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TITRIMETRIC ANALYSIS OF KETOPROFEN IN THE BULK DRUG SAMPLE USING SODIUM CITRATE AS HYDROTROPIC AGENT

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ABSTRACT

The present investigation illustrates the application of hydrotropy. There was a miraculous synergistic effect on enhancement in solubility of a practically water insoluble drug by using hydrotropic agents. The enhancement in the solubility of ketoprofen by using hydrotropic solution 1.25 M sodium citrate was more than 180 fold (as compared to the solubility in distilled water). This proved a synergistic enhancement in solubility of a practically water insoluble drug due to hydrotropy. Hydrotropic agent was employed to solublize 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 presenter of hydrotropic agents (sodium citrate) did not interfere with the analysis.

KEY WORDS: **Keoprofen, Hydrotropy, sodium citrate, solubility enhancement.**

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INTRODUCTION

The 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 solublization technique because of the easy recovery of dissolved solute and possible re-use of hydrotropic solutions. Various hydrotropic agents such as sodium citrate, sodium acetate and urea have been employed to enhance the aqueous solubility of the large number of poorly water soluble drugs.[1-20] Various organic solvents like methanol, chloroform, alcohol, dimethy forma-mide and benzene have been employed for the solublization of poorly water soluble drugs for their analysis. Drawbacks of organic solvents include higher cost, toxicity, pollution and error in the analysis due to volatility. The primary objective of this study was to employ the concept of hydrotropy and preclude the use of organic solvents.

MATERIALS AND METHODS

Analysis of ketoprofen bulk drug by IP (1996) method[21]: 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 content 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 as weighed and transferred to 250 ml conical flask. 25 ml of a solution of 1.25 M sodium citrate 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 as indicator. Blank titration was performed 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 content 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 hydrotropic solution containing 1.25 M sodium citrate was more than 180 fold as compared to its solubility in distilled water. It is evident from the Table 1. that the values of mean percent of ketoprofen estimated in the drug sample was 99.14 ± 1.377 and 98.45 ± 1.550 by the Indian Pharmacopoeial and proposed titrimetric method respectively. The amounts of drug estimated by Indian Pharmacopoeial and proposed titrimetric method (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 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

CONCLUSIONS

It is, thus, concluded that the proposed method is new, simple, environmentally 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 a 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 the future.

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