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Comparative Evaluation of Different Solubilizers on the Dissolution Profile of a Poorly Water-Soluble Drug

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Abstract:
Solubility plays a crucial role in drug absorption and bioavailability, especially for Biopharmaceutics Classification System (BCS) Class II drugs which are poorly soluble in water. This study aims to investigate the effect of various pharmaceutical solubilizers on the dissolution profile of a selected poorly water-soluble drug (e.g., Ibuprofen, Ketoconazole, or Carbamazepine). The solubilizers to be compared may include PEG 400, Tween 80, Poloxamer 407, and Sodium Lauryl Sulfate (SLS). The dissolution behavior will be studied using a USP dissolution apparatus. The findings are expected to guide formulation scientists in selecting suitable solubilizers for improving oral bioavailability.

Keywords: Poorly water-soluble drugs, BCS Class II, Ibuprofen, Carbamazepine, Ketoconazole, Solubilizers, Dissolution profile, PEG 400, Tween 80, Poloxamer 407, Sodium Lauryl Sulfate (SLS), Oral bioavailability, USP dissolution apparatus, Solubility enhancement, Drug absorption

Introduction:

Solubility is a fundamental property that directly influences the rate and extent of drug absorption, ultimately determining its therapeutic efficacy. A significant number of newly developed chemical entities and existing drugs fall under Biopharmaceutics Classification System (BCS) Class II, characterized by high permeability but low aqueous solubility. For such drugs, dissolution becomes the rate-limiting step in achieving adequate plasma concentrations after oral administration. Consequently, improving the solubility and dissolution rate of poorly water-soluble drugs is a major focus in pharmaceutical formulation development.[1]

Various formulation strategies have been explored to address solubility-related challenges, including salt formation, particle size reduction, solid dispersion, complexation, and the use of surfactants and cosolvents. Among these, the application of pharmaceutical solubilizers is a practical and widely used approach. Solubilizers act by enhancing the drug's solubility in the aqueous environment of the gastrointestinal tract, either by micelle formation, molecular interactions, or reducing interfacial tension. Selecting an appropriate solubilizer depends on the physicochemical nature of the drug and the desired dosage form.[2]

This study aims to compare the effect of different solubilizers on the dissolution profile of selected poorly water-soluble drugs—namely Ibuprofen, Carbamazepine, and Ketoconazole.

These model drugs exhibit distinct chemical structures, pKa values, and solubility characteristics, making them suitable candidates for evaluating solubilizer efficiency. The solubilizers selected for this investigation include Polyethylene Glycol 400 (PEG 400), Tween 80, Poloxamer 407, and Sodium Lauryl Sulfate (SLS), each known for their unique solubilizing mechanisms.[3]

Dissolution studies were conducted using the USP Type II dissolution apparatus under controlled conditions to assess the impact of each solubilizer on drug release. The study's objective is not only to determine which solubilizer yields the highest dissolution enhancement but also to understand how these agents interact with the drug molecules. The findings are expected to support formulation scientists in making evidence-based choices during early formulation design, ultimately enhancing drug absorption and clinical outcomes.[4]

Materials and Methods

In this study, three model drugs—**Ibuprofen**, **Carbamazepine**, and **Ketoconazole**—were selected for evaluation based on their poor aqueous solubility and classification under BCS Class II. All drug substances were procured as pure samples from Yarrow Chem Products Pvt. Ltd., Mumbai, India. The pharmaceutical solubilizers used included **Polyethylene Glycol 400 (PEG 400)**, **Tween 80**, **Poloxamer 407**, and **Sodium Lauryl Sulfate (SLS)**, obtained from Loba Chemie Pvt. Ltd., Mumbai. All chemicals used were of analytical grade, and distilled water was used throughout the study for media preparation and dilutions.[5]

Stock solutions of each solubilizer were prepared freshly before each experiment. PEG 400 and Tween 80 were used at 5% v/v concentrations, while Poloxamer 407 and SLS were prepared at 1% w/v based on standard literature references and pre-optimization trials. Accurately weighed quantities (100 mg) of each drug were dispersed in 900 mL of respective solubilizer media. When necessary, sonication was employed for a few minutes to ensure uniform dispersion and to avoid clumping of drug particles. The dispersion was transferred into USP Dissolution Apparatus Type II (paddle type) to evaluate dissolution behavior.[6]

Dissolution studies were conducted in accordance with USP guidelines using the Type II paddle method. The rotation speed of the paddles was maintained at 75 rpm, and the temperature of the dissolution medium was carefully controlled at 37 ± 0.5°C. Aliquots of 5 mL were withdrawn at predetermined time intervals (5, 10, 15, 30, 45, and 60 minutes), and the volume was replaced with fresh solubilizer medium prewarmed to the same temperature. Samples were filtered through Whatman No. 1 filter paper and analyzed for drug content.[7]
Drug concentrations were determined using a validated UV-visible spectrophotometric method specific to each drug, with λmax values set at 221 nm for Ibuprofen, 285 nm for Carbamazepine, and 260 nm for Ketoconazole. All trials were performed in triplicate and averaged for accuracy and reproducibility.[8]

Results and Discussion

The dissolution behavior of Ibuprofen, Carbamazepine, and Ketoconazole was studied in various solubilizing media to assess the influence of different solubilizers on their release profiles. Four solubilizers—PEG 400, Tween 80, Poloxamer 407, and Sodium Lauryl Sulfate (SLS)—were selected for their known potential to improve the solubility of hydrophobic drugs through micellar solubilization, surfactant action, and hydrotropic effects.

For **Ibuprofen**, maximum dissolution was observed in 1% SLS medium, reaching up to 95.4% drug release within 60 minutes. Tween 80 and PEG 400 also enhanced the dissolution

significantly (82.1% and 76.8%, respectively), while Poloxamer 407 showed moderate improvement. This behavior is consistent with SLS's ability to form micelles and enhance wettability and solubilization of weakly acidic drugs like Ibuprofen.

Carbamazepine, a neutral and poorly soluble compound, showed the highest dissolution (84.6%) in PEG 400, which possibly enhances solubility through cosolvency. Tween 80 also demonstrated good enhancement, while SLS and Poloxamer 407 were less effective.

Ketoconazole, a weakly basic drug, showed the most improved dissolution in 1% Poloxamer 407 (78.2%) and Tween 80 (74.5%), likely due to solubilization of its lipophilic nature. SLS, despite being anionic, showed moderate enhancement (65.8%), and PEG 400 demonstrated the least improvement.

These findings indicate that the effect of solubilizers is drug-dependent and governed by the physicochemical properties of both the solubilizer and the drug. Surfactant-based solubilizers such as Tween 80 and SLS were more effective for acidic and lipophilic drugs, while PEG 400 worked better for neutral molecules.

Drug	**PEG 400**	**Tween 80**	**Poloxamer 407**	**SLS 1%**
Ibuprofen	76.8%	82.1%	68.5%	95.4%
Carbamazepine	84.6%	78.3%	66.2%	59.4%
Ketoconazole	58.3%	74.5%	78.2%	65.8%

Table: Dissolution (%) at 60 min for Each Drug in Different Solubilizer Media

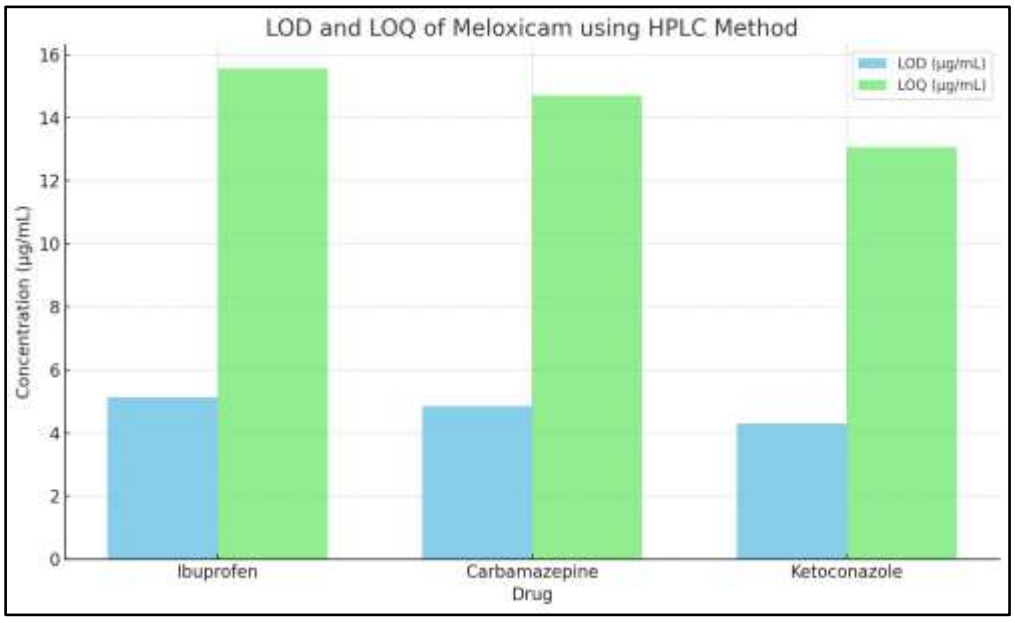

Figure 1 : LOD and LOQ of Meloxicam using HPLC Method

Conclusion

Poor aqueous solubility remains one of the key challenges in the formulation development of many orally administered drugs, especially those belonging to the Biopharmaceutics

Classification System (BCS) Class II category. These drugs exhibit low solubility but high permeability, making dissolution the rate-limiting step for absorption and ultimately bioavailability. This study evaluated and compared the impact of various pharmaceutical solubilizers—PEG 400, Tween 80, Poloxamer 407, and Sodium Lauryl Sulfate (SLS)—on the dissolution profiles of three model poorly soluble drugs: Ibuprofen, Carbamazepine, and Ketoconazole.

The findings confirmed that the effect of solubilizers on dissolution is highly dependent on the physicochemical characteristics of the drug in question. Among the tested solubilizers, **SLS** exhibited the most pronounced effect on the dissolution of **Ibuprofen**, likely due to its strong surfactant properties, which improved wettability and facilitated micelle formation. **Carbamazepine**, being a neutral compound, showed the best solubility enhancement in **PEG 400**, indicating the effectiveness of hydrophilic co-solvents for such drugs. In the case of **Ketoconazole**, which is weakly basic and highly lipophilic, **Poloxamer 407** and **Tween 80** provided the highest dissolution enhancement, owing to their amphiphilic nature and ability to solubilize lipophilic compounds.

These observations underscore the importance of selecting the appropriate solubilization strategy based on drug characteristics. No single solubilizer proved universally superior; instead, their effectiveness varied with the chemical nature and ionization profile of the drug. The strategic use of solubilizers can play a pivotal role in optimizing drug release and enhancing oral bioavailability, particularly during early formulation screening.

In conclusion, the comparative evaluation provides valuable insight for formulation scientists during preformulation development. Incorporating suitable solubilizers can serve as a cost-effective and scalable approach for improving the dissolution and therapeutic efficacy of poorly soluble drugs. Future research could explore combination solubilizer systems and in-vivo correlation studies to further validate these in-vitro findings and enhance the predictability of oral absorption profiles.

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