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Original Article

ENHANCING WATER SOLUBILITY OF A BCS CLASS II DRUG USING HYDROTROPY, MIXED SOLVENCY, CO-SOLVENCY, AND NANOSUSPENSION TECHNIQUES

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ABSTRACT

Diclofenac sodium, a BCS Class II drug, exhibits high permeability but poor solubility, limiting its bioavailability. This study investigates solubility enhancement techniques such as hydrotropy, co-solvency, mixed solvency, and nanosuspension using agents such as urea, sodium acetate, sodium citrate, polyethylene glycol 400 (PEG 400), and glycerin at concentrations of 10–60 ppm. Solubility was evaluated via Shimadzu UV-1800 UV-Vis spectrophotometry. All methods showed a linear increase in solubility, with nanosuspension demonstrating the highest enhancement. The eco-friendly, non-toxic agents used make these techniques suitable for pharmaceutical applications. Overall, the findings support nanosuspension as a promising strategy to improve the bioavailability and therapeutic efficacy of poorly soluble drugs like diclofenac sodium.

KEYWORDS: diclofenac sodium, hydrotropy, nanosuspension, co-solvency, solubility enhancement.

1. Introduction

The maximum amount of solutes that may dissolve in a certain volume of the solvent is known as solubility. It is defined as the solute concentration at a saturated concentration at a specific temperature. A qualitative definition of solubility is the spontaneous interaction of two or more substances to produce a homogeneous molecular dispersion [1]. Solubility, according to the International Union of Pure and Applied Chemistry, involves the analytical characterization of a saturated solution, typically expressed as the percentage of a specified solute within a particular solvent [2]. A solution is considered saturated when the solute and solvent are in a state of dynamic equilibrium, meaning no additional solute can dissolve under the given conditions. The solubility of a drug or compound can be expressed using various units, including molarity, volume percentage, molar fraction, and other concentration terms, depending on the context and requirements of the analysis [3]. The Indian Pharmacopoeia also explains this in terms of the number of solvent components needed for one portion of the solute as shown in Fig 1.

Descriptive Term	Parts of Solvent Required for One Part of Solute
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1000
Very slightly soluble	From 1000 to 10,000
Practically insoluble, or insoluble	10,000 or more

Fig. 1. Expression of solubility according to the Indian Pharmacopoeia [4].

Additionally, drugs can be categorized into four classes using the Biopharmaceutics Classification System (BCS) as shown in Fig 2, which is based on their aqueous solubility and intestinal membrane permeability. The BCS was developed in the mid-1990s to classify pharmaceutical compounds according to these two key parameters, aiding in the prediction of drug absorption and guiding formulation strategies [5,6].

	High solubility	Low solubility
High permeability	**Class 1 (Amphiphilic)** glucose Enalapril L-Dopa captopril Diltiazem	**Class 2 (Lipophilic)** Diclofenac Verapamil Ketoprofen Phenytoin Naproxen
Low permsability	**Class 3 (Hydrophilic)** Acyclovir Atenolol Nadolol Ranitidine Cimetidine	**Class 4** Furosemide Cyclosporine Terfenadine

Fig. 2. Drugs as per biopharmaceutical classification system.

Several factors can limit the absorption of drugs in the gastrointestinal tract (GIT). Among the most critical are poor membrane permeability and low aqueous solubility of the drug molecules. For an active pharmaceutical ingredient (API) to reach systemic circulation and cross the GIT membranes, it must first dissolve in the gastric or intestinal fluids. Consequently, enhancing the dissolution rate and water solubility of poorly soluble drugs has become a key focus in pharmaceutical research, particularly in efforts aimed at improving the oral bioavailability of active compounds [7,8]. Making the medication available at the right site of action at the ideal dosage is the main goal of the section on future formulation and development.

Solubilization is the process by which the interionic or intermolecular bonds of a solute are disrupted, allowing the solvent molecules to separate and create space for the solute. This is followed by interactions between the solvent and the solute molecules or ions, ultimately leading to the formation of a homogeneous solution [9—11].

1.1. Methods used for the improvement of diclofenac sodium solubility in water [12,27].

1.1.1. Addition of hydrotropic agents

Hydrotropy is a solubilization technique in which the aqueous solubility of a poorly water-soluble drug is enhanced by the addition of a substantial amount of a secondary solute, known as a hydrotropic agent. These agents are typically ionic compounds, such as salts of organic acids combined with alkali or alkaline earth metals. The process increases solubility through a phenomenon referred to as “salting in,” in contrast to “salting out,” where certain salts reduce solubility. Hydrotropic agents may be organic or inorganic, solid or liquid, and are non-micelle-forming substances capable of solubilizing otherwise insoluble compounds [13]. The term “hydrotropism” describes the property of certain water-soluble salts, especially those containing bulky cations or anions, to enhance the solubility of nonelectrolytes. The mechanism behind hydrotropy is thought to involve complexation and weak molecular interactions between the drug and hydrotropic agents, facilitated by the presence of numerous molecules in close proximity that promote interaction with the solvent. Common hydrotropic agents include sodium benzoate, sodium acetate, sodium alginate, and urea. These compounds form loose associations with drug molecules, thereby improving their solubility in aqueous media [14].

Hydrotropy refers to the ability of hydrotropic substances to improve the solubility of poorly soluble compounds, such as diclofenac sodium. These agents typically possess both hydrophilic (water-attracting) and hydrophobic (water-repelling) components, which work synergistically to disrupt solute-solvent interactions, thereby increasing solubility. One significant mechanism by which hydrotropic agents achieve this is through the formation of non-covalent complexes with diclofenac sodium, which reduces the intermolecular forces among the drug molecules and enhances their solubility in aqueous solutions. Additionally, certain hydrotropic agents can aggregate in solution to form micelles, effectively encapsulating diclofenac sodium and further increasing its apparent solubility. This micellar formation not only aids in dissolution but also improves the delivery of the drug. Furthermore, hydrotropic agents can reduce the activity coefficient of diclofenac sodium in solution, enhancing the solvent's capacity to solubilize the drug. Another important factor is the alteration of pH by specific hydrotropic agents, which can enhance the ionization of diclofenac sodium. Since the ionized forms of the drug are typically more soluble in water, this pH modification contributes significantly to the overall increase in solubility. Collectively, these mechanisms underscore the potential of hydrotropic agents in enhancing diclofenac sodium's bioavailability and solubility in medicinal formulations [15].

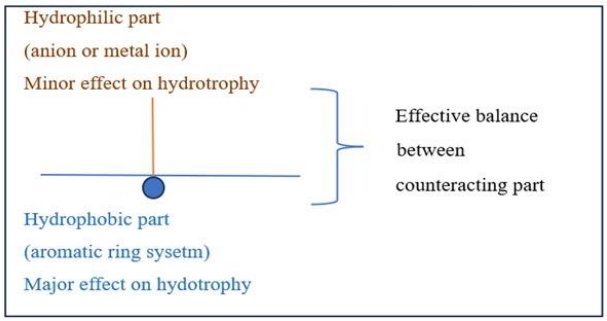

Fig. 3. Structure of hydrotropic agents.

Hydrotropes offer numerous advantages in pharmaceutical formulations and industrial applications, making them valuable agents for solubilizing hydrophobic compounds. One of their key benefits is their ability to complement other solubilization techniques, such as salting, micellar solubilization, and miscibility enhancement, due to their independent mode of action as solubilizing agents as shown in Fig 3 [16]. This versatility enables hydrotropes to be effectively employed alongside a variety of approaches. A significant advantage of hydrotropy is that it does not require chemical modification of the drug molecule, thereby preserving the chemical integrity of active pharmaceutical ingredients. Furthermore, hydrotropes do not induce temperature changes upon dissolution in water, simplifying processing conditions by eliminating the need for temperature control. The method of application is straightforward, involving only the mixing of the drug with the hydrotrope in an aqueous medium, thus streamlining the formulation process. Unlike other solubilization techniques, hydrotropy does not necessitate the use of organic solvents, complex emulsion systems, or chemical alteration of the drug, making it a more efficient and environmentally friendly

alternative. Hydrotropes are typically non-toxic, non-reactive, readily available, and cost-effective, which enhances their suitability for both pharmaceutical and large-scale industrial applications [17].

1.1.2. Co-solvency

Co-solvency is a solubilization technique that involves the use of one or more miscible liquids, known as co-solvents, to enhance the solubility of poorly water-soluble substances. The addition of co-solvents can significantly improve the solubility, miscibility, and dissolution rate of a drug in a given solution. In some cases, the solubility of a poorly soluble drug has been reported to increase by more than a thousandfold using co-solvent systems compared to its solubility in water alone [18].

This method is particularly suitable for highly crystalline compounds with good solubility in solvent mixtures, as well as lipophilic molecules that exhibit poor aqueous solubility. Co-solvents are especially valuable in parenteral formulations due to their low toxicity and effectiveness in solubilizing nonpolar drugs. However, formulations intended for intravenous administration may require dilution with water or aqueous media before delivery to reduce solvent concentration.

Co-solvency is an effective solubilization technique that involves the use of one or more water-miscible organic solvents to enhance the solubility of poorly water-soluble drugs. Common low-toxicity co-solvents used in pharmaceutical formulations include polyethylene glycol (PEG-400), glycerin, ethanol, and propylene glycol, which are particularly effective for drugs with poor aqueous solubility. These solvents are especially valuable in formulations containing lipophilic or highly crystalline drugs.

The enhancement of drug solubility through co-solvency is primarily attributed to changes in the physicochemical properties of the solvent system. Co-solvents reduce the interfacial tension between hydrophobic solutes and water, allowing drug molecules to disperse more efficiently [19]. Their molecular structure typically consisting of hydrophobic hydrocarbon groups and hydrophilic hydrogen-bonding sites enables them to disrupt the structured hydrogen-bonding network of water while maintaining miscibility with it. This dual behavior significantly facilitates the solubilization of nonpolar and weakly polar drugs. In addition, co-solvents can be used in combination with other solubilization methods, such as pH adjustment, to improve the solubility of weakly ionizable compounds.

A variety of co-solvents, including glycerin, ethanol, propylene glycol, N,N-dimethylformamide (DMF), and dimethyl sulfoxide (DMSO), have been widely employed because of their ability to solubilize hydrophobic drugs while maintaining acceptable safety profiles for pharmaceutical use [20].

In oral formulations, glycerol and polyethylene glycol are among the most frequently used co-solvents. Glycerol (glycerin), a triol with three hydroxyl groups, is fully miscible with water and forms hydrogen bonds with both water and drug molecules, making it an efficient solubilizing agent. It also exhibits co-solvency behavior similar to ethanol and is commonly used in polymer gel preparations. Polyethylene glycol (PEG), composed of repeating ethylene oxide units ($HO-(CH_2CH_2O)_n-H$), displays solubilizing properties that depend on its molecular weight. Lower molecular weight grades such as PEG 200 and PEG 400, which are liquid at room temperature, are particularly preferred for pharmaceutical solutions [21].

The mechanism of co-solvency involves several complementary physicochemical interactions that enhance solubility. These include modification of the overall polarity of the solvent system, hydrogen bonding between co-solvents and solutes, disruption of the structured hydrogen-bonding network of water, and alteration of the dielectric constant. Such changes reduce the energy barrier for solvation and may increase system entropy, making dissolution thermodynamically favorable. Collectively, these effects demonstrate that co-solvency is a powerful and versatile strategy for increasing the solubility of poorly water-soluble drugs in pharmaceutical and chemical formulations [24].

1.1.3. Mixed solvency

Hydrotropic solubilization shares similarities with co-solvency and is considered a manifestation of the mixed-solvency concept. According to this concept, all substances possess inherent solubilizing potential, and any soluble material — whether in the form of a solid, liquid, or gas — can enhance the solubility of poorly water-soluble drugs. In a solubility enhancement study using salicylic acid (a model drug known for its poor aqueous solubility), solubility tests were carried out using various solubilizing agents. These included co-solvents such as glycerin, propylene glycol, PEG 300, and PEG 400; hydrotropic agents like urea and sodium citrate; and water-soluble solids such as PEG 4000 and PEG 6000. The tests were performed both individually and in ten randomly formulated blends composed of solubilizers from the aforementioned categories, maintaining a constant total concentration of 40% w/v. The results demonstrated that seven out of ten combinations exhibited a synergistic enhancement of solubility, confirming the potential effectiveness of the mixed- solvency approach for improving the aqueous solubility of poorly soluble drugs [22].

Mixed solvency enhances solubility through multiple mechanisms involving interactions between different solvents. A central aspect of this approach is the synergistic effect observed when various solvents interact not only with the solute but also with each other. This interaction can result in solubility enhancement that surpasses the sum of the individual effects of each solvent. By combining solvents of varying polarities and hydrogen-bonding capacities, the solvation environment is optimized, allowing for more effective interaction with the solute. This tailored environment improves the dissolution of compounds, particularly those that are poorly soluble in water. Additionally, the process of solvent mixing leads to an increase in system entropy, which thermodynamically favors the dissolution of solutes by enhancing the overall free-energy change of the system. Mixed solvency also contributes to the disruption of structured hydrogen-bonding networks present in primary solvents such as water, enabling easier incorporation of solute molecules into the solution. Moreover, the modification of the dielectric constant of the solvent mixture plays a crucial

role in solubilizing ionic and polar compounds by influencing solvation dynamics [23].

1.1.4. Nanosuspension

This method is employed for drugs that exhibit poor solubility in both water and oil. Nanosuspensions are biphasic systems consisting of nanosized drug particles dispersed in an aqueous medium, stabilized by suitable surfactants. These formulations are particularly beneficial for enhancing the bioavailability of poorly soluble drugs intended for oral, pulmonary, parenteral, and topical administration. The particle-size distribution in nanosuspensions is generally below 1 micron, with the average particle size typically ranging between 200—600 nm. This nanosizing significantly increases the surface area of the drug particles, improving dissolution rates and absorption. Nanosuspension technology has been successfully applied to various poorly soluble drugs, including buparvaquone, amphotericin B, paclitaxel, atovaquone, and tarazepide. Common techniques utilized for the preparation of nanosuspensions include Nanocrystal, DissoCubes, Nanopore, and Nanoedge technologies, each offering specific advantages in particle size reduction and stability enhancement [25,26].

2. Materials and methods

The experimental study was conducted using a variety of laboratory instruments and chemicals to ensure accurate and reproducible results. A Shimadzu UV-1800 UV-Visible spectrophotometer was employed for the spectral analysis of samples, while an Aczet ultrasonic homogenizer was used to achieve uniform dispersion of components. An analytical weighing balance facilitated the precise measurement of chemical substances. The chemicals utilized in the study included distilled water, diclofenac sodium, urea, sodium acetate, sodium citrate, polyethylene glycol (PEG 400), and glycerin. Various laboratory apparatuses such as volumetric flasks, spatulas, beakers, and magnetic stirrers were employed for the preparation and thorough mixing of solutions. A stock solution of diclofenac sodium was prepared by dissolving 10 mg of the drug in 100 mL of distilled water, resulting in a 100 ppm solution. From this stock, serial dilutions were prepared to obtain concentrations of 10, 20, 30, 40, 50, and 60 ppm by mixing 1, 2, 3, 4, 5, and 6 mL of the stock solution, respectively, with distilled water to make up a final volume of 10 mL in each case. The required volume of stock solution was accurately measured using a pipette and transferred to a clean graduated cylinder or volumetric flask, followed by the addition of distilled water. Each solution was thoroughly mixed using a magnetic stirrer to ensure homogeneity. The prepared dilutions were then stored in properly labeled volumetric flasks at room temperature for 2 hours and marked with their respective concentrations and date of preparation. This procedure was consistently followed for all subsequent blends of diclofenac sodium (Tables 1-3) to ensure uniformity across different concentrations.

Table 1. Blends for the addition of hydrotropic agents.

Sr. No.	Blend preparation
1	10 mg diclofenac sodium + 10 mg urea
2	10 mg diclofenac sodium + 10 mg sodium acetate
3	10 mg diclofenac sodium + 10 mg sodium citrate
4	10 mg diclofenac sodium + 10 mg urea + 10 mg dium sodium acetate

Table 2. Blends for addition of co-solvents.

Sr. No.	Blend preparation
1	diclofenac + 1 ml PEG 400
2	diclofenac + 1 ml glycerin
3	diclofenac + 1 ml PEG 400 + 1 ml glycerin

Table 3. Blends for mixed solvency.

Sr. No.	Blend preparation
1	10 mg diclofenac + 5 mg sodium citrate + 1 ml PEG 400
2	10 mg diclofenac + 5 mg sodium citrate + 1 ml glycerin
3	10 mg diclofenac + 5 mg urea + 5 mg sodium acetate + 5 mg sodium citrate + 1 mL PEG 400

2.2.1. Preparation of nanosuspension

1. Make the solution of 10 mg of diclofenac in distilled water of 100 mL

2. Make 100 mL of the stock solution.

3. Make the dilution of 30, 40, 50 & 60 ppm wisely.

4. Set the parameters in the homogenizer as per Table 4.

Table 4. Parameter criteria for the homogenizer.

Sr. No.	Parameters	Set at
1	Process time	0h 5m 0s
2	On the pulse	2.0 seconds
3	Pulse off	2.0 seconds
4	Alarm temperature	500 c
5	Probe temperature	310 c
6	Program no	1@6
7	Power rate	70%

3. Results and discussion

3.1. Spectra of diclofenac sodium

Initially, the UV spectrum of diclofenac sodium was recorded to determine its maximum absorption wavelength (λmax), which was found to be 276 nm. This wavelength was subsequently used for the analysis of all parameters throughout the study.

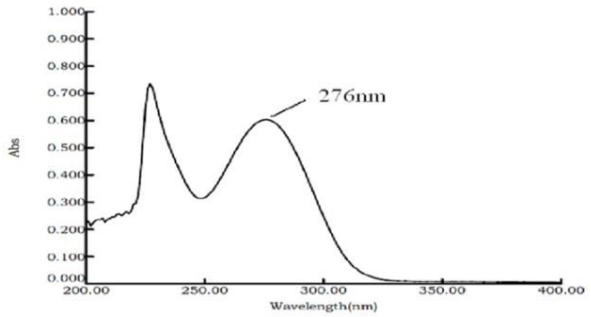

Fig. 4. UV spectrum of diclofenac sodium.

3.2. Addition of Hydrotropic Agents

According to the results, the incorporation of hydrotropic agents — particularly sodium citrate, sodium acetate, and urea — significantly enhanced the solubility of poorly water-soluble substances. This improvement was demonstrated by increased absorbance values as per Table 5-8, indicating that the use of these agents is an effective strategy for enhancing drug solubility and, consequently, improving bioavailability as shown in Fig 5.

Table 5. Addition of urea to diclofenac.

Sr. No.	Concentration	Absorbance of only diclofenac	Absorbance of diclofenac + urea
1	10 ppm	0.266	0.310
2	20 ppm	0.535	0.548
3	30 ppm	0.803	0.817
4	40 ppm	1.075	1.138
5	50 ppm	1.415	1.459
6	60 ppm	1.650	1.754

Table 6. Addition of sodium acetate to diclofenac.

Sr. No.	Concentration	Absorbance of only diclofenac	Absorbance of diclofenac + sodium acetate
1.	10 ppm	0.266	0.303
2.	20 ppm	0.535	0.618
3.	30 ppm	0.803	0.876
4.	40 ppm	1.075	1.148
5.	50 ppm	1.415	1.489
6.	60 ppm	1.650	1.804

Table 7. Addition of sodium citrate to diclofenac.

Sr. No.	Concentration	Absorbance of only diclofenac	Absorbance of diclofenac + sodium citrate
1	10 ppm	0.266	0.311
2	20 ppm	0.535	0.684
3	30 ppm	0.803	0.898
4	40 ppm	1.075	1.259
5	50 ppm	1.415	1.554
6	60 ppm	1.650	1.849

Table 8. Addition of urea & sodium acetate to diclofenac.

Sr. No.	Concentration	Absorbance of only diclofenac	Absorbance of diclofenac + urea + sodium acetate
1	10 ppm	0.266	0.402
2	20 ppm	0.535	0.714
3	30 ppm	0.803	0.925
4	40 ppm	1.075	1.298
5	50 ppm	1.415	1.633
6	60 ppm	1.650	1.895

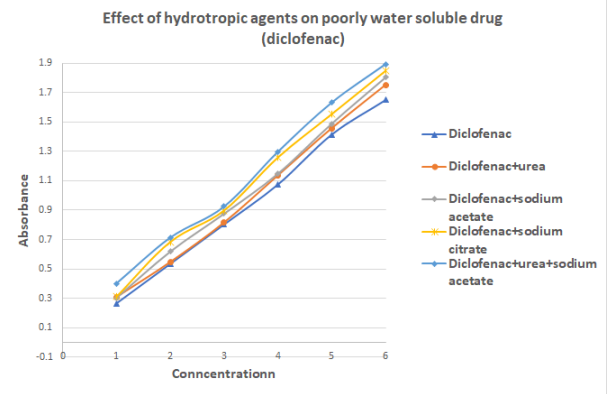

Fig. 5. Effect of hydrotropic agent on diclofenac sodium.

3.3. Addition of co-solvents

Table 9. Addition of glycerin to diclofenac.

Sr. No.	Concentration	Absorbance of only diclofenac	Absorbance of diclofenac + glycerin
1	10 ppm	0.266	0.295
2	20 ppm	0.535	0.543
3	30 ppm	0.803	0.828
4	40 ppm	1.075	1.136
5	50 ppm	1.415	1.438
6	60 ppm	1.650	1.819

Table 10. Addition of PEG 400 to diclofenac.

Sr. No.	Concentration	Absorbance of only diclofenac	Absorbance of diclofenac + PEG 400
1	10 ppm	0.266	0.346
2	20 ppm	0.535	0.651
3	30 ppm	0.803	0.951
4	40 ppm	1.075	1.260
5	50 ppm	1.415	1.563
6	60 ppm	1.650	1.884

Table 11. Addition of PEG 400 and glycerin to diclofenac.

Sr. No.	Concentration	Absorbance of only diclofenac	Absorbance of diclofenac + PEG 400+glycerin
1	10 ppm	0.266	0.382
2	20 ppm	0.535	0.699
3	30 ppm	0.803	0.993
4	40 ppm	1.075	1.287
5	50 ppm	1.415	1.604
6	60 ppm	1.650	1.948

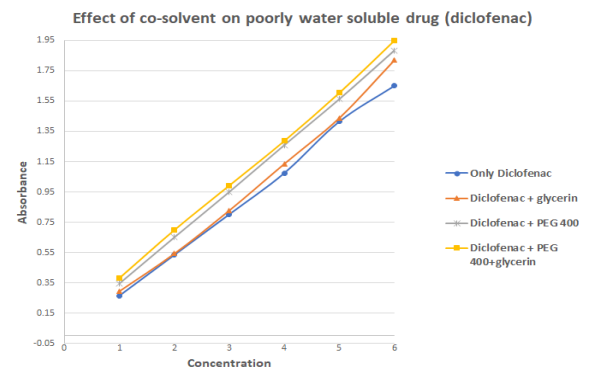

Fig 6. Effect of co-solvent on diclofenac sodium.

The incorporation of co-solvents such as glycerin and PEG 400 significantly enhances the aqueous solubility of diclofenac sodium, as demonstrated by increased absorbance values as shown in fig 6 and Table 9-11. This improvement underscores the potential of co-solvency as an effective strategy for developing improved drug delivery systems, which may contribute to enhanced therapeutic efficacy and better patient outcomes for formulations containing diclofenac sodium.

3.4. Addition of Mixed Solvents

The application of mixed solvency, utilizing agents such as urea, sodium acetate, sodium citrate, PEG 400, and glycerin, significantly enhances the solubility of diclofenac sodium, as evidenced by increased absorbance measurements as shown in Fig 7 and Tables 12-14. This innovative approach demonstrates strong potential for the development of more effective drug delivery systems, ultimately improving the therapeutic efficacy of diclofenac sodium.

Table 12. Addition of glycerin and sodium citrate to diclofenac.

Sr. No.	Concentration	Absorbance of only diclofenac	Absorbance of diclofenac + glycerin + sodium citrate
1	10 ppm	0.266	0.330
2	20 ppm	0.535	0.618
3	30 ppm	0.803	0.964
4	40 ppm	1.075	1.243
5	50 ppm	1.415	1.553
6	60 ppm	1.650	1.819

Table 13. Addition of PEG 400 and sodium citrate to diclofenac.

Sr. No.	Concentration	Absorbance of only diclofenac	Absorbance of diclofenac + PEG 400 +Sodium Citrate
1	10 ppm	0.266	0.384
2	20 ppm	0.535	0.682
3	30 ppm	0.803	0.996
4	40 ppm	1.075	1.358
5	50 ppm	1.415	1.701
6	60 ppm	1.650	1.920

Table 14. Addition of PEG 400, sodium citrate and sodium acetate to diclofenac.

Sr. No.	Concentration	Absorbance of only diclofenac	Absorbance of diclofenac + PEG 400 + sodium citrate + sodium acetate
1	10 ppm	0.266	0.466
2	20 ppm	0.535	0.742
3	30 ppm	0.803	1.059
4	40 ppm	1.075	1.448
5	50 ppm	1.415	1.758
6	60 ppm	1.650	2.165

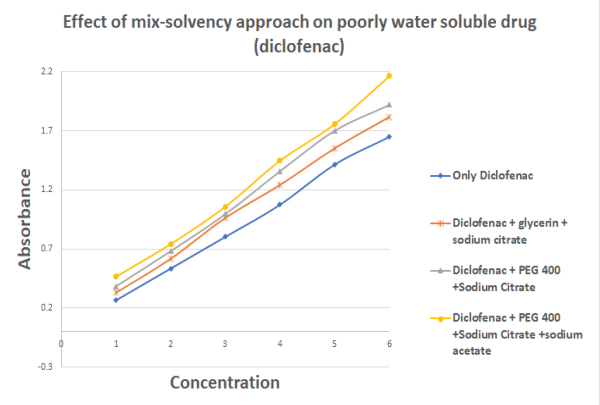

Fig. 7. Effect of mixed solvency on diclofenac sodium.

3.5. Nanosuspension

The application of the nanosuspension technique has demonstrated a significant enhancement in the solubility of diclofenac sodium, as reflected by increased absorbance measurements as shown in Fig. 8 and Table 15. This innovative approach not only improves the drug's solubility but also presents substantial potential for the development of more efficient drug delivery systems. Ultimately, such advancements may lead to improved therapeutic efficacy, better patient outcomes, and broader clinical applications for diclofenac sodium.

Table 15. Nanosuspension of different concentration.

Sr. No.	Concentration	Absorbance of only diclofenac	Absorbance of nanosuspension
1	10 ppm	0.266	0.389
2	20 ppm	0.535	0.757
3	30 ppm	0.803	1.088
4	40 ppm	1.075	1.383
5	50 ppm	1.415	2.332
6	60 ppm	1.650	2.454

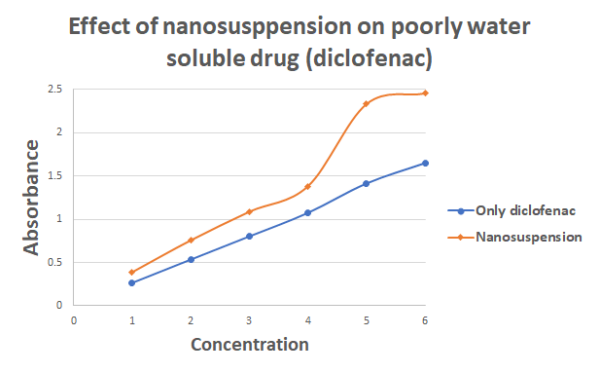

Fig. 8. Effect of nanosuspension on diclofenac sodium.

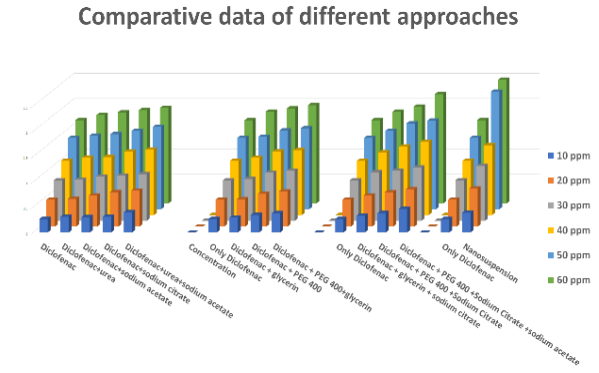

Fig. 9. Comparison of all techniques of solubility enhancement on diclofenac sodium.

4. Limitations and Future Directions

Despite the promising results, this study has certain limitations. The solubility enhancement was evaluated only through in vitro spectrophotometric analysis, and no in vivo studies were conducted to confirm improved bioavailability. Furthermore, the study utilized a limited set of solubilizing agents and concentration ranges, which may not capture the full potential of each technique. The nanosuspension system, while effective, was not assessed for long-term physical or chemical stability. Future research should include pharmacokinetic studies to validate bioavailability enhancement, expand the scope of solubilizing agents and concentrations, and investigate formulation stability and scalability for industrial application.

5. Conclusion

This research successfully demonstrated the potential of multiple strategies such as hydrotropy, co-solvency, mixed solvency, and nanosuspension for enhancing the water solubility of poorly soluble drugs. All four techniques showed a consistent and measurable increase in solubility, as indicated by elevated absorbance values. Among them, nanosuspension proved to be the most effective approach, primarily due to its ability to reduce particle size and increase surface area, thereby significantly improving solubility. These results highlight the promising role of solubility-enhancement techniques in increasing the bioavailability of insoluble drugs. The study offers valuable insights for the development of more efficient drug delivery systems and sets the groundwork for future pharmaceutical innovations aimed at improving therapeutic efficacy and patient outcomes.

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