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## QUANTITATIVE ANALYSIS OF BULK SAMPLE OF IBUPROFEN BY USING HYDROTROPIC SOLUBILIZATION TECHNIQUE

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### ABSTRACT

Numerous drugs available in the market are poorly water soluble. Majority of the failures in new drug development are because of the poor aqueous solubility of the drug. The present study illustrates the application of hydrotropic solubilization technique to increase the solubility of poorly water-soluble non-steroidal antiinflammatory drug, ibuprofen. Sodium salicylate (2M) and sodium acetate (2M) solutions were employed as hydrotropic solubilizing agents to solubilize the ibuprofen to facilitate its titrimetric analysis, excluding the use of organic solvent. Solubility study exhibited enhancement of solubility of a drug in 2M sodium salicylate and sodium acetate solutions as compared to solubility in water. The drug was analyzed successfully. The results of analysis obtained by employing the proposed method involving the use of hydrotropic agents were found to be very close to the results of the standard Indian Pharmacopoeial method. The proposed method was validated statistically which proved the accuracy, precision, and reproducibility of the method.

**Keywords:** Hydrotrophy, Ibuprofen, Sodium salicylate, Sodium acetate, Titrimetric analysis

### INTRODUCTION

Most of the newly developed chemical entities or drug molecules are lipophilic in nature and one of the most difficult

problems of these drugs is their poor aqueous solubility. Aqueous solubility of drugs is the most important parameter

considered in the fields of pharmaceutical analysis and formulation development. Different techniques have been employed to enhance the aqueous solubility of poorly water soluble drugs and hydrotrophy is one of them. Hydrotropic solubilization is a phenomenon in which the addition of a large amount of second solute increases the solubility of poorly water soluble solute [1-3]. Hydrotropic solubilization phenomenon has been employed to analyze various drugs having poor aqueous solubility like aceclofenac [3], salicylic acid [4], tinidazole [5], frusemide [6], piroxicam [7], ketoprofen [8], cefixime [9]. Concentrated solutions of hydrotropic agents like sodium benzoate, ibuprofen, urea, nicotinamide, sodium citrate, and sodium acetate have been used to enhance the aqueous solubility of a large number of poorly water-soluble compounds [4-15].

Organic solvents such as methanol, ethanol, chloroform, benzene, dimethylformamide and acetone have been used for dissolving drugs having poor aqueous solubility to facilitate their titrimetric analysis. But organic solvents are associated with some drawbacks like toxicity, higher cost, pollution, and error in the analysis due to volatility. An organic solvent, ethanol is used for the solubilization of ibuprofen, a poorly water soluble non-steroidal antiinflammatory drug (NSAID), in its titrimetric analysis as per the Indian

Pharmacopoeial method. Hydrotrophy is a proper choice to preclude the use of organic solvents. The objective of the present study was to employ solutions of hydrotropic solubilizing agents, sodium salicylate (2M) and sodium acetate (2M) for the purpose of solubilization of ibuprofen and to facilitate its titrimetric analysis, precluding the use of unsafe and costlier organic solvent.

## MATERIALS & METHODS

Pure sample of Ibuprofen was supplied by Cipla Ltd. Mumbai. Analytical grade chemicals and solvents were used. UV-visible spectrophotometer, Shimadzu model-1700, was used to carry out the spectrophotometric analysis. Incubator shaker, HMQ India made was used to perform solubility study.

### Preliminary Solubility Study

Solubility of Ibuprofen was determined in distilled water, sodium salicylate (2M) and sodium acetate (2M) solutions at the temperature of  $28 \pm 1^\circ$ . An excess amount of ibuprofen was added to 25 ml volumetric flasks containing distilled water, 2M sodium salicylate, and 2M sodium acetate solutions. These flasks were shaken using mechanical shaker for 12 hr at  $28 \pm 1^\circ$ . These solutions were then equilibrated for the next 24hr and centrifuged at 2000 rpm for 5 min. The supernatant liquid was taken from each flask and filtered through Whatman filter paper. After appropriate dilution the solutions were

analyzed spectrophotometrically against corresponding solvent blank.

#### **Titrimetric Analysis of a drug by Indian Pharmacopoeial method**

##### **[IPM][15]:**

An accurately weighed (0.3gm) ibuprofen was dissolved in 50ml of ethanol. The solution was then titrated with 0.1M sodium hydroxide (NaOH) using phenolphthalein as an indicator. By conducting blank determination, necessary correction was made and the amount of drug was determined.

#### **Titrimetric Analysis of a drug by Proposed method**

An accurately weighed (0.3gm) ibuprofen was solubilized in 50ml of 2M sodium salicylate solution. The solution was then titrated with 0.1M sodium hydroxide (NaOH) using phenolphthalein as an indicator. By conducting blank determination, necessary correction was made and the amount of drug was determined. For another hydrotropic agent, i.e., sodium acetate (2 M) the same procedure was applied.

## **RESULTS & DISCUSSION**

The solubility study exhibited a more than 20-fold enhancement of solubility of ibuprofen bulk drug in sodium salicylate (2M) and sodium acetate (2M) solutions as compared to distilled water. Compared to sodium acetate, ibuprofen was found to be more soluble in 2 M sodium salicylate solution.

As shown in **Table 1**, the mean percent of ibuprofen estimated in the bulk sample by I.P. method was 98.56% while the mean percent of drug estimated by the proposed method of analysis, by using 2 M sodium salicylate and 2 M sodium acetate solutions, were 98.94 and 98.67% respectively. The results of analysis obtained by employing the proposed method were comparable to the results obtained by standard I.P. method. The proposed method was validated statistically. Low values of standard deviation, % coefficient of variation and standard error confirmed the accuracy of the proposed method.

**Table 1: Results of titrimetric estimation of ibuprofen in bulk drug sample (n=3)**

Method of analysis	Percent drug Estimated (Mean ± S.D.)	% CV	SE
IPM	98.56±0.495	0.502	0.285
PMSS	98.94±0.371	0.374	0.216
PMSA	98.67±0.482	0.488	0.282

IPM: Indian pharmacopoeial method, PMSS: Proposed method using sodium salicylate solution, PMSA: Proposed method using sodium acetate solution, SD: Standard deviation, CV: Coefficient of variation, SE: Standard error

**CONCLUSION:**

The proposed method involving the use of sodium salicylate and sodium acetate as hydrotropic solubilizing agents can be used successfully in the analysis of ibuprofen bulk drug sample. This method is simple, safe, rapid, accurate, reproducible, cost-effective, and most importantly eco-friendly. Thus, hydrotrophy technique can be used for solubilization of poorly water soluble drugs to facilitate their quantitative estimation excluding the use of unsafe and costlier organic solvents.

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**CONFLICTS OF INTEREST**

The authors declare that they have no conflicts of interest.

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