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QUANTITATIVE ANALYSIS OF FAMOTIDINE BULK SAMPLE USING SODIUM SALICYLATE HYDROTROPE

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ABSTRACT

Solubilization of poorly water-soluble drugs has been a very important issue in screening studies of new chemical entities as well as formulation research. A novel, safe and sensitive method of titrimetric estimation has been developed using 2 M sodium salicylate as a hydrotropic solubilizing agent for the quantitative determination of famotidine in bulk, a sparingly water-soluble keratolytic drug. There was more than a 25-fold enhancement in aqueous solubility of famotidine in 2 M sodium salicylate solution. The hydrotrope used in this work is freely soluble in water, non toxic and do not interfere in analysis. The results of analysis obtained by the present method are comparable with that by the Indian Pharmacopoeial Method. The present method is new, simple, accurate and reproducible. Results of the analysis were validated statistically. Statistical data proved the accuracy, reproducibility and precision of the present method.

INTRODUCTION

Hydrotropy refers to the process of solubilization of sparingly soluble hydrophobic compounds in the aqueous phase by addition of certain substances (called hydrotropes) to the aqueous phase. Common hydrotropes include urea, citric acid, sodium benzoate, sodium salicylate, aromatic sulfonic acids and their sodium salts etc. (Neuberg, 1916) [1,2]. The chemical structure of the conventional Neuberg's hydrotropic salts (prototype,sodium salicylate) consists generally of two essential parts, an anionic group and a hydrophobic aromatic ring or- ring system [3] . The anionic group is obviously involved in bringing about high aqueous solubility which is a pre-requisite for a hydrotropic substance. The type of anion or metal ion appeared to have a minor effect on the phenomenon [4, 5]. On the other hand, planarity of the hydrophobic part has been emphasized as an important factor in the mechanism of hydrotropic solubilization. These compounds are also useful to solubilize insoluble or poorly soluble drugs and detergent industry [6, 7]. However, the molecular mechanism of hydrotropic solubilization has not been completely under stood yet. Easy recovery of the dissolved solute and the possible reuse of hydrotrope solutions make this method the most effective one particularly at pharmaceutical industries levels[8].

This potentially attractive technique can also be adapted to separate close boiling isomeric/non-isomeric mixtures. At the same time, the problem of emulsification, which is normally encountered with conventional surfactant solution is not found with hydrotrope solutions [9]. Hydrotropes have been used to increase the rate of heterogeneous reactions and have also been used for the separation of close boiling mixture through extractive separation and liquid-liquid extraction[10, 11]. The solubility enhancement of organic compounds through hydrotropy could be due to the formation of the molecular structures in the form of complexes. Since this aggregation process is driven by hydrophobic interactions, the parameters associated with the hydrocarbon part of the hydrotrope, such as surface area and volume of the hydrophobic part, may play a significant role in the solubility change and perhaps in extractive separations [12-14]. The advantage of certain properties, such as absence of emulsification, inexpensive aqueous base, absence of solvent and fire hazard technique makes this technique superior to other solubilization methods such as micellar solubilization, miscibility, co-solvency, salting-in, etc.

Maheshwari *et al*. have applied the use of hydrotropy in titrimetric and spectrophotometric estimation of a large number of poorly water-soluble drugs, hence discouraging the use of

organic solvents [16]. Sodium benzoate, sodium salicylate, sodium ascorbate, sodium glycinate, niacinamide, sodium citrate and urea are widely used hydrotropes agents that have been used to solubilize a large number of poorly water-soluble compounds [15]. 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 [16-20]. Demerits of organic solvents include higher cost, toxicity, pollution, and possible error in analysis due to volatility [21]. The present study aims to apply hydrotropic solution of sodium salicylate as a solubilizing agent to analyze a sparingly water-soluble drug, famotidine, by titrimetric estimation [22]. There was a tremendous increase in solubility of famotidine (a widely used keratolytic agent) in 2 M sodium salicylate solution. Hence, it was thought worthwhile to solubilize the drug with the help of sodium salicylate solution to carry out the estimation.

MATERIALS AND METHODS

Analysis of famotidine bulk sample by I.P. (2007) method:-

Accurately weighed (0.3 g) famotidine bulk sample was dissolved in 50 ml of ethanol (95%) and 20 ml of distilled water was added. It was titrated against sodium hydroxide solution (0.1 M) using phenol red solution as an indicator until a reddish violet color was obtained. 1 ml of 0.1 M sodium hydroxide is equivalent to 0.01801 g of $C_8H_{15}N_7O_2S_3$. Necessary blank runs were carried out to get drug content (Table-1).

Analysis of famotidine bulk sample by proposed titrimetric method:-

In the proposed method, accurately weighed (0.3 g) famotidine bulk sample was solubilized in 40 ml of 2 M famotidine solution in a conical flask by shaking for about 5 min and titrated against sodium hydroxide solution (0.1 M) using phenolphthalein as an indicator until a reddish violet color was obtained. Necessary correction was done by conducting blank runs and amount of famotidine was calculated (Table -1).

RESULTS AND DISCUSSION

Results of solubility studies of famotidine revealed that enhancement in solubility in 2 M sodium salicylate solution was more than 25-fold. The results of analysis of famotidine by proposed titrimetric method are given in Table-I. It is evident from Table-II that the values of mean percent drug (famotidine) estimated by Indian Pharmacopoeial and proposed titrimetric methods

are 96.47 and 99.26 respectively. The results of analysis by the present titrimetric method are comparable to the results obtained from the Indian Pharmacopoeial method. The amounts of drug estimated by Indian Pharmacopoeial and Present Titrimetric Methods are very close to each other and very near to 100.0, indicating the accuracy of the present method of analysis. Low values of standard deviation, percent coefficient of variation and standard error (Table-2), further validated the proposed titrimetric method.

Table 1 - Analysis data of famotidine bulk sample

Amount of Drug Analyzed (mg)	Amount of Drug Found (mg)		% Drug Estimated	
	I.P.M	P.T.M	I.P.M	P.T.M
300	284.38	293.57	94.79	97.85
300	297.96	296.95	99.32	98.98
300	287.52	303.70	95.84	101.23
300	287.84	296.95	95.94	98.98

P.T.M. = Present Titrimetric Method

I.P.M. = Indian Pharmacopoeial Method.

Table 2- Statistical evaluation of analysis of famotidine bulk sample

Method of Analysis	% Drug Estimated	Coefficient of Variation (mean + SD)	Standard Error (%)
I.P.M	96.47±1.968	1.968	0.984
P.T.M	99.26±1.417	1.417	0.709

CONCLUSION

Hence, it can be concluded that the hydrotropic method is new, simple, cost effective, accurate, safe and precise and can be successfully employed in the routine analysis of famotidine in bulk drug sample. Decisive advantage is that the organic solvent is precluded but not at the expense of accuracy. There is a good scope for other poorly water-soluble drugs which may be tried to get solubilized in 2 M sodium salicylate solution (as hydrotropic agent) to carry out their titrimetric and/or spectrophotometric analysis excluding the use of costlier and unsafe organic solvents. The present method is worth adopting in the respective Pharmacopoeia.

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