



Research Article

Analysis of benzoic acid bulk sample using sodium saccharin as hydrotropic solubilizing agent

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Abstract

In the present investigation, hydrotropic solubilization technique has been employed to solubilize the slightly water soluble topical antifungal drug, benzoic acid (by 2 M sodium saccharin solution), for its titrimetric analysis. There was more than 20 fold enhancement in aqueous solubility of benzoic acid in 2 M sodium saccharin solution as compared to the solubility in distilled water. The hydrotropic agent did not interfere in the analysis. The proposed method is new, simple, accurate and reproducible. Statistical data proved the accuracy, reproducibility and precision of the proposed method.

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. This technique also facilitates the separation of close boiling isomeric components from their binary mixtures forming simple eutectics¹ and non-isomers in mixtures besides increasing the rate of heterogeneous reactions.² Neuberger (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-solvency¹¹ 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. 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.¹³⁻¹⁹ 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 present study

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aims to apply hydrotropic solution of sodium saccharin as a solubilizing agent to analyze a sparingly water-soluble drug, benzoic acid, by titrimetric estimation. There was tremendous increase in solubility of benzoic acid in 2 M sodium saccharin solution. Therefore, it was thought worthwhile to solubilize the drug with the help of sodium saccharin solution to carry out the estimation.

Experimental

Chemicals

Benzoic acid was obtained as gift sample from Alkem Lab. Ltd., Mumbai. All other chemicals and solvents used were of analytical grade.

Preliminary solubility studies of drug

Solubility of benzoic acid was determined in distilled water and 2 M sodium saccharin solution at $27 \pm 1^\circ\text{C}$. Solubility was found to be increased by more than 20 fold in 2 M sodium saccharin solution as compared to the solubility in distilled water.

Analysis of benzoic acid bulk sample by I.P. (1996) method

Accurately weighed (1.0 g) benzoic acid bulk sample was dissolved in 15 ml of warm ethanol (95%) previously neutralized to phenolphthalein solution, 20 ml of distilled water was added to it and it was titrated with 0.5 M sodium hydroxide solution using phenolphthalein solution as indicator. Necessary blank determination was adjusted to get drug content. (Each ml of 0.5 M sodium hydroxide is equivalent to 0.06106 g of benzoic acid).²⁰

Analysis of salicylic acid bulk sample by proposed titrimetric method

In the proposed method, accurately weighed (1.0 g) benzoic acid bulk sample was solubilized in 40 ml of 2 M sodium saccharin solution in a conical flask by shaking for about 5 min and titrated with sodium hydroxide solution (0.1 M) using phenolphthalein solution as indicator until a reddish violet color was obtained. Necessary correction was done by conducting blank determination and amount of salicylic acid was calculated.

Results and Discussion

Results of solubility studies of benzoic acid revealed that enhancement in solubility in 2 M sodium saccharin solution was more than 20-fold as compared to its solubility in distilled water. The results of analysis of salicylic acid by proposed

titrimetric method are given in Table 1. It is evident that the values of mean percent drug (benzoic acid) estimated by Indian Pharmacopoeial and proposed titrimetric methods are 100.97 and 99.93 respectively. The results of analysis by the proposed titrimetric method are comparable to the results obtained from the Indian Pharmacopoeial method. The amounts of drug estimated by Indian Pharmacopoeial and proposed titrimetric methods are very close to each other and very near to 100.0, indicating the accuracy of the proposed method of analysis. This indicates the accuracy of the proposed method. Low values of standard deviation, percent coefficient of variation and standard error, further validated the proposed titrimetric method.

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

Amount of bulk drug taken (mg)	Method of analysis*	Percent drug estimated (Mean $\pm$ S.D.)	Coefficient of variation (%)	Standard error
1000.0	I.P.M.	100.97 $\pm$ 1.22	0.975	0.489
1000.0	P.T.M.	99.93 $\pm$ 0.64	0.718	0.301

*I.P.M.: Indian Pharmacopoeial Method; P.T.M.: Proposed Titrimetric Method

Conclusion

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

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