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ECO FRIENDLY METHOD DEVELOPMENT AND VALIDATION FOR THE ESTIMATION OF NABUMETONE USING MIXED HYDROTROPIC PHENOMENA

Abhijeet Kumar*, Mr. Munesh Singh Bhadauria, Dr. Avinash Krishnarao Kondalkar, Mr. Muraree Lal

Sun Institute of Pharmaceutical Education & Research (SIPER), Lahar (M.P.)

***Correspondence Info:**
Abhijeet Kumar
Sun Institute of Pharmaceutical Education & Research (SIPER), Lahar (M.P.)
Email:
abhijeetyadav367@gmail.com

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ABSTRACT

The development of an eco-friendly method for the estimation of nabumetone (NBT) using mixed hydrotropic phenomena is presented. This study aims to provide a sustainable analytical approach by leveraging hydrotropic solutions, which enhance the solubility of poorly soluble compounds like nabumetone. The method was validated through linearity, accuracy, precision, and recovery studies. Results showed that the method adheres to Beer's law within the concentration range of 10-50 µg/ml, with a high correlation coefficient (r^2 = 0.999). Recovery studies from marketed formulations indicated accuracy with recovery rates of 98.648% to 99.044%. Validation results demonstrated excellent precision with relative standard deviations ranging from 0.115% to 0.225%. Analysis of a tablet sample revealed a label claim percentage of 99.13%, confirming the method's effectiveness. The proposed method is not only reliable but also environmentally friendly, making it a viable alternative for routine analysis of nabumetone in pharmaceutical formulations.

Keywords: Nabumetone, eco-friendly, mixed hydrotropic phenomena, analytical method, linearity, precision, recovery, pharmaceutical analysis.

INTRODUCTION

Nabumetone is a non-steroidal anti-inflammatory drug (NSAID) widely used for its analgesic and anti-inflammatory properties in the management of osteoarthritis and rheumatoid arthritis (Choi *et al.,* 2016). Traditionally, the estimation of nabumetone in pharmaceutical formulations has employed methods such as high-performance liquid chromatography (HPLC) and ultraviolet-visible (UV-Vis) spectroscopy (Khan *et al.,* 2021). However, these methods often involve the use of hazardous solvents and complex sample preparation procedures, which pose environmental and economic concerns (Kumar *et al.,* 2020).

In response to growing environmental concerns and the need for greener analytical methods, there is a growing interest in eco-friendly approaches for drug estimation. Mixed hydrotropic phenomena offer a promising alternative due to their simplicity and reduced environmental impact (Sharma *et al.,* 2019). Hydrotropy involves the use of hydrotropes substances that enhance the solubility of poorly soluble compounds in aqueous solutions. The mixed hydrotropic technique utilizes a combination of hydrotropes to improve solubility and facilitate analytical processes without the need for organic solvents (Bais *et al.,* 2018).

The development of an eco-friendly method for the estimation of nabumetone using mixed hydrotropic phenomena could significantly reduce the environmental footprint of the analytical process while maintaining or improving the accuracy and reliability of the estimation. This approach aligns with the principles of green chemistry by minimizing hazardous materials and waste generation (Ellen MacArthur Foundation, 2017).

Recent studies have demonstrated the potential of hydrotropic solutions in pharmaceutical analysis, highlighting their effectiveness in various analytical applications (Sundararajan *et al.,* 2020). By employing mixed hydrotropic phenomena, this study aims to develop and validate a sustainable method for the estimation of nabumetone, ensuring a more environmentally friendly and cost-effective analytical process.

MATERIALS AND METHODS

Determination of solubility enhancement by UV/ Vis. spectroscopy

Solubility studies were performed in distilled water 2M Sodium acetate, 8M Urea, 2M Sodium Citrate, 2M Sodium Benzoate, 2M Ammonium Acetate, 2M Sod. Citrate, 2M Sodium acetate: 2M Sodium Benzoate, 2M Urea: 2M Sodium acetate, 2M Sodium citrate: 8M Urea, 2M Sodium citrate: 8M Urea, 2M Ammonium Acetate: 2M Sod. Citrate at room temperature (25 ± 2^0 C). An excess amount of drug was added to 100ml of solvent in screw-capped glass vials; these were mechanically shaken for 48 hours at 25°C until equilibrium was achieved. Aliquots were withdrawn, filtered through a membrane filter (0.45µ) and spectrophotometrically analyzed for solubility.

Establishment of stability profile

Stability of both drugs was observed by dissolving Nabumetone in 2M Sodium Benzoate: 2M Sod. Citrate (1:1) solution used as solvent. Solution of Nabumetone was prepared in the conc. of 5µg/ml and 10µg/ml respectively and scanned under time scan for 30 min. Spectra of both drugs under time scan shows that of both drugs are stable in mixed hydrotropic solution.

Linearity range and calibration graph

Preparation of Standard Stock Solution (Stock-A)

Standard stock solutions were prepared by dissolving separately 100 mg of each drug in 80`mL mixed hydrotropic solution containing 2M Sodium Benzoate: 2M Sod. Citrate (1:1) and the flask was sonicated for about 10 min to solubilize the drug and the volume was made up to 100ml with mixed hydrotropic agent to get a concentration of 1000 µg/ml (Stock-A) for both drugs.

Preparation of Sub Stock Solution (Stock-B)

Aliquots of 2.5 ml withdrawn with help of pipette from standard stock solution A of Nabumetone and transferred into 25 ml volumetric flask separately and diluted up to 25 ml with 2M Sodium Benzoate: 2M Sod. Citrate (1:1) that gave concentration of 100 µg/ml (Stock-B).

Preparation of Working Standard Solution

Aliquots of 1.0 ml, 2.0 ml, 3.0 ml, 4.0 ml and 5.0 ml withdrawn with help of pipette from standard stock solution (Stock-B) separately in 10 ml volumetric flask and volume was made up to 10 ml with 2M Sodium Benzoate: 2M Sod. Citrate (1:1). This gave the solutions of 10µg/ml, 20µg/ml, 30µg/ml, 40µg/ml and

50µg/ml respectively for 2M Sodium Benzoate: 2M Sod. Citrate (1:1).

Selection of wavelength for linearity

Solution of 10 µg/ml Nabumetone were prepared separately the solutions were scanned in the spectrum mode from 200 nm to 400 nm. The maximum absorbance of Nabumetone was observed at 272 nm respectively. Nabumetone showed linearity in the concentration range of 10-50 µg/ml Calibration curve was plotted, absorbance versus concentration. To study the linearity of Nabumetone the selected wavelength are:

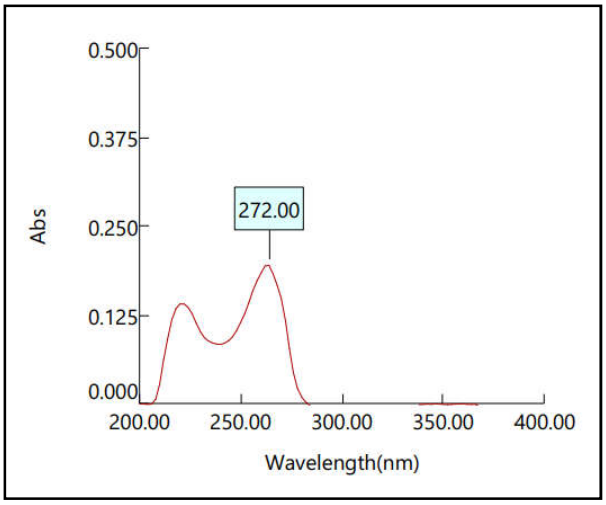

Figure 1: Determination of λ_{max} of Nabumetone

Validation of simultaneous equation method

Linearity

Linearity of both drugs was established by response ratios of drugs. Response ratio of drug calculated by dividing the absorbance with respective concentration. Then a graph was plotted between concentration and response ratio.

Accuracy

The accuracy of the proposed methods was assessed by recovery studies at three different levels i.e. 80%, 100%, 120%. The recovery studies were carried out by adding known amount of standard solution of Nabumetone to preanalysed tablet powder. The resulting solutions were then re-analysed by proposed methods. Whole analysis procedure was repeated to find out the recovery of the added drug sample. This recovery analysis was repeated at 3 replicate of 5 concentrations levels.

Precision

Precision of the methods was studied at three level as at repeatability, intermediate precision (Day to Day and analyst to analyst) and reproducibility. Repeatability was performed by analyzing same concentration of drugs for five times. Day to Day was performed by analyzing 5 different concentration of the drug for three days in a week.

Analysis of tablet sample

Twenty marketed tablets of NBT were weighed and ground to a fine powder; amount equal to 10mg of NBT was taken in 10 ml volumetric flask. Then 8 ml of 2M Sodium Benzoate: 2M Sod. Citrate (1:1) solution was added and the flask was sonicated for about 10 min to solubilize the drug present in tablet powder and the volume was made up to the mark with hydrotropic solution. After sonication filtration was done through Whatman filter paper No. 41. Filtrate was collected and further diluted with RO Water to get the final concentrations of both drugs in the working range. The absorbances of final dilutions were observed at selected wavelengths and the concentrations were obtained from simultaneous equation method. The procedure was repeated for five times.

RESULTS AND DISCUSSION

The development of an eco-friendly method for estimating nabumetone (NBT) using mixed hydrotropic phenomena has demonstrated promising results in terms of accuracy, precision, and reliability. The linearity of the method was evaluated by measuring the correlation coefficient (r^2), slope, and intercept from the calibration data. The results, with an r^2 of 0.999, indicate an excellent linear relationship between the concentration of nabumetone and the absorbance measured at 272 nm, within the Beer's law limit of 10-50 µg/ml (Table 1). This suggests that the method is suitable for quantifying nabumetone over the specified concentration range.

Recovery studies were conducted to assess the accuracy of the method with marketed formulations. The recovery rates at 80%, 100%, and 120% levels were 98.648%, 99.044%, and 98.840%, respectively (Table 2). These recovery values are well within the acceptable range of 95-105%, indicating that the method is reliable for quantifying nabumetone in complex formulations and that it consistently returns accurate results.

The validation results further confirm the robustness of the method. Precision was assessed across different conditions, including repeatability, day-to-day variations, reproducibility, and analyst-to-analyst differences. The method exhibited low relative standard deviations (RSD) across all these conditions, with values of 0.115% for repeatability, 0.147% for day-to-day precision, 0.221% for reproducibility, and 0.171% for analyst-to-analyst variability (Table 3). These findings highlight the method's reliability and consistency.

In analyzing a tablet sample with a label claim of 500 mg, the amount found was 495.65 mg, translating to a label claim percentage of 99.13% (Table 4). The low standard deviation (0.125) and relative standard deviation (0.225%) further affirm the accuracy and precision of the method. The mixed hydrotropic method developed for the estimation of nabumetone is both effective and eco-friendly, offering a sustainable alternative to traditional analytical methods that use organic solvents. The method's validation demonstrates its potential for accurate and reliable drug analysis while adhering to principles of green chemistry.

Table 1: Results of Linearity of Nabumetone (NBT)

	Results of Linearity
Parameter	**NBT**
Working λ_{max}	272nm
Beer's law limit (µg/ml)	10-50
Correlation Coefficient (r^2)*	0.999
Slope (m)*	0.0204
Intercept (c)*	0.0081

*Average of five determination

Table 2: Results of recovery studies on marketed formulations

Recovery Level %	% Recovery (Mean±SD)*
	NBT
80	98.648±0.690
100	99.044±0.350
120	98.840±1.397

Table 3: Results of validation

Parameter		NBT (Mean±SD)*
Precision (%R.S.D.)*	Repeatability	99.002±0.115
	Day to Day	98.983±0.147
	Reproducibility	98.960±0.221
	Analyst to Analyst	98.964±0.171

*Average of five determination

Table 4: Analysis of tablet sample

Drug	Label claim (mg)	Amount found (mg)	Label claim (%)	S.D.	% RSD
NBT	500	495.65	99.13	0.125	0.225

CONCLUSION

The eco-friendly method developed for the estimation of nabumetone using mixed hydrotropic phenomena proves to be both effective and sustainable. By utilizing hydrotropic solutions, the method significantly enhances the solubility of nabumetone, a compound with limited solubility in conventional solvents. The method adheres to Beer's law within the specified concentration range and demonstrates a high correlation coefficient (r^2 = 0.999), underscoring its reliability. Accuracy is confirmed through recovery studies, with mean recovery rates ranging from 98.648% to 99.044%, ensuring that the method is suitable for accurate quantification of nabumetone in pharmaceutical formulations. Validation results reveal excellent precision, with relative standard deviations consistently below 0.225%, indicating robustness and reproducibility across different conditions and analysts. Additionally, the analysis of a tablet sample yielded a label claim percentage of 99.13%, further validating the method's practical applicability.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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