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Research Article

QUANTITATIVE ANALYSIS OF MEBENDAZOLE BULK SAMPLE USING SODIUM SALICYLATE HYDROTROPIC AGENT

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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 mebendazole in bulk, a sparingly water-soluble keratolytic drug. There was more than a 50-fold enhancement in aqueous solubility of mebendazole 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.

Keywords: Mebendazole, Sodium salicylate, Solubility enhancement, Solubilization.

INTRODUCTION

Increasing the aqueous solubility of insoluble and slightly soluble drugs is of major importance. Various techniques have been employed to enhance the aqueous solubility of poorly water-soluble drugs. Various techniques have been employed to enhance the aqueous solubility of poorly water-soluble drugs. Hydrotropy is a unique and unprecedented solubilization technique in which certain chemical compounds termed as hydrotropes can be used to effect a several fold increase in the solubility of sparingly soluble solutes under normal conditions [1-4]. The phenomenon of hydrotropy, i.e., the increase in solubility of sparingly soluble compounds in aqueous solutions was first reported by Neuberg. Hydrotropes are "short chain organic compounds with a polar group [that] could serve as agents to dissolve poorly water soluble substances into water, if added in high concentrations." The ability of hydrotropes to increase the solubility of organics in water is often strongest when the hydrotrope concentration is sufficient to induce the formation of associated structures [5-7]. This increase in solubility in water is probably due to the formation of organized assemblies of hydrotrope molecules at critical concentrations. Hydrotropes exhibit a higher and often more selective ability to solubilized guest molecules [8-10].

The self aggregation of the hydrotropes has been considered to be a pre-requisite for a number of applications in various fields such as drug solubilization, chemical reactions, separation of organic compounds, extraction of curcuminoids from turmeric,piperine from piper nigrum and boswellic acids from boswellia serrata resins.Hydrotropes in general are water-soluble and surface-active compounds which can significantly enhance the solubility of organic solutes such as esters, acids, alcohols, aldehydes, ketones, hydrocarbons, and fats [11-12]. The solubility enhancement in the organic compounds could be due to the formation of molecular structures in the form of complexes. The concentration at which self association begins is denoted as Minimum Hydrotrope Concentration (MHC) and is often indicated by changes in solution properties such as viscosity, conductivity, surface tension, or solubility[13-14]. The relatively high concentrations required to reach the MHC, however, often restrict the commercial application of hydrotropes. Despite this extensive study and the numerous commercial and pharmaceutical applications many ambiguities regarding their classification and molecular association still exist [15].

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. 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. 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. Demerits of organic solvents include higher cost, toxicity, pollution, and possible error in analysis due to volatility. The present study aims to apply hydrotropic solution of sodium salicylate as a solubilizing agent to analyze a sparingly water-soluble drug, mebendazole, by titrimetric estimation. There was a tremendous increase in solubility of mebendazole (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 [16-19].

MATERIALS AND METHODS

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

Accurately weighed (0.3 g) mebendazole 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 0.0296 g of $C_{16}H_{13}N_3O_3$. Necessary blank runs were carried out to get drug content (Table-1).

Analysis of Mebendazole bulk sample by proposed titrimetric method:-

In the proposed method, accurately weighed (0.3 g) mebendazole bulk sample was solubilized in 40 ml of 2 M mebendazole 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 mebendazole was calculated (Table -1).

RESULTS AND DISCUSSION

Results of solubility studies of mebendazole revealed that enhancement in solubility in 2 M sodium salicylate solution was more than 21-fold. The results of analysis of mebendazole by proposed titrimetric method are given in Table-0I. It is evident from Table-2 that the values of mean percent drug (mebendazole) estimated by Indian Pharmacopoeial and proposed titrimetric methods are 96.91 and 98.49 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 mebendazole 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	289.15	295.29	96.38	98.43
300	292.76	297.18	97.87	99.06
300	288.62	296.14	96.20	98.71
300	291.54	293.26	97.18	97.75

P.T.M. = Proposed Titrimetric Method; I.P.M. = Indian Pharmacopoeial Method.

Table 2: Statistical evaluation of analysis of Mebendazole bulk sample

Method of Analysis	% Drug Estimated (mean + SD)	Coefficient of Variation	Standard Error (%)
I.P.M	96.91±0.770	0.00795	0.979
P.T.M	98.49±0.555	0.00564	0.989

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 mebendazole 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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