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A simple spectrophotometric estimation of Ketoprofen in tablets using mixed hydrotrophy

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Abstract

The present investigation illustrates the application of mixed hydrotrophy. A novel, safe and sensitive method of spectrophotometric estimation in the ultraviolet region has been developed using a mixed hydrotropic solution, containing a blend of 30% w/v urea, 13.6% w/v sodium acetate and 11.8% w/v sodium citrate for the quantitative determination of ketoprofen, a poorly water soluble drug, in tablet dosage form. Beer's law was obeyed in the concentration range of 4–20 µg/ml. There was more than 570-fold enhancement in aqueous solubility of ketoprofen in mixed hydrotropic solution as compared with the solubility in distilled water precluding the use of organic solvents. Hydrotropic agents and commonly used tablet excipients did not interfere in spectrophotometric estimation. Results of the analysis were validated statistically and by recovery studies. Statistical data proved accuracy, reproducibility and the precision of the proposed method.

Keywords: Ketoprofen, Mixed hydrotrophy, Sodium acetate, Sodium citrate, Spectrophotometry, Urea

INTRODUCTION

Hydrotropes are a class of chemical compounds that cause a several fold increase in the solubility for sparingly soluble solute under normal conditions. This phenomenon termed hydrotrophy is considered as a unique and unprecedented solubilization technique because of the easy recovery of dissolved solute and possible re-use of hydrotropic solutions. This technique also facilitates the separation of close boiling isomeric components from their binary mixtures forming simple eutectics [1] and non-isomers in mixtures besides increasing the rate of heterogeneous reactions [2]. Neuberg (1916) identified this pioneering technique for very large solubility enhancements for a variety of sparingly soluble organic solutes. Hydrotropes in

general are water-soluble and surface-active compounds that enhance the solubility of organic solutes like acids, esters, alcohols, aldehydes, ketones, hydrocarbons, and fats [3, 4]. Hydrotropes have been widely used in detergent formulation, health care, household applications [5, 6] and also as an extraction agent for fragrances [7]. Each hydrotrope has a selective ability towards a particular component in the mixture to facilitate easy recovery of the hydrotrope solution by controlled dilution with distilled water [8]. The solubility enhancement of organic solute is due to the formation of molecular structures in the form of complexes [9, 10]. The previous experimental findings concluded that hydrotropy is a process which goes beyond conventional solubilization methods, such as miscibility, co-solvency [11] and the salting-in effect, since the solubilization affected by hydrotropy is higher and more selective compared to other solubilization methods [12].

Maheshwari *et al.* have applied the use of hydrotropy in titrimetric and spectrophotometric estimation of a large number of poorly water-soluble drugs, discouraging the use of organic solvents [13-28]. Sodium benzoate, sodium salicylate, sodium ascorbate, sodium glycinate, niacinamide, sodium citrate and urea are the most popular examples of hydrotropic agents that have been used to solubilize a large number of poorly water-soluble compounds [13-33]. Various organic solvents like methanol, chloroform, alcohol, dimethyl formamide, and benzene have been employed for the solubilization of poorly water soluble drugs for their analysis. Drawbacks of organic solvents include higher cost, toxicity, pollution, and error, in analysis due to volatility. Hydrotropic agents act only at higher concentrations (30%, 40%, 45%) therefore in mixed hydrotropy we use mixture of two or more hydrotropic agents in place of one, so that higher concentration of one hydrotropic agent can be replaced by smaller amounts of two or more hydrotropic agents thus minimizing individual toxic concentration of single hydrotropic agent and at the same time utilizing synergistic effect of mixed hydrotropes to obtain even greater solubility than one hydrotrope. The present study aims to apply the concept of mixed hydrotropic solution of urea, sodium citrate and sodium acetate as a solubilizing agent to analyze a poorly water soluble drug ketoprofen in tablet, by spectrophotometric estimation. Earlier studies showed the application of mixed hydrotropy in spectrophotometric analysis of aceclofenac [34] and titrimetric analysis of ibuprofen [35]. There was more than 570-fold increase in solubility of ketoprofen (a commonly used NSAID) in the mixed hydrotropic solution. Therefore, it was thought worthwhile to solubilize the drug with the help of mixed hydrotropy to carry out the estimation. Chemically, ketoprofen is 2-[3-(benzoyl)phenyl]propanoic acid.

RESULTS AND DISCUSSION

Results of solubility studies of ketoprofen revealed that enhancement in solubility in a mixed hydrotropic solution of urea (30% w/v), sodium acetate (13.6% w/v) and sodium citrate (11.8% w/v) was more than 570-fold as compared with its solubility in distilled water.

It is evident from Table-1 that the value of mean percent drug (ketoprofen) estimated by proposed spectrophotometric method for formulation I and II are 99.71 and 98.15, respectively. The amount of drug estimated, by the proposed method for both formulations are very close to 100.0, indicating the accuracy of the proposed method of analysis. Low values of standard deviation, percent coefficient of variation and standard error [Table-1] further validated the proposed method.

Table -1: Analysis data of ketoprofen tablet formulations with statistical evaluation. (n=3)

Tablet formulation	Label claim (mg/tablet)	Percent drug estimated (Mean \pm SD)	Percent coefficient of variation	Standard error
I	100	99.71 \pm 1.629	1.634	0.943
II	100	98.15 \pm 1.296	1.320	0.762

The mean percent recoveries estimated ranged from 98.77 to 100.54. The values are close to 100.0 indicating the accuracy of the proposed method. The values of standard deviation, percent coefficient of variation and standard error are statistically low and thus validate the proposed method [Table-2].

Table -2: Recovery studies using the proposed spectrophotometric method with statistical evaluation (n=3)

Tablet formulation	Drug present in pre-analyzed tablet powder (mg)	Spiked drug added (mg)	Percent recovery estimated (Mean \pm SD)	% Coefficient of variation	Standard error
I	100	30	98.77 \pm 0.828	0.838	0.478
I	100	60	100.54 \pm 0.917	0.912	0.529
II	100	30	100.42 \pm 1.620	1.613	0.935
II	100	60	99.77 \pm 1.453	1.456	0.839

MATERIALS AND METHODS

All chemicals and solvents used were of analytical grade. A spectrophotometer (Model UV-160A) (Shimadzu, Kyoto, Japan) with 1 cm matched silica cells was used for spectrophotometric analysis. Ketoprofen was obtained as a gift sample from Alkem Laboratories Limited, Mumbai, and ketoprofen tablets were purchased from the local market.

Experimental

Preparation of calibration curve of ketoprofen: Accurately weighed 100 mg of ketoprofen was solubilized by 20 ml of a mixed hydrotropic solution containing a blend of 30% w/v urea, 13.6% w/v sodium acetate and 11.8% w/v sodium citrate in a 50 ml volumetric flask, and distilled water was added to make up the volume. This stock solution was further diluted with distilled water to get various dilutions containing 4, 8, 12, 16, and 20, μ g/ml of drug. Absorbances of these solutions were noted at 260 nm against corresponding reagent blanks.

Preliminary solubility studies of ketoprofen: Solubility of ketoprofen was determined in distilled water and mixed hydrotropic solution of urea (30%), sodium acetate (13.6%) and sodium citrate (11.8%) at 28°C \pm 1°C. There was more than 570-fold enhancement in the solubility of drug in the mixed hydrotropic solution, as compared with the solubility in distilled water.

Analysis of ketoprofen tablets by the proposed method: Twenty tablets of ketoprofen (formulation-I) were weighed and finely powdered. Powder equivalent to 100 mg of ketoprofen was taken in a 50 ml volumetric flask. Twenty milliliters of mixed hydrotropic solution containing urea (30% w/v), sodium acetate (13.6% w/v) and sodium citrate (11.8% w/v) was added and the flask was shaken properly for 10 min. to solubilize the drug; and the volume was made up to the mark with distilled water. After filtration through a Whatmann filter paper no. 41, the filtrate was appropriately diluted with distilled water for spectrophotometric estimation against reagent blank to calculate the drug content. The similar procedure was followed for formulation-II of ketoprofen also.[Table-1]

Recovery studies: To evaluate the validity and reproducibility of the proposed method, recovery experiments were carried out. For recovery studies, in pre-analyzed tablet powder equivalent to 100 mg ketoprofen, bulk drug samples 30 and 60 mg were added as spiked concentrations and drug contents were determined by the proposed spectrophotometric method. The results of analysis of recovery studies are presented in Table-2.

CONCLUSION

It is, thus, concluded that the proposed method is new, simple, environment friendly, accurate and reproducible. The proposed method can be successfully employed in the routine analysis of ketoprofen in tablets. Like this method, other hydrotropes can also be tried by combining them to improve the solubility of poorly water soluble drugs to be applied in different fields of analysis. Mixed hydrotropy may find wide use in development of aqueous formulations of poorly water soluble drugs in future.

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