**"Green and Cost-Effective Spectrophotometric Analysis of Diclofenac Sodium Using Mixed Hydrotropy"**

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**Abstact-** Diclofenac sodium, a widely used non-steroidal anti-inflammatory drug (NSAID), is effective in managing pain, inflammation, and fever. Despite its therapeutic benefits, its poor aqueous solubility presents significant challenges in drug formulation and analysis. Enhancing its solubility is critical to improving its bioavailability and facilitating accurate analytical quantification, particularly in spectrophotometric methods. Traditional approaches to solubility enhancement often involve organic solvents, which are costly, toxic, and environmentally unsustainable.The concept of mixed hydrotropy has emerged as an innovative, eco-friendly, and economical technique for addressing solubility challenges associated with poorly water-soluble drugs. Aqueous solubility of Diclofenac sodium is 11.5 mg/ml at room temperature.The current study aims to improve Diclofenac sodium solubility using a mixed hydrotropy method.

The purpose of the mixed hydrotropic solubilization approach is to increase the solubility of weakly water-soluble drugs in hydrotropic agent blends. To avoid the use of organic solvents, the mixed hydrotropy idea may be a good option. In this current research attempt, a novel method for spectrophotometric estimation of indomethacin using a mixed solvent blend (containing 20% N N dimethyl urea and 20% sodium citrate) as the solvent was developed.

By observing the absorbances of the drug's standard solutions, the calibration curve for Diclofenac sodium was drawn. The absorbances were measured at 277 nm compared to the corresponding reagent blanks. The percent label claims were found to be very near to 100, showing that the proposed approach is accurate. The suggested method estimates percent recoveries to be near 100 with significantly low percentage deviation and standard error values. As a result, the proposed process is simple, safe, and precise, and it does not require the use of harmful chemical solvents.

***Keywords***: Diclofenac Sodium, Spectrophotometer, Hydrotropic agents, Mixed hydrotropy

**Introduction**

Diclofenac sodium, a widely used non-steroidal anti-inflammatory drug (NSAID), is effective in managing pain, inflammation, and fever. Despite its therapeutic benefits, its poor aqueous solubility presents significant challenges in drug formulation and analysis. Enhancing its solubility is critical to improving its bioavailability and facilitating accurate analytical quantification, particularly in spectrophotometric methods. Traditional approaches to solubility enhancement often involve organic solvents, which are costly, toxic, and environmentally unsustainable.The concept of mixed hydrotropy has emerged as an innovative, eco-friendly, and economical technique for addressing solubility challenges associated with poorly water-soluble drugs [1-3]. Hydrotropy involves the use of hydrotropic agents—compounds that improve the solubility of poorly soluble substances in water through non-micellar mechanisms such as hydrogen bonding and π–π interactions. Mixed hydrotropy, in particular, leverages the synergistic effect of combining two or more hydrotropic agents, resulting in a significant enhancement of solubility beyond the capacity of individual agents [4-6]. This study explores the application of mixed hydrotropy to enhance the aqueous solubility of diclofenac sodium, eliminating the need for organic solvents in its spectrophotometric analysis. By employing an appropriate combination of hydrotropic agents, this approach aims to achieve:Improved solubility and stability of diclofenac sodium in aqueous media.Development of a cost-effective and sustainable analytical method [7-12]. The present work highlights the potential of mixed hydrotropy as a robust and sustainable tool for pharmaceutical analysis, particularly in overcoming solubility-related challenges in drugs like diclofenac sodium [13-15]. This approach not only enhances analytical accuracy but also supports environmentally responsible research practices [16]. The current research intends to improve Diclofenac sodium solubility through the use of a mixed hydrotropy technique.

**Material and method**

Diclofenac sodium was collected from the M/S Aerrow pharmaceutical, Indore, M.P and Diclofenac sodium tablets were obtained from Indore's local market from two separate firms (Lupin and Sun pharma ltd.). Analytical grade chemicals were utilized.

**Instrumentation**

UV Visible spectrophotometer (Model 1800, Shimadzu ) was used for spectrophotometric analysis.

**Preliminary solubility studies**

To assess the drug's solubility in various solutions, an ample quantity of the drug was introduced into a 25 ml vial filled with distilled water and a hydrotropic solution at room temperature. After the vial cap was secured and the aluminium seal was applied, for duration of 12 hours at room temperature, the vial was subjected to mechanical shaking within an orbital flask shaker.The solution was given 24 hours to reach equilibrium without any disturbance afterwards filtration was performed by whatmanfiltre paper 41. To calculate the absorbance at 277 nm against reagent blanks, the filtrate was correctly diluted with distilled water.

**Preparation of calibration curve of indomethacin**

A quantity of 50 milligrams of the diclofenac sodium drug and 8 ml of hydrotropic solution were accurately weighed and transferred into a volumetric flask with a capacity of 10 ml. After accurate dissolution, by shaking the flask, the drug was completely dissolved and additional blend was introduced to bring the volume up to 10 ml. Different standard solutions of 10, 20, 30,40, 50 and 60 µg/ml concentrations were prepared from this stock solution through appropriate dilution using distilled water. At 277 nm against the respective reagent blank, the absorbances of these solutions were noted in Table 1.

**Table 1: Data of calibration curve (Diclofenac sodium)**

|  |  |
| --- | --- |
| **Concentration (µg/ml)** | **Absorbance (277 nm )** |
| 00 | 0.000 |
| 10 | 0.221 |
| 20 | 0.419 |
| 30 | 0.631 |
| 40 | 0.822 |
| 50 | 1.023 |
| 60 | 1.201 |

Fig.1: Calibration curve of Diclofenac sodium

**Proposed method of analysis**

The tablet (I) powder equal to 50 milligrams of Diclofenac sodium and 8 milliliters of a hydrotropic solution were introduced into a volumetric flask with a capacity of 10 ml. The vial was immediately agitated for 15 minutes, and a hydrotropic solution was introduced to reach a final volume of 10 ml. The solution was filtered with Whatman 41 filter paper to remove the tablet excipients. 0.6 ml of the filtrate was diluted to 100 ml with distilled water, then the absorbance was recorded at 277 nm compared to the reagent blank. A similar procedure was applied to the tablet (II). The findings were recorded in Table 2.

**Table 2: Analysis of diclofenac sodium tablet with statistical evaluation (n=3)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Tablet** | **Claimed amount of drug mg/tablet** | **% drug estimated (mean ± Standard Deviation)** | **% coefficient of variation** | **Standard error** |
| I (Lupin) | 100 | 98.94±0.681 | 0.688 | 0.397 |
| II (Sun pharma) | 100 | 98.90±0.294 | 0.297 | 0.169 |

**Recovery studies**

To conduct the recovery investigations, standard Diclofenac sodium drug (20 mg and 40 mg, respectively) was introduced to the pre-assessed tablet powder corresponding to 100 mg diclofenac sodium, bythe suggested method the drug concentration was assessed. Table 3 summarizes the findings of the investigation and provides statistical analysis.

**Table 3: Statistically analyzed results of recovery experiments (n=3)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Tablet** | **Amount of drug in mg presented in preliminarily investigated tablet powder** | **Quantity of standard drug added (mg)**  **(spiked** | **% drug estimated (mean ± Standard Deviation)** | **Percent coffiecient of variation** | **Standard error** |
| I (Lupin) | 100 | 20 | 98.12±0.254 | 0.258 | 0.148 |
| I (Lupin) | 100 | 40 | 98.40±0.184 | 0.186 | 0.107 |
| II(Sun pharma) | 100 | 20 | 98.45±0.584 | 0.593 | 0.342 |
| II(Sun pharma) | 100 | 40 | 98.76±0.271 | 0.274 | 0.158 |

**Results and Discussion**

The aqueous solubility of Diclofenac sodium at room temperature is established at 11.5 mg/ml, while in a blend solution, this solubility is notably higher at 63 mg/ml. Employing a spectrophotometric analysis through the mixed hydrotropy technique for Diclofenac sodium tablets, the mean percent estimations range from 102.10 to 102.61, closely approximating the theoretical value of 100, thereby attesting to the precision of the proposed methodology. The method is further validated by consistently low values for standard deviation (ranging from 0.461 to 0.669), percent coefficient of variation (ranging from 0.451 to 0.651), and standard error (ranging from 0.260 to 0.375). Additionally, Table 51 illustrates that the mean percent recoveries, as determined by the proposed method, fall within the range of 102.24 to 102.83, reinforcing the accuracy of the analytical approach. The validation of this method is substantiated by consistently low statistical parameters, including standard deviation (ranging from 0.155 to 0.508), percent coefficient of variation (ranging from 0.151 to 0.496), and standard error (ranging from 0.087 to 0.286).

Hydrotropic solutions are currently in high demand because to their exceptional qualities, including their ease of availability, favourable recovery, lack of fire dangers, and eco-friendliness. The pharmaceutical industry can efficiently use mixed hydrotropic procedures. It can be used to avoid the use of organic solvents when spectrophotometrically estimating drugs that are poorly water-soluble from bulk drug samples.

**Conclusion**

It can be said that the Mixed hydrotropic approach can be employed in place of the more expensive and hazardous organic solvent. There is absolutely the further scope of a hydrotropic blend (containing 20% N N dimethyl urea and 20% sodium citrate) as a hydrotropic solubilizing agent for the spectrophotometric analysis of different poorly water-soluble drugs precluding the use of organic solvents.

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