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SIMPLE ECOFRIENDLY METHOD DEVELOPMENT & VALIDATION FOR THE ESTIMATION OF ANTIEMETIC DRUG USING MIXED HYDROTROPIC PHENOMENA

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ABSTRACT

Aprepitant is a widely used drug for the prevention of chemotherapy-induced nausea and vomiting. The present study focuses on the development and validation of a simple and ecofriendly method for the estimation of aprepitant using mixed hydrotropic phenomena. The proposed method offers an alternative to traditional analytical techniques, reducing the use of hazardous organic solvents and promoting green analytical chemistry principles. The method development involved the optimization of various parameters, including the concentration of hydrotropic agents, pH of the solution, and temperature. Aprepitant was found to exhibit good solubility in a mixed hydrotropic solution composed of sodium benzoate and sodium acetate. The UV-visible spectrophotometric analysis was performed at the wavelength of maximum absorption (λmax) determined using a standard aprepitant solution. The proposed method was validated as per International Conference on Harmonization (ICH) guidelines. The validation parameters such as linearity, accuracy, precision, specificity, robustness, and limits of detection and quantitation were evaluated. The method exhibited excellent linearity over the concentration range of aprepitant, with a correlation coefficient (r2) of >0.99. The accuracy of the method was confirmed by recovery studies conducted at different concentration levels, with percentage recoveries ranging from 98 to 102%. The precision of the method, assessed in terms of repeatability and intermediate precision, yielded relative standard deviation (RSD) values below 2%. The developed method offers several advantages, including simplicity, cost-effectiveness, reduced analysis time, and the use of ecofriendly hydrotropic agents. It provides a reliable and accurate estimation of aprepitant, making it suitable for routine analysis in pharmaceutical laboratories. The proposed method aligns with the principles of green chemistry, contributing to sustainable and environmentally friendly analytical practices.

Keywords: Aprepitant, mixed hydrotropic solution, UV-visible spectrophotometry, method validation, green analytical chemistry.

INTRODUCTION

Aprepitant is a selective neurokinin-1 receptor antagonist widely used in the prevention of chemotherapy-induced nausea and vomiting (CINV) (Kucerova *et al.*, 2018). It exhibits low water solubility and poses challenges in its estimation due to its poor solubility in commonly used solvents (Kulkarni *et al.*, 2012).

Traditional analytical methods for the estimation of aprepitant often involve the use of organic solvents, which can be hazardous to health and the environment.

In recent years, there has been an increasing emphasis on the development of ecofriendly analytical methods that adhere to green chemistry principles. Hydrotropy is a concept that involves the solubilization of poorly soluble compounds using high concentrations of hydrotropic agents, which are generally biodegradable and non-toxic (Nanda *et al.*, 2014). The use of mixed hydrotropic solutions offers a promising approach to enhance the solubility of Aprepitant and enable its estimation in an ecofriendly manner.

This study aims to develop a simple and ecofriendly method for the estimation of aprepitant using mixed hydrotropic phenomena. The method will be validated following the guidelines provided by the International Conference on Harmonization (ICH), ensuring its reliability and accuracy in pharmaceutical analysis.

MATERIALS AND METHODS

Establishment of stability profile

Stability of both drugs was observed by dissolving Aprepitant in 2M Sodium acetate: 2M Sodium Benzoate (1:1) solution used as solvent. Solution of Aprepitant was prepared in the conc. 10 µg/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 (Maheshwari *et al.*, 2010).

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 acetate: 2M Sodium Benzoate (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 Aprepitantand transferred into 25 ml volumetric flask separately and diluted up to 25 ml with 2M Sodium acetate: 2M Sodium Benzoate (1:1) that gave concentration of 100 µg/ml (Stock-B) (Maheshwari *et al.*, 2010).

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 acetate: 2M Sodium Benzoate (1:1). This gave the solutions of 10µg/ml, 20µg/ml, 30µg/ml, 40µg/ml and 50µg/ml respectively for 2M Ammonium Acetate: 2M Sod. Citrate (1:1).

Selection of wavelength for linearity

Solution of 10 µg/ml Aprepitant were prepared separately the solutions were scanned in the spectrum mode from 200 nm to 400 nm. The maximum absorbance of Aprepitant was observed at 264 nm respectively.

Aprepitant showed linearity in the concentration range of 10-50 µg/ml Calibration curve was plotted, absorbance versus concentration (Sundari *et al.,* 2012).

Validation of simultaneous equation method (ICH, 2005)

Linearity

Linearity of drug 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 Aprepitant 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 APT were weighed and ground to a fine powder; amount equal to 10mg of APT was taken in 10 ml volumetric flask. Then 8 ml of 2M Ammonium Acetate: 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 Distilled 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.

Table 1: Results of Linearity of Aprepitant (APT)

Results of Linearity	
Parameter	**APT**
Working λ_{max}	264nm
Beer's law limit (µg/ml)	10-50
Correlation Coefficient (r^2)*	0.999
Slope (m)*	0.015
Intercept (c)*	0.004

*Average of five determination

Table 2: Results of recovery studies on marketed formulations

Recovery Level %	% Recovery (Mean±SD)*
80	98.95±0.547
100	99.12±0.404
120	99.32±0.704

Table 3: Results of validation

Parameter		
		APT (Mean±SD)*
Precision (%R.S.D.)*	Repeatability	99.416±0.107
	Day to Day	99.06±0.110
	Analyst to Analyst	98.98±0.233
	Reproducibility	99.34±0.111

*Average of five determination

Table 4: Analysis of tablet sample

Drug	Label claim (mg)	Amount found (mg)	Label claim (%)	S.D.	% RSD
APT	80	79.45	99.31	0.225	0.341

RESULTS AND DISCUSSION

Based on the solubility, stability and spectral characteristics of the drugs, 2M Sodium acetate: 2M Sodium Benzoate (1:1) solution was selected as hydrotropic agent. Presence of hydrotropic agent do not shows any significant interference in the spectrophotometric assay thus further confirming the applicability and reproducibility of the developed method.

The developed methods were found to be linear. The values of mean percent recoveries were found to shown in Table 2 and results of validation were shown in Table 3.

The mean percent label claims of tablets by the proposed methods were close to 100, indicating the accuracy of the proposed method and low values of standard deviation, percent coefficient of variation and standard error further validated the proposed method.

CONCLUSION

In conclusion, the present study successfully developed a spectrophotometric method for the quantitative estimation of Aprepitant using a hydrotropic agent. The method demonstrated good linearity, precision, accuracy, and robustness. The developed method can be considered as a reliable and effective tool for the estimation of Aprepitant in pharmaceutical formulations and quality control processes.

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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