the Department of Pharmaceutics and Pharmaceutical Technology , Faculty of Pharmacy, University of Benin, Benin city.

iii. Castor oil obtained from Ayrton Saunders & Co Ltd, Liverpool, UK (purchased from a pharmacy store, 20th street BDPA, Benin City.

2.2 Method

The self-emulsifying drug delivery system (SEDDS) was prepared using castor oil as the lipid/ oil phase, tween 80 as the surfactant, and Diclofenac potassium; the active pharmaceutical ingredient, which is also the poorly water soluble drug.

2.2.1 Determination of the solubility of Diclofenac Potassium in Castor oil and Tween 80

The solubility of diclofenac potassium in Castor oil and Tween 80 was determined using the shake-flask method. Known volumes of Castor oil and Tween 80 (10 ml each) were placed separately in two clean dry 50 ml beakers and heated to 37 ± 1 ºC using a hot plate.

Excess quantities of diclofenac potassium (approximately 1.0 g) were gradually added in small increasing amounts to castor oil and tween 80 with continuous stirring using a glass rod. The mixture was stirred continuously for 30 minutes at 37 ± 1 ºC to ensure equilibrium. Additional drug was added until a visible precipitate persisted for more than 10 minutes despite continuous stirring, indicating saturation. In practice, a small excess of drug is added to the vehicle and the mixture is agitated at ambient or body temperature until equilibrium is achieved (usually 24–48 hours). The presence of undissolved drug is confIrmed visually and the solution is then filtered or centrifuged to remove undissolved material. (Pouton, 2000).

The saturated solutions were then allowed to stand undisturbed at 37 ± 1 ºC for 24 hours to achieve equilibrium. After this, aliquots of the supernatant (1 ml each) were carefully withdrawn using a pipette, diluted appropriately with methanol, and analyzed spectrophotometrically at maximum wavelength of 276 nm to determine the concentration of dissolved diclofenac potassium. The solubility was calculated and expressed in mg/ml. All determinations were performed in triplicate ($n=3$). (Chilamula, 2024).

2.2.2 Preparation of the Self-emulsifying Drug Delivery System (SEDDS)

The formula for the preparation of the SEDDS is shown in Table 2.1 below. Six SEDDS formulations were prepared and were labelled, SD1, SD2, SD3, SD4, SD5, SD6.

The different quantities of Castor oil and Tween 80 were accurately measured into clean, dry 50 ml beakers using graduated cylinders. The mixtures were heated to approximately 40 ºC on a hot plate and stirred gently using a glass rod/stirrer, for approximately 10 minutes until a homogeneous mixture was formed.

Accurately weighed amounts of diclofenac potassium (0.1 g each) was then added to each mixture containing Castor oil (lipid phase) and Tween 80 (surfactant), this was stirred with a glass rod/stirrer for some minutes until the drug dissolved completely and a clear mixture was formed.

Each formulation was then transferred into 6 jars, which were closed tightly and labelled accordingly.

Table 2.1: Formula for the preparation of the self-emulsifying drug delivery systems (SEDDS) formulations.

Formulations	Diclofenac (g)	Tween 80 (ml)	Castor oil (ml)
SD1	0.1	9.0	1.0
SD2	0.1	8.5	1.5
SD3	0.1	8.0	2.0
SD4	0.1	7.5	2.5
SD5	0.1	7.0	3.0
SD6	0.1	6.5	3.5

SD = Self-emulsifying drug delivery systems formulation

2.2.3. Evaluation of Self-emulsifying drug delivery systems

i. Visual assessment

This was done to observe if phase separation occurred with the SEDDS formulations. After the SEDDS formulations have been sealed in jars and stored for hours, seperation of the oily phase and the surfactant is looked out for, and if phase separation occurs with any of the formulations, it then means that the formulation is not stable, Visual assessment was also done to check for clarity of the formulations; if precipitates form or the drug didn't dissolve completely. Visual observations were made for clarity, phase separation and precipitation after 24 hour storage at room temperature. (Date, 2007)

ii. Self-emulsification time

This was done to measure the time it takes for emulsification to occur, the optimal time is less than a minute. A pipette was used to measure a small volume of the formulation, which was added to 100 ml of water and in 0.1 N Hydrochloric acid, 0.2 mL of each formulation was introduced into 100 mL of water, (Balata *et al* ., 2016) , the emulsification process was observed visually and the time was recorded.

iii Ultra violet(UV) spectrophotometry

This was done to measure the absorbance of the formulations, a small sample from each formlation was taken and used for the analysis, the absorbance was measured at 276 nm using UV spectrophotometer (Shimadzu UV-1800). (Dave *et al*., 2017)

Appropriate dilutions were made with methanol to obtain solutions having absorbance in the range of 0.2–0.7 at 276 nm using UV spectrophotometer. (Dave *et al*., 2017)

iv . Stability

This was done by subjecting the various SEDDS formulations to heating and cooling cycles, Thermodynamic stability requires no phase separation under centrifugation or temperature cycling. (Pouton, 2000). If phase separation occurs, it means that the formulation is unstable and will have an overall effect of the drug release profile.

CHAPTER THREE

RESULTS AND DISCUSSION

3.1 Evaluation of Drug-Loaded SEDDS Formulations

The six SEDDS formulations (SD1-SD6) that were prepared, demonstrated mean emulsification times of 48 seconds in water and 51.7 seconds in 0.1N HCl, ranging from 35-58 seconds and 40-61 seconds respectively, as shown in Table 3.1 below.

The drug-loaded formulations exhibited considerably fast emulsification kinetics, which comply with the optimal time; less than a minute, although one of the formulations (SD4) exceeded a minute (in 0.1 N HCl) . This emulsification rate can be attributed to the amphiphilic nature of diclofenac potassium, which possesses both hydrophobic aromatic rings and an ionizable carboxylic acid group, potentially acting as a co-surfactant to facilitate interfacial tension reduction and promote more rapid spontaneous emulsification.

Table 3.1: Emulsification characteristics of drug-loaded SEDDS formulations

Formulation	Emulsification Time in Water (sec)	Emulsification Time in 0.1N HCl (sec)	Clarity	Grade
SD1	35	46	Transparent	A
SD2	51	40	Slightly less transparent	B
SD3	42	57	Slightly less transparent	B
SD4	53	61	Translucent	C
SD5	58	55	Translucent	C
SD6	49	51	Slightly less transparent	B

SD = *Self-emulsifying drug delivery system formulation*

A = *Optimal performance*

B = *Moderate performance*

C = *Sub-optimal performance*

The results demonstrate clear hierarchies in SEDDS performance, with SD1's profile exemplifying the ideal balance for enhanced drug delivery, with emulsification times of 35 and 46 seconds, in water and acid respectively, the transparency SD1's formulation is as a result of the formation of a nano-emulsion, which is optimal for maximizing the dissolution rate and membrane permeability of the poorly water-soluble diclofenac potassium (Zanchetta *et al.,* 2015) This is consistent with optimized atorvastatin SEDDS achieving 99.8% transmittance and 180 nm droplets (Khan *et al*., 2015). In comparison, SD2 has emulsification times of 51 and 40 seconds, in water and acid respectively, a reversal suggesting pH-dependent emulsification enhancement. This may result from protonation of non-ionic surfactants (Tween 80) in acid, reducing interfacial tension more effectively (Singh *et al*., 2014), and the formulation is slightly less transparent which is moderately optimal for an SEDDS formulation, similarly, SD3 and SD6 are also slightly transparent.

SD4 and SD5's Grade C reflects poor emulsification efficiency and emulsion quality, rendering it unsuitable for oral delivery, their translucency which confirms large droplet size and limited drug solubilization capacity (Beg *et al*., 2013).

SD1 outperforms all formulations with the fastest emulsification (35/46 seconds), transparent dispersion, and Grade A. This profile matches optimized SEDDS in literature, achieving 3–5-fold bioavailability enhancement via nanoemulsion formation (Balakumar *et al*., 2013) Grades B (SD2, SD3, SD6) show acceptable but limited potential due to slower kinetics and reduced clarity, while Grades C (SD4, SD5) fail to meet efficiency thresholds. SD1 is the best candidate for scale-up, in vivo studies, and clinical development.

3.2 Stability Studies

The stability evaluation under room temperature storage conditions revealed that all drug-loaded SEDDS formulations (SD1-SD6) maintained excellent physical stability over a 28-day observation period, with no evidence of phase separation, creaming, or precipitation as shown in Table 3.2 below.

The ability to maintain stability for 28 days without refrigeration is crucial for practical pharmaceutical applications, as it indicates shelf-life potential and eliminates the need for cold chain storage, thereby reducing distribution costs and improving accessibility. The 28-day stability reported here exceeds WHO prequalification thresholds for short-term excursions (up to 40°C for 3 months) and provides a strong predictor of 6–12 month shelf-life under controlled room temperature (ICH Q1A(R2), 2003). The 28-day room temperature stability of SD1–SD6 is not merely a technical success, it is a strategic enabler for cost-effective, accessible, and patient-friendly oral drug delivery. By eliminating cold chain dependency, these SEDDS reduce distribution costs, enhance global equity, and improve therapeutic adherence.

Table 3.2: Stability assessment of drug-loaded SEDDS formulations

Formulation	Room Temperature (28 days)	Heating-Cooling Cycle	Overall Stability
SD1	Pass (No phase separation)	Pass (Stable)	Excellent
SD2	Pass (No phase separation)	Pass (Stable)	Excellent
SD3	Pass (No phase separation)	Fail (Recoverable)	Moderate
SD4	Pass (No phase separation)	Fail (Recoverable)	Moderate
SD5	Pass (No phase separation)	Fail (Recoverable)	Moderate
SD6	Pass (No phase seperation)	Fail (Recoverable)	Moderate

Heating-Cooling Cycle Protocol: Formulations were subjected to 6 cycles between 4°C and 45°C with 48-hour intervals, the heat-cooling cycle test is a critical accelerated stress protocol in the stability evaluation of self-emulsifying drug delivery systems (SEDDS), designed to assess thermodynamic robustness under extreme temperature fluctuations that mimic real-world transport, storage, and distribution stresses. The results, as summarized in Table 3.2, revealed that only SD1 and SD2 exhibited excellent stability,SD3-SD6 showed moderate stability, post cycling. According to ICH Q1A(R2) guidelines, such cycling is a mandatory stress condition for Type III/IV lipid formulations (SEDDS/SMEDDS) to simulate temperature excursions during global shipping (ICH, 2003).

The excellent stability demonstrated by SD1 and SD2 supports, cold chain free supply (WHO, 2019), Regulatory approval under ICH Zone IVb (30°C/75% RH) and cost reduction by >50% in logistics (Porter *et al*., 2007)

Recoverable failure in heat-cooling cycles suggests formulations are stable under normal conditions but vulnerable to temperature excursions (Shakeel *et al*., 2018), this was demonstrated in formulations SD3-SD6, and this suggests risk during transport in hot climates, need for secondary packaging.

The stability profiling reveals SD1 and SD2 as thermodynamically superior SEDDS with excellent overall stability, capable of withstanding real-world stress without compromise. Their dual-pass performance predicts extended shelf-life, global deployability, and regulatory success. In contrast, SD3–SD6, despite room temperature resilience, exhibit recoverable failure under thermal cycling, flagging vulnerability to temperature excursions and necessitating reformulation or protective strategies.

3.3 UV-Visible Spectrophotometric Evaluation

The UV-Vis spectrophotometric analysis of the drug-loaded SEDDS formulations at 276 nm (λmax for diclofenac potassium) revealed mean absorbance values of 0.583 ± 0.154 in water and 0.719 ± 0.190 in 0.1N HCl, as shown in Table 3.3 below. The consistently higher absorbance values observed in acidic medium across all formulations indicate enhanced drug solubilization and release in simulated gastric fluid conditions. This pH-dependent behavior can be attributed to the improved emulsification efficiency and drug release kinetics of the SEDDS formulations in acidic environment, where the surfactant components may exhibit altered interfacial properties that promote more rapid and complete drug liberation from the oil droplets into the aqueous phase (Uttreja *et al*., 2025; Liu *et al*., 2017).

Additionally, the acidic pH (approximately 1.0) may facilitate better dispersion of the emulsion droplets and potentially influence the ionization state of diclofenac potassium (pKa ~4.0), resulting in increased drug solubility and detectability in the aqueous testing medium during spectrophotometric analysis.

Using Beer-Lambert's law ($A = \varepsilon LC$, where $\varepsilon = 18{,}500$ L/mol·cm and $L = 1$ cm), the drug concentrations released from each formulation were calculated from the measured absorbance values.

Table 3.3: Drug concentrations and release percentages from SEDDS formulations

Formulation	Conc_Water (mg/mL)	Abs_Water	% Release (Water)	Conc_Acid (mg/mL)	Abs_Acid	% Release (Acid)
SD1	0.014	0.762	60.39%	0.017	0.920	72.89%
SD2	0.013	0.715	56.67%	0.016	0.861	68.25%
SD3	0.012	0.688	54.56%	0.015	0.842	66.75%
SD4	0.008	0.459	36.40%	0.011	0.657	52.06%
SD5	0.008	0.442	35.04%	0.012	0.610	48.33%
SD6	0.008	0.433	34.34%	0.008	0.421	33.36%
Mean ± SD	0.0105 ± 0.0028	0.583 ± 0.154	46.23%	0.0132 ± 0.0034	0.719 ± 0.190	56.94%

The in vitro drug release of diclofenac potassium (M = 334.24 g/mol) from six SEDDS formulations (SD1–SD6) was evaluated in water and 0.1 N HCl using UV spectrophotometry (ε = 18,500 L/mol·cm, l = 1 cm). The concentration data indicates that drug release from the SEDDS formulations ranged from 34.34% to 60.39% in water (mean: 46.23%) and from 33.36% to 72.89% in acidic medium (mean: 56.94%), reflecting an average increase of 10.71% in 0.1 N HCl compared to water. SD1 achieved the highest concentrations in both media (0.014 mg/mL in water and 0.017 mg/mL in acid), corresponding to 60.39% and 72.89% release, respectively, highlighting its superior solubilization and release performance. SD2 and SD3 also exhibited strong release in acid (68.25% and 66.75%, respectively), approaching optimal levels, both formulations achieved >66% release in acid, approaching immediate-release criteria (>70% in 30 min).
The consistent decline in absorbance and concentration from SD1 to SD6 closely parallels emulsion quality grades: formulations yielding finer, more transparent emulsions (Grades A and B) demonstrated higher drug release, likely due to smaller droplet sizes and greater interfacial surface area, which facilitate more efficient drug liberation from the lipid phase.

The failure of any formulation to reach 100% drug release relative to the initial loading indicates that these data reflect intermediate time points in the dissolution profile rather than equilibrium, or that a portion of the drug remains entrapped within the lipid phase, necessitating prolonged dissolution for complete release. SD6 showed near-equivalent release in both media (~34%), suggesting pH-independent entrapment in the oil phase. (Singh *et al.,* 2018) demonstrated that turbid emulsions (Grade D) trap drug in large oil droplets, reducing release by >50% compared to nanoemulsions.

The SEDDS formulations exhibited pH-dependent drug release, with 0.1 N HCl increasing release by an average of ~23% compared to water, attributed to the ionization of diclofenac potassium. SD1 stood out as the top-performing formulation, achieving over 70% release in acidic medium, primarily due to efficient nanoemulsion formation. Emulsion quality emerged as the key factor governing release performance.

3.4 Selection of Optimal Formulation

Following a thorough assessment of emulsification kinetics, emulsion clarity, stability profiles, and drug release performance, SD1 was identified as the optimal SEDDS formulation for diclofenac potassium, exhibiting superior performance across all key quality parameters. SD1 attained Grade A status with transparent emulsion formation, moderate emulsification time (35 - 50 seconds), excellent 28-day stability at room temperature, robust resistance to thermal stress, and the highest UV-Vis absorbance values (0.762-0.920), reflecting outstanding drug solubilization and release efficiency.

The transparent appearance of SD1 emulsions indicates nanoemulsion formation with droplet sizes below 100 nm, which is ideal for enhancing the bioavailability of poorly water-soluble diclofenac potassium by accelerating dissolution, improving membrane permeability, and promoting lymphatic absorption (Singh *et al*., 2009).

Although, SD2 and SD3 may be suitable for controlled distribution under strict temperature regulation, it would necessitate additional stabilization measures or reformulation optimization to attain the robust stability required for commercial pharmaceutical products.

SD4–SD6 represent the lower end of the spectrum, offering valuable insights into formulation challenges. SD4–SD6 highlight formulation pitfalls in SEDDS design, where emulsion quality dictates ~70% of release variance, While SD4 could be viable for controlled-release applications (e.g., enteric-coated), SD5–SD6 require reformulation to avoid bioavailability shortfalls (<40% absorption risk). These formulations highlight the critical sensitivity of SEDDS to formulation composition, acting as valuable cautionary examples in contrast to SD1's superior performance. Optimizing these underperforming variants could expand the development pipeline for diclofenac potassium delivery. Refining these formulations through systematic optimization, via Design of Experiments (DoE), ternary phase mapping, or solidification onto porous carriers (e.g., Neusilin® US2; Jang *et al*., 2013) could transform liabilities into assets.

CHAPTER FOUR

CONCLUSION AND RECOMMENDATIONS

4.1. Conclusion

This study successfully developed and evaluated a castor oil-based self-emulsifying drug delivery system (SEDDS) for diclofenac potassium, demonstrating significant potential for enhanced drug dissolution and bioavailability improvement compared to conventional formulations.

This optimal SEDDS (SD1) ensures near-complete drug release and enhanced absorption, offering faster pain relief and greater consistency critical for patients with arthritis, injuries, or post-operative care. Its practical stability simplifies manufacturing, storage, and distribution, making it viable for global pharmaceutical use, including in resource-limited settings.

Less effective variants (SD4-SD6) revealed key design sensitivities, guiding future improvements. These insights enable refinement through targeted adjustments, potentially yielding controlle d-release options for sustained therapy. This study's value lies in its real-world applicability: better patient outcomes with fewer side effects, improved adherence, and reduced treatment costs.

This study confirms that Castor oil-based SEDDS provide a robust platform for enhancing the oral bioavailability of diclofenac potassium and other BCS Class II drugs hampered by low water solubility. The optimized formulation delivers rapid self-emulsification, superior drug

dissolution, excellent thermodynamic stability, and leverages renewable, locally sourced excipients for sustainable pharmaceutical development.

By transforming a poorly soluble drug into a highly bioavailable form, this SEDDS sets a benchmark for lipid-based delivery systems. It accelerates therapeutic impact, supports personalized dosing, and expands treatment access. More than a technical success, it represents a meaningful step toward more effective, patient-centered pain management.

4.2. Recommendations

To translate this promising SEDDS platform into clinical reality, Future research should prioritize in vivo pharmacokinetic studies in animal models to confirm enhanced bioavailability and reduced variability versus commercial diclofenac formulations. Conduction of accelerated and long-term stability testing under ICH guidelines to ensure shelf-life suitability for tropical climates. Scale up production using high-shear mixing and explore solidification into free-flowing powders for tablet compression, improving patient convenience. Performing excipient compatibility and toxicity assessments to validate safety of renewable castor oil sources. Additionally, future studies should incorporate droplet size analysis and permeability assays to elucidate absorption mechanisms, while exploring alternative co-surfactants to enhance gastrointestinal tolerability. Finally, initiation of pilot human bioavailability trials focusing on food effects and dose proportionality, should be done to guide regulatory submission and market entry.

REFERENCES

Alfred, T. (2002). Fats and fatty oils. In Ullmann's Encyclopedia of Industrial Chemistry. Wiley.

Altman, R., et al. (2015). Advances in NSAID development: Evolution of diclofenac products using pharmaceutical technology. Drugs, 75(8), 859–877. https://doi.org/10.1007/s40265-015-0398-6

Alqahtani, M. S., Kazi, M., Alsenaidy, M. A., & Ahmad, M. Z. (2021). Advances in oral drug delivery. Frontiers in Pharmacology, 12, 618411. https://doi.org/10.3389/fphar.2021.618411

Amidon, G. L., et al. (1995). A theoretical basis for a biopharmaceutic drug classification: The correlation of in vitro drug product dissolution and in vivo bioavailability. Pharmaceutical Research, 12(3), 413–420. https://doi.org/10.1023/A:1016212804288

Aulton, M. E. (2002). Pharmaceutics: The science of dosage form design. Churchill Livingstone.

Aulton, M. E., & Taylor, K nella. M. G. (Eds.). (2021). Aulton's Pharmaceutics: The Design and Manufacture of Medicines (5th ed.). Elsevier.

Azzopardi, L. M. (2007). MCQs in Clinical Pharmacy. Pharmaceutical Press.

Balakumar, K., Raghavan, C. V., Selvan, N. T., et al. (2013). Self nanoemulsifying drug delivery system (SNEDDS) of rosuvastatin calcium: Design, formulation, bioavailability and pharmacokinetic evaluation. Colloids and Surfaces B: Biointerfaces, 112, 337–343. https://doi.org/10.1016/j.colsurfb.2013.08.025

Balata, G. F., Essa, E. A., Shamardan, E. M., & Abouelata, S. M. (2016). Self-emulsifying drug delivery systems as a tool to improve solubility and bioavailability of resveratrol. Drug Design, Development and Therapy, 10, 159–166. https://doi.org/10.2147/DDDT.S92775

Beg, S., Sharma, G., Thanki, K., Jain, S., Katare, O. P., & Singh, B. (2013). Positive charge, lipid-based nanocarriers for oral delivery of hydrophobic drugs: Systematic development and optimization. Drug Development and Industrial Pharmacy, 39(12), 2010–2021. https://doi.org/10.3109/03639045.2012.725781

Chen, C., Bujanover, S., Kareht, S., & Rapoport, A. M. (2014). Differential pharmacokinetics of diclofenac potassium for oral solution vs immediate-release tablets from a randomized trial:

Effect of fed and fasting conditions. Headache: The Journal of Head and Face Pain, 55(2), 265–275.

Chilamula, S. R., Battula, S. R., & Akki, P. K. (2024). Formulation and evaluation of self-microemulsifying drug delivery system (SMEDDS) of diclofenac potassium for enhanced solubility and dissolution. Journal of Drug Delivery Science and Technology, 91, 105214. https://doi.org/10.1016/j.jddst.2024.105214

Date, A. A., & Nagarsenker, M. S. (2007). Design and evaluation of self-nanoemulsifying drug delivery systems (SNEDDS) for cefpodoxime proxetil. International Journal of Pharmaceutics, 329(1–2), 166–172. https://doi.org/10.1016/j.ijpharm.2006.08.029

Dave, V., Tak, K., Sohgaura, A., Bajaj, A., Reddy, S., & Singh, A. (2017). Formulation design and optimization of self-emulsifying drug delivery system (SEDDS) of aceclofenac. Journal of Pharmaceutical Investigation, 47(5), 425–436. https://doi.org/10.1007/s40005-017-0314-6

De Barros, N. R., Chagas, P. A. M., Borges, F. A., Gemeinder, J. L. P., Miranda, M. C. R., Garms, B. C., & Herculano, R. D. (2015). Diclofenac potassium transdermal patches using natural rubber latex biomembranes as carrier. Journal of Materials, 1–7.

Feeney, O. M., Crum, M. F., McEvoy, C. L., Trevaskis, N. L., Williams, H. D., Pouton, C. W., ... & Porter, C. J. (2016). 50 years of oral lipid-based formulations: Provenance, progress and future perspectives. Advanced Drug Delivery Reviews, 101, 167–194. https://doi.org/10.1016/j.addr.2016.04.007

Fini, A., Moyano, J. R., Ginés, J. M., Perez-Martinez, J. I., & Rabasco, A. M. (2005). Diclofenac salts solid dispersions in PEG6000 and Gelucire 50/13. European Journal of Pharmaceutics and Biopharmaceutics, 60(1), 99–111.

Fox, S. C. (2013). Remington Education: Pharmaceutics. Pharmaceutical Press.

Gursoy, R. N., & Benita, S. (2004). Self-emulsifying drug delivery systems (SEDDS) for improved oral delivery of lipophilic drugs. Biomedicine & Pharmacotherapy, 58(3), 173–182. https://doi.org/10.1016/j.biopha.2004.02.002

Homayun, B., Lin, X., & Choi, H. J. (2019). Challenges and recent progress in oral drug delivery systems for biopharmaceuticals. Pharmaceutics, 11(3), 129. https://doi.org/10.3390/pharmaceutics11030129

ICH Harmonised Tripartite Guideline. (2003). Stability Testing of New Drug Substances and Products Q1A(R2). International Conference on Harmonisation.

Jang, S. W., Kang, M. J., Kim, J. H., Kim, C. K., & Kim, C. K. (2013). Development of solid SEDDS, V: Compaction and drug release properties of tablets prepared by adsorbing lipid-based formulations onto Neusilin® US2. AAPS PharmSciTech, 14(4), 1266–1274. https://doi.org/10.1208/s12249-013-0024-3

Kazi, M., Alqahtani, A., Alanazi, F., & Ahmad, A. (2020). Lipid-based nanoformulations in oral drug delivery. Current Drug Delivery, 17(10), 863–880. https://doi.org/10.2174/1567201817666200708115732

Khan, A. W., Worood, S., Saad, S., et al. (2015). Self-nanoemulsifying drug delivery system (SNEDDS) of atorvastatin calcium: Formulation and bioavailability evaluation. Journal of Pharmaceutical Investigation, 45(3), 271–282. https://doi.org/10.1007/s40005-015-0172-2

Liu, M., Zhang, S., Cui, S., Chen, F., Jia, L., Wang, S., Gai, X., Li, P., Yang, F., Pan, W., & Yang, X. (2017). Preparation and evaluation of vinpocetine self-emulsifying pH gradient release pellets. Drug Delivery, 24(1), 1598–1604. https://doi.org/10.1080/10717544.2017.1388453

Löbenberg, R., & Amidon, G. L. (2000). Modern bioavailability, bioequivalence and biopharmaceutics classification system: Scientific and regulatory aspects. European Journal of Pharmaceutics and Biopharmaceutics, 50(1), 3–12. https://doi.org/10.1016/S0939-6411(00)00066-7

Müller, R. H., Shegokar, R., & Keck, C. M. (2019). 20 years of lipid nanoparticles (SLN & NLC): Present state of development & industrial applications. Current Drug Discovery Technologies, 16(3), 254–268. https://doi.org/10.2174/1570163815666180821141005

Mutlu, H., & Meier, M. A. R. (2010). Castor oil as a renewable resource for the chemical industry. European Journal of Lipid Science and Technology, 112(1), 10–30.

Peretz, A., Degani, N., Nachman, R., Uziyel, Y., Gibor, G., Shabat, D., & Attali, B. (2004). Meclofenamic acid and diclofenac, novel templates of KCNQ2/Q3 potassium channel. Journal of Biological Chemistry, 279(43), 44416–44424.

Porter, C. J., Pouton, C. W., Cuine, J. F., & Charman, W. N. (2008). Enhancing intestinal drug solubilisation using lipid-based delivery systems. Advanced Drug Delivery Reviews, 60(6), 673–691. https://doi.org/10.1016/j.addr.2007.10.014

Pouton, C. W. (2000). Lipid formulations for oral administration of drugs: Non-emulsifying, self-emulsifying and 'self-microemulsifying' drug delivery systems. European Journal of Pharmaceutical Sciences, 11(Suppl 2), S93–S98. https://doi.org/10.1016/S0928-0987(00)00167-6

Pouton, C. W. (2006). Formulation of poorly water-soluble drugs for oral administration: Physicochemical and physiological issues and the lipid formulation classification system. European Journal of Pharmaceutical Sciences, 29(3–4), 278–287.

PubChem. Diclofenac potassium. https://pubchem.ncbi.nlm.nih.gov/compound/Diclofenac-Potassium

Shakeel, F., Ramadan, W., & Ahmed, M. A. (2018). Investigation of nanoemulsion system for transdermal delivery of glibenclamide. Journal of Molecular Liquids, 250, 300–308. https://doi.org/10.1016/j.molliq.2017.12.002

Shaw, J. P., Gauld, N. J., Emmerton, L. M., Tucker, I. G., & Pethica, B. D. (2000). Usage of diclofenac potassium (Cataflam®) when purchased as a non-prescription medicine in New Zealand. Contraindications for Diclofenac Potassium, 17(3), 169–175.

Sheng, J. J., et al. (2006). Solubilization and stabilization of poorly soluble drugs in self-emulsifying drug delivery systems. Journal of Pharmacy and Pharmacology, 58(9), 1181–1189. https://doi.org/10.1211/jpp.58.9.0005

Sinatra, R. S. (2009). Acute Pain Management. Cambridge University Press.

Singh, B., Bandopadhyay, S., Kapil, R., Singh, R., & Katare, O. P. (2014). Self-emulsifying drug delivery systems (SEDDS): Formulation development, characterization, and applications. Critical Reviews in Therapeutic Drug Carrier Systems, 31(2), 121–185.

Tang, B., Cheng, G., Gu, J. C., & Xu, C. H. (2008). Development of solid self-emulsifying drug delivery systems: Preparation techniques and dosage forms. Drug Discovery Today, 13(13–14), 606–612.

Thanki, K., Date, T., & Jain, S. (2021). Lipid-based oral formulation approaches for bioactives and drug molecules. Drug Delivery and Translational Research, 11(5), 1845–1868. https://doi.org/10.1007/s13346-021-00987-3

Thanki, K., Gangwal, R. P., Sangamwar, A. T., & Jain, S. (2019). Oral delivery of proteins and peptides: Challenges, status, and future prospects. Drug Discovery Today, 24(5), 1097–1113. https://doi.org/10.1016/j.drudis.2019.02.008

Trevaskis, N. L., Charman, W. N., & Porter, C. J. (2008). Lipid-based delivery systems and intestinal lymphatic drug transport: A mechanistic update. Advanced Drug Delivery Reviews, 60(6), 702–716.

Trevaskis, N. L., Charman, W. N., & Porter, C. J. (2015). Targeted drug delivery to lymphocytes in the lymphatic system using lipid-based formulations. Advanced Drug Delivery Reviews, 91, 65–81. https://doi.org/10.1016/j.addr.2015.03.003

Uttreja, P., Karnik, I., Youssef, A. A. A., Narala, N., Elkanayati, R. M., Baisa, S., Alshammari, N. D., Banda, S., Vemula, S. K., & Repka, M. A. (2025). Self-emulsifying drug delivery systems (SEDDS): Transition from liquid to solid, A comprehensive review of formulation, characterization, applications, and future trends. *Pharmaceutics, 17(1), 63.

Wallace, J. L., Caliendo, G., Santagada, V., Cirino, G., & Fiorucci, S. (2006). Gastrointestinal safety and anti-inflammatory effects of a hydrogen sulfide–releasing diclofenac derivative in the rat. Gastroenterology, 132(1), 261–271.

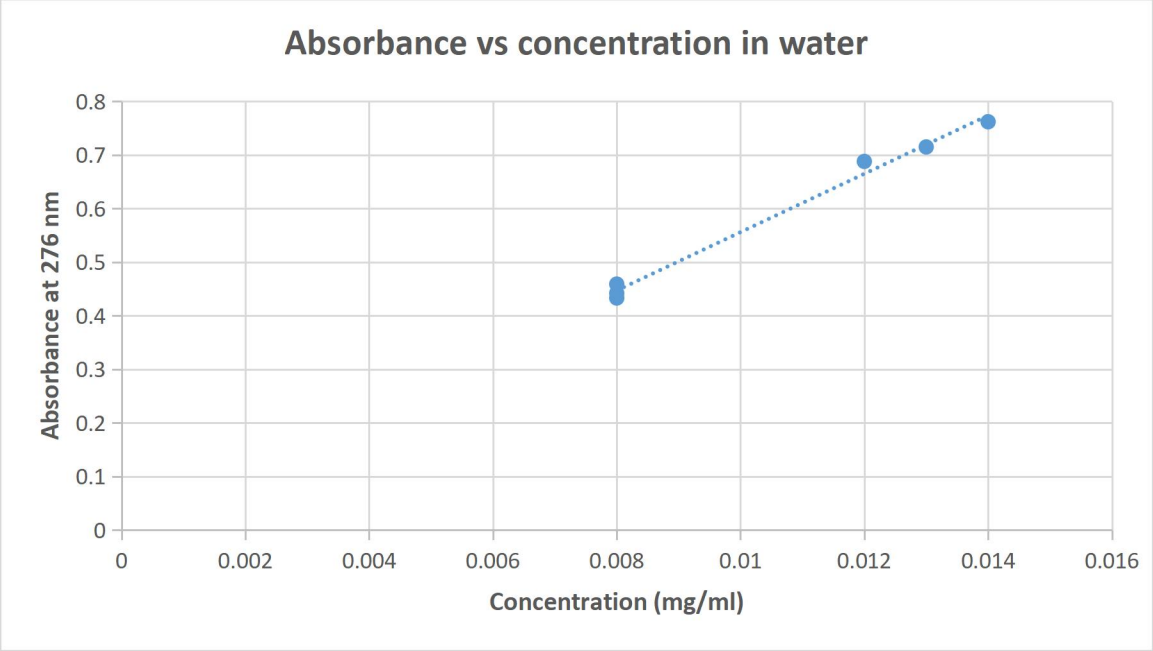
World Health Organization. (2019). Temperature sensitivity of vaccines (WHO/IVB/19.05). Geneva: WHO.

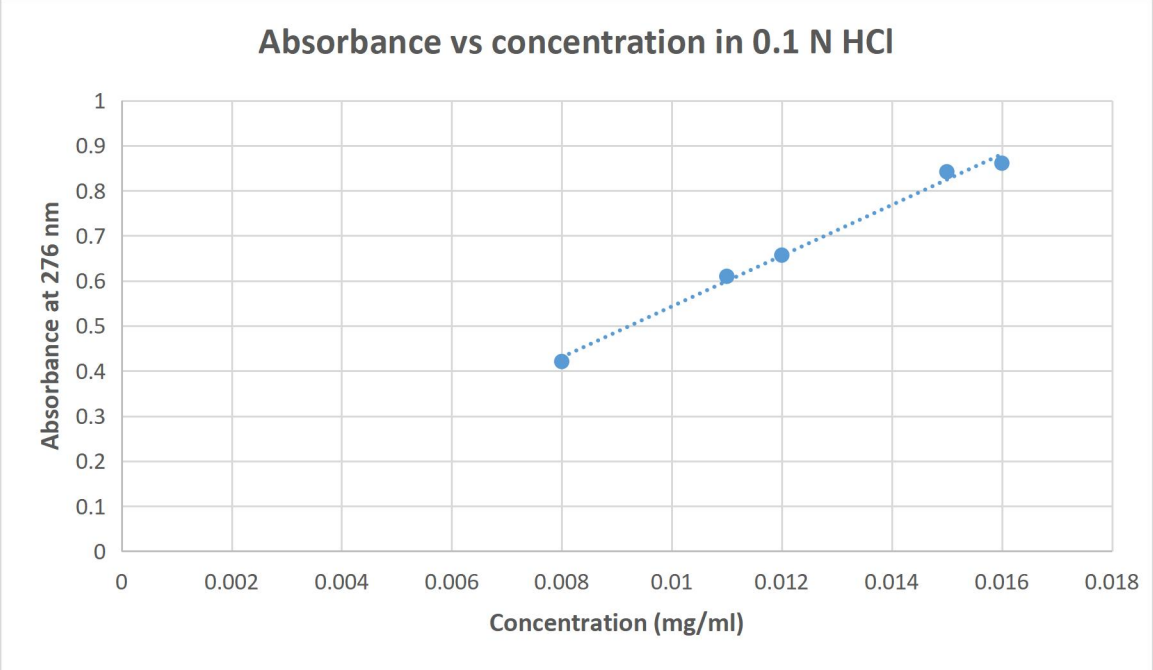
Zanchetta, B., Chaud, M. V., & Santana, M. H. A. (2015). Self-emulsifying drug delivery systems (SEDDS) in pharmaceutical development. Journal of Advanced Chemical Engineering, 5(3), 130. https://doi.org/10.4172/2090-4568.1000130

APPENDIX

UV-Vis absorbance values of drug-loaded SEDDS formulations at 276 nm

Formulation	Absorbance in Water	Absorbance in 0.1N HCl	Difference (ΔA)
SD1	0.762	0.920	0.158
SD2	0.715	0.861	0.146
SD3	0.688	0.842	0.154
SD4	0.459	0.657	0.198
SD5	0.442	0.610	0.168
SD6	0.433	0.421	0.012
Mean ± SD	0.583 ± 0.154	0.719 ± 0.190	0.136 ± 0.036


Absorbance vs concentration in water
Absorbance at 276 nm
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.002
0.004
0.006
0.008
0.01
0.012
0.014
0.016
Concentration (mg/ml)


Absorbance vs concentration in 0.1 N HCl
Absorbance at 276 nm
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.002
0.004
0.006
0.008
0.01
0.012
0.014
0.016
0.018
Concentration (mg/ml)