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A SIMPLE ECOFRIENDLY TITRIMETRIC ANALYTICAL METHOD TO ESTIMATE KETOPROFANE IN THE BULK DRUG SAMPLE USING MIXED HYDROTROPHY

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ABSTRACT

The present investigation illustrates the application of mixed hydrotropy. There was a miraculous synergistic effect on enhancement in solubility of a practically water insoluble drug by mixing three hydrotropic agents. The enhancement in the solubility of ketoprofen in a mixed hydrotropoic solution containing 30% urea, 11.8% sodium citrate and 13.6% sodium acetate was more than 560 fold (as compared to the solubility in distilled water). This proved a synergistic enhancement in solubility of a practically water insoluble drug due to mixed hydrotropy. Mixed hydrotropic solution was employed to solubilize a practically water insoluble drug, ketoprofen, in bulk to carry out titrimetric analysis precluding the use of organic solvents. The bulk containing ketoprofen was analyzed successfully. Statistical data proved accuracy, reproducibility and the precision of the proposed method. The presence of hydrotropic agents (urea, sodium acetate and sodium citrate) did not interfere in the analysis.

KEY WORDS

Ketoprofen, mixed hydrotropy, urea, sodium citrate, sodium acetate, solubility enhancement

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 hydrotropy is considered as a unique and unprecedented solubilization technique because of the easy recovery of dissolved solute and possible re-use of hydrotropic solutions. Various hydrotropic agents such as sodium benzoate, niacinamide, sodium salicylate, sodium acetate, sodium citrate, and urea, have been employed to enhance the aqueous solubility of large number of poorly water soluble drugs[1-20]. 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. The primary objective of this study was to employ the concept of mixed

hydrotropy of hydrotropic solubilizing agents, urea and sodium citrate for the estimation of ketoprofen bulk drug to preclude the use of organic solvents.

Synergistic effect on enhancement in solubility of a practically water insoluble drug by mixing two hydrotropic agents represents the concept of mixed hydrotropy. Earlier studies showed the application of mixed hydrotropy in spectrophotometric analysis of aceclofenac[21] and titrimetric analysis of ibuprofen[22]. There was tremendous increase in solubility of ketoprofen (a widely used NSAID) in a mixed hydrotropoic solution containing 30% urea, 11.8% sodium citrate and 13.6% sodium acetate. Therefore, it was thought worthwhile to solubilize the drug with the help of mixed hydrotropy to carry out the estimation.

MATERIALS AND METHODS

Analysis of ketoprofen bulk drug by I.P. (1996) method[23]: About 500 mg of ketoprofen bulk drug was accurately weighed and dissolved in 25 ml of ethanol (95%) previously neutralized to phenolphthalein solution, 25 ml of water was added and titrated with 0.1 M sodium hydroxide using phenolphthalein solution as indicator. Each ml of 0.1 M sodium hydroxide is equivalent to 0.02543 g of $C_{16}H_{14}O_3$. Drug contents were determined (n=3) and presented in Table 1.

Analysis of ketoprofen bulk drug by the proposed method: About 500 mg of ketoprofen bulk drug was weighed and transferred to 250 ml conical flask. Twenty five ml of blend consisting of 30% urea, 11.8% sodium citrate and 13.6% sodium acetate was added and the flask was shaken for about 10 min to dissolve the drug. Titration was performed with 0.1 M sodium hydroxide using phenolphthalein solution as indicator. Blank titration was performed using 25 ml of blend consisting of 30% urea, 11.8% sodium citrate and 13.6% sodium acetate for necessary correction. Each ml of 0.1 M sodium hydroxide is equivalent to 0.02543 g of $C_{16}H_{14}O_3$. Drug contents were determined (n=3) and presented in **Table 1**.

RESULTS AND DISCUSSION

Results of solubility studies of ketoprofen revealed that enhancement in solubility in a mixed hydrotropic solution containing 30% urea, 11.8% sodium citrate and 13.6% sodium acetate was more than 560 fold as compared to its solubility in distilled water.

It is evident from Table 1 that the values of mean percent ketoprofen estimated in the drug sample was 99.14 ± 1.377 and 98.45 ± 1.550 by the Indian Pharmacopoeial and proposed titrimetric methods, respectively . The amounts of drug estimated by Indian Pharmacopoeial and proposed titrimetric methods (Table 1) are very close to each other and very near 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 titrimetric method.

Table 1.
Analysis data of bulk drug sample with statistical evaluation (n= 3)

Amount of bulk drug taken (mg)	Method of analysis	Percent drug estimated (Mean ± S.D.)	Coefficient of variation (%)	Standard error
500	IPM	99.14 ± 1.377	1.389	0.795
500	PTM	98.45 ± 1.550	1.574	0.895

IPM = Indian Pharmacopoeial Method; PTM = Proposed Titrimetric Method

CONCLUSION

It is, thus, concluded that the proposed method is new, simple, environment friendly, accurate and reproducible. Decided advantage is that the organic solvent is precluded but not at the expense of accuracy. The proposed method can be successfully employed in the routine analysis of ketoprofen in bulk drug sample. There is a good scope for other poorly water soluble drugs which may be tried to get solubilized by suitable hydrotropic agents to carry out their titrimetric analysis precluding the use of costlier and unsafe organic solvents. Like this method, other hydrotropes can also be tried by combining them to exert synergestic effect on 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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