

Estimation of Ibuprofen in Bulk and Tablets Using Ibuprofen Sodium as Hydrotropic Solubilizing Agent

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In the present investigation, hydrotropic solubilization phenomenon has been employed to solubilize the poorly water-soluble antiinflammatory drug, ibuprofen by use of 0.5 M of ibuprofen sodium (an economic drug) solution to carry out titrimetric analysis (in bulk drug sample and tablets) precluding the use of organic solvents. The methods are new, simple, accurate, reproducible, inexpensive and eco-friendly. The results of analysis by proposed methods of analysis compared well with the results of standard pharmacopoeial methods. Recovery studies and statistical parameters validated the proposed methods.

Key Words: Ibuprofen, Ibuprofen sodium, Hydrotropy, Titrimetry.

INTRODUCTION

It is well documented that concentrated aqueous solutions of a large number of hydrotropic agents *viz.* sodium gluconate, niacinamide, urea, sodium benzoate, sodium salicylate, sodium ascorbate and sodium glycinate have been employed to enhance the aqueous solubilities of poorly water-soluble drugs¹⁻¹⁴. Maheshwari *et al.*¹⁻¹¹ have analyzed several poorly water-soluble drugs quantitatively by use of hydrotropic agents.

Various organic solvents like methanol, chloroform, dimethyl formamide and ethanol have been employed for solubilization of poorly water-soluble drugs to conduct their titrimetric analyses. Drawbacks of organic solvents include their higher costs, toxicities and pollution. There was more than 290 times enhancement in the aqueous solubility of ibuprofen (a poorly water-soluble drug) in 0.5 M ibuprofen sodium solution, as compared to its aqueous solubility. Therefore, it was thought worthwhile to employ 0.5 M ibuprofen sodium solution to solubilize ibuprofen for its titrimetric analysis. Determination of solubility of ibuprofen in 0.5 M ibuprofen sodium solution and water were carried out at room temperature. Ibuprofen showed more than 290 fold enhancement in solubility in 0.5 M ibuprofen sodium solution as compared to the solubility in distilled water.

EXPERIMENTAL

Ibuprofen bulk drug sample was obtained as gift sample from Alkem Laboratories Limited, Mumbai. Commercial tablets of ibuprofen, Brufen of Knoll Pharmaceuticals Ltd (formulation-I) and Ibugesic of Cipla Ltd. (formulation- II) were purchased from the local market. All other chemicals and solvents used were of analytical grade.

Preparation of 0.5 M ibuprofen sodium solution: Ibuprofen (87.25 g) was suspended in 450 mL distilled water in a 1000 mL beaker, sodium hydroxide (15.0 g) was dissolved in 150 mL distilled water separately. Sodium hydroxide solution was added in ibuprofen slurry in successive portions. Slurry was stirred after each addition of sodium hydroxide solution. When a clear solution was obtained due to conversion of all ibuprofen in ibuprofen sodium, the pH of solution was adjusted to 7.5-8.0 with sodium hydroxide solution and the volume of solution was made up to 750 mL with distilled water.

Analysis of ibuprofen bulk sample by the proposed method¹⁵: Ibuprofen bulk sample (0.4 g) was accurately weighed and solubilized in 100 mL of 0.5 M ibuprofen sodium solution in a conical flask by shaking. This solution was titrated with 0.1 M sodium hydroxide using 0.2 mL of the phenolphthalein solution as indicator. Necessary correction was done by conducting the blank determination (using 100 mL of 0.5 M ibuprofen sodium solution) and amount of ibuprofen was calculated (Table-1). (Each mL of 0.1 M sodium hydroxide is equivalent to 20.63 mg of ibuprofen).

TABLE-1
ANALYSIS DATA OF BULK DRUG SAMPLE OF IBUPROFEN
WITH STATISTICAL EVALUATION (n = 3)

Amount of drug taken (mg)	Method of analysis	Per cent drug estimated (mean \pm SD)	% Coefficient of variation	Standard error
400	I.P. Method	99.13 \pm 1.244	1.255	0.718
400	Proposed method	100.69 \pm 2.070	2.056	1.195

Analysis of ibuprofen bulk sample by Indian Pharmacopoeial method¹⁶: Ibuprofen bulk sample (0.4 g) was weighed and dissolved in 100 mL of ethanol (95 %) in a conical flask and titration was done with 0.1 M sodium hydroxide using 0.2 mL of phenolphthalein solution as indicator. Blank titration was carried out and necessary correction was made to calculate the drug content. (Each mL of 0.1 M sodium hydroxide is equivalent to 20.63 mg of ibuprofen).

Analysis of ibuprofen tablets by the proposed method: Twenty tablets of ibuprofen (formulation I and II) were weighed and finely powdered. Tablet powder equivalent to about 500 mg of ibuprofen was taken in a conical flask. Hundred mL of 0.5 M ibuprofen sodium solution was added and the flask was shaken for about 10 min to solubilize ibuprofen from tablet powder and titration was performed with 0.1 M sodium hydroxide using 0.2 mL phenolphthalein solution as indicator. Necessary correction was made by conducting blank determination and amount of ibuprofen

was calculated (Table-2). For recovery studies, same procedure was repeated using 60 and 100 mg of ibuprofen bulk drug as the spiked drug together with the pre-analyzed tablet powder equivalent to 500 mg of ibuprofen (Table-3).

TABLE-2
ANALYSIS DATA OF TABLET FORMULATIONS WITH
STATISTICAL EVALUATION (n = 3)

Tablet formulation	Label claim (mg/tab)	Method of analysis	% Label claim estimated (mean \pm SD)	% Coefficient of variation	Standard error
I	400	I.P. method	102.31 \pm 0.771	0.754	0.445
I	400	Proposed method	100.77 \pm 0.935	0.928	0.540
II	200	I.P. method	100.72 \pm 2.013	1.999	1.162
II	200	Proposed method	99.11 \pm 1.771	1.787	1.023

TABLE-3
RESULTS OF RECOVERY STUDIES OF TABLET FORMULATIONS
WITH STATISTICAL EVALUATION (n = 3)

Tablet formulation	Label claim (mg/tab)	Drug added (spiked) (mg)	%Recovery estimated (mean \pm SD)	% Coefficient of variation	Standard error
I	500	60	98.74 \pm 1.397	1.415	0.807
I	500	100	99.42 \pm 0.993	0.938	0.539
II	500	60	98.31 \pm 1.210	1.231	0.699
II	500	100	100.71 \pm 1.447	1.437	0.835

Analysis of ibuprofen tablets by Indian Pharmacopoeial method¹⁶: Tablet powder equivalent to 0.5 g ibuprofen was accurately weighed and extracted with 60 mL of chloroform for 15 min and filtered. Residue was washed with 3 quantities each of 10 mL of chloroform. Chloroform was evaporated in a current of air. Residue was dissolved in 100 mL of ethanol (95 %) previously neutralized to phenolphthalein solution and titrated with 0.1 M sodium hydroxide solution. Ibuprofen content was then determined (Table-2). (Each mL of 0.1 M sodium hydroxide is equivalent to 20.63 mg of ibuprofen). Each type of analysis was performed thrice.

RESULTS AND DISCUSSION

The values of mean per cent drug estimated in the bulk sample of ibuprofen by the proposed and IP methods were 100.69 and 99.13, respectively. The values are comparable and close to 100 indicating the accuracy of the proposed method. Low values of statistical parameters *viz.* standard deviation, % coefficient of variation and standard error (Table-1) confirms the accuracy of the proposed method. In case of tablets, the values of the mean per cent drug estimated by the IP method were 102.31 (formulation-1) and 100.72 (formulation-2) while the values of mean per cent drug estimated by the proposed method were 100.77 (formulation-1) and 99.11 (formulation-2). These values are comparable and close to 100 indicating the accuracy of the proposed method. Low values of statistical parameters *viz.* standard

deviation, % coefficient of variation and standard error (Table-2) confirms the accuracy of the proposed method. The values of the mean per cent recoveries estimated (Table-3) by the proposed method ranged from 98.31 to 100.71 which are close to 100, further confirmed the accuracy of the proposed method. The low values of standard deviation, % coefficient of variation and standard error validated the method. Thus, it may be concluded that the proposed method of analysis is new, rapid, simple, cost-effective, eco-friendly, safe, accurate and reproducible.

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