

APPLICATION OF MIXED-HYDROTROPIC SOLUBILIZATION CONCEPT IN SPECTROPHOTOMETRIC ANALYSIS OF FRUSEMIDE IN TABLET DOSAGE FORM

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ABSTRACT

In the present investigation, a poorly water-soluble drug, frusemide has been solubilized using hydrotropic blend containing 5 M urea, 1 M sodium acetate and 0.4 M sodium citrate for the spectrophotometric analysis precluding the use of organic solvents. These hydrotropes are economic and pollution-free. The mean percent frusemide estimated in frusemide tablets were 101.22 (formulation I) and 99.75 (formulation II). These values are very close to 100, indicating the accuracy of the proposed method. The proposed method was validated statistically by low values of statistical parameters viz. standard deviation, percent coefficient of variation and standard error. The proposed method is new, accurate, simple and economic.

Keywords: Frusemide, Mixed-Hydrotrophy, Urea, Sodium Acetate, Sodium Citrate, Spectrophotometry

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1.0 INTRODUCTION

Hydrotropy refers to the ability of a concentrated solution of a chemical compound to increase the aqueous solubility of another compound (usually a sparingly soluble organic compound). Compounds that have this property are called 'hydrotropes'. Sodium benzoate, sodium salicylate, sodium acetate, sodium glycinate, sodium ascorbate, niacinamide and sodium citrate are the most popular examples of hydrotropic agents which have been used to solubilize a large number of poorly water-soluble

compounds¹⁻²⁶. Maheshwari et al¹⁻²¹ analyzed various poorly water-soluble drugs, using hydrotropic solubilization phenomenon and mixed-solvency phenomenon including ibuprofen, salicylic acid aspirin, frusemide, tinidazole, ketoprofen, cefixime, hydrochlorothiazide, cephalixin and piroxicam.

There was tremendous increase in solubility of frusemide in hydrotropic blend containing 5 M urea, 1 M sodium acetate and 0.4 M sodium citrate in distilled water. Therefore, it was thought worthwhile to solubilize this drug in aforementioned hydrotropic blend to carry out the spectrophotometric analysis.

2.0 MATERIALS AND METHODS

All chemicals and solvents used were of analytical grade. Frusemide bulk drug was obtained as a gift sample from Alkem Laboratories Limited, Mumbai. Frusemide tablets were purchased from the local market.

2.1 Preliminary solubility studies of drug:

Solubility of frusemide was determined spectrophotometrically at 277 nm in distilled water and in blend of hydrotropic agents (5 M urea, 1 M sodium acetate and 0.4 M sodium citrate in distilled water) at $27\pm 1^\circ\text{C}$. There was more than 15 fold enhancement in the solubility of frusemide in hydrotropic blend containing 5 M urea, 1 M sodium acetate and 0.4 M sodium citrate in distilled water as compared to its aqueous solubility.

2.2 Preparation of calibration curve of drug:

Accurately weighed 50 mg of frusemide was transferred to a volumetric flask containing 20 ml of hydrotropic blend (containing 5 M urea, 1 M sodium acetate and 0.4 M sodium citrate in distilled water). The flask was shaken for 5 minutes to solubilize the drug and volume was made up to 25 ml using distilled water. Using this stock solution, various standard solutions of concentrations 4, 8, 12, 16 and 20 $\mu\text{g/ml}$ were prepared using distilled water as diluents. Absorbances of these solutions were noted against

corresponding reagent blanks at 277 nm to obtain the calibration curve.

2.3 Analysis of frusemide tablets by the proposed method:

Marketed tablets (formulation I) of frusemide were analysed by the proposed method. To do this, 20 tablets were weighed accurately and were finely powdered. Tablet powder equivalent to 50 mg of frusemide was transferred to a volumetric flask containing 20 ml of hydrotropic blend containing 5 M urea, 1 M sodium acetate and 0.4

M sodium citrate in distilled water. The flask was shaken for 5 minutes to solubilize the drug and the volume was made up to 25 ml using distilled water. After filtration, the filtrate was appropriately diluted with distilled water and the absorbance of this solution was noted at 277 nm against corresponding reagent blank. The results of analysis are presented in Table 1. Each type of analysis was performed in triplicate. The same procedure was repeated for formulation II of the frusemide tablets.

Table 1. Results of analysis of marketed tablets of frusemide tablet formulations

Tablet formulation	Label claim (mg per tablet)	% drug estimated * (mean±S.D.)	% Coefficient of variation	Standard error
I	40	101.22±0.907	0.896	0.524
II	40	99.75±1.623	1.627	0.937

* Mean of three determinations. S.D- Standard deviation

2.4 Recovery studies:

To evaluate the validity and reproducibility of the proposed method, recovery studies were carried out by adding known quantities of frusemide bulk drug sample in the preanalyzed tablet powder containing known amounts of drug and performing the analysis using the same procedure and percent recoveries were calculated (Table 2). Each type of analysis was performed in triplicate for both formulations of frusemide tablets.

3.0 Results and Discussion

From the solubility studies, it was found that there was more than 15 fold enhancement in

the solubility of frusemide in hydrotropic blend containing 5 M urea, 1 M sodium acetate and 0.4 M sodium citrate in distilled water (as compared to its solubility in distilled water). As evident from Table 1, the mean per cent drug estimated were 101.22 (formulation I) and 99.75 (formulation II). These values are very close to

100, indicating the accuracy of the proposed method. The values of standard deviation (0.907 and 1.623), % coefficient of variation (0.896 and 1.627) and standard error (0.524 and 0.937) were satisfactorily low and validated the proposed method.

The values of the mean per cent recoveries (Table 2) were 100.84 and 100.92 in case of formulation

I and 101.55 and 99.69 in case of formulation II. The values are close to 100, indicating the accuracy of the proposed method. Low values of standard deviation (0.942 to 1.339), % coefficient of variation (0.933 to 1.319) and standard error (0.544 to 0.773) further validated the proposed method.

Table 2. Recovery study for spiked concentration of frusemide added to the preanalyzed tablet powders

Tablet formulation	Drug present in preanalyzed tablet powder taken (mg)	Pure drug taken (mg)	% Recovery estimated* (mean±S.D.)	% Coefficient of variation	Standard error
I	50	10	100.84±1.246	1.236	0.719
I	50	20	100.92±0.942	0.933	0.544
II	50	10	101.55±1.339	1.319	0.773
II	50	20	99.69±1.008	1.011	0.582

* Mean of three determinations. S.D- Standard deviation

4.0 Conclusions

It is, thus, concluded that the proposed method is new, simple, accurate, cost-effective, safe, economic, precise and can be successfully employed in the routine analysis of frusemide in bulk and tablets. There is definitely further scope of hydrotropic blend containing 5 M urea, 1 M sodium acetate and 0.4 M sodium citrate as a

hydrotropic solubilizing agent for the spectrophotometric analysis of other poorly water-soluble drugs precluding the involvement of organic solvents.

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