

## The determination of pharmaceutically important ibuprofen by non-aqueous potentiometric titration method

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**Abstract :** The determination of pharmaceutically important ibuprofen by non-aqueous potentiometric titration method using isopropyl alcohol as the solvent and KOH in isopropyl alcohol as the titrant has been established. The study of effect of solvent and concentration on potentiometric determination of ibuprofen has been carried out followed by the estimation of ibuprofen in single component tablets. The titrations were carried out using a pair of glass and calomel electrode. The method was found to be precise for assay of ibuprofen and results obtained are comparable with those obtained by I.P. method.

**Keywords :** Ibuprofen, non-aqueous, potentiometric titration.

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### Introduction

The potentiometric determination in non-aqueous media has been reported earlier using different electrode pairs<sup>1</sup>. Literature is enriched with different methods for the determination of ibuprofen<sup>2</sup>. The potentiometric determination of ibuprofen in non-aqueous solvents like methanol and dimethyl formamide has been reported earlier using sodium methoxide as the titrant and a pair of glass and calomel electrodes<sup>3</sup>. I.P. and B.P. methods involved the titration of ibuprofen in alcohol with aqueous alkali using phenolphthalein indicator. The methods described in these pharmacopoeias are mostly of visual titrations. The potentiometric titration method using glass and calomel electrode pair is also recommended by these pharmacopoeias but the calomel electrode is modified by filling it with methanol saturated with potassium chloride<sup>4</sup>. Spectrophotometric estimation of ibuprofen has been carried out by many workers<sup>5</sup>. Ibuprofen has also been analyzed by conductometric, potentiometric, enthalpimetric and coulometric methods<sup>6</sup>. Determination of ibuprofen by chromatographic techniques was carried out earlier<sup>7</sup>. As the ibuprofen is distinctly acidic, it could not be titrated directly with aqueous alkali due to its easy hydrolysis. The basic titrant is also superior to the alkoxide solvents which are more susceptible to the atmospheric moisture and carbondioxide. The present work is aimed

at finding out simple analysis procedure for common drugs. This will help the analysis of raw materials and products for quick check of spurious drugs which are feared to penetrate the markets. In this communication, determination of ibuprofen by potentiometric titration using isopropyl alcohol as the solvent and KOH in isopropyl alcohol as the titrant has been reported. Efforts have also been made to study the effect of solvent, concentration and the estimation of ibuprofen in single component tablets.

### Results and discussion

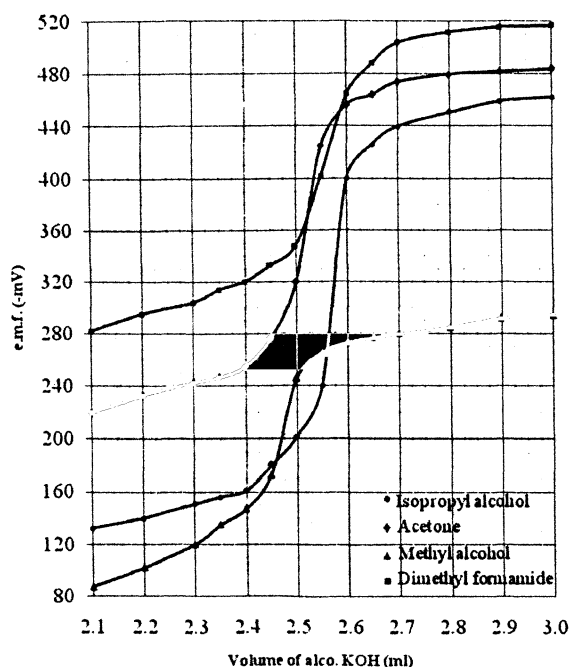
#### *Effect of solvent and concentration on potentiometric determination of ibuprofen :*

In the study of effect of solvent, the accuracy of results in determination of ibuprofen by using different solvents was checked by potentiometric titration method. The required volumes of the stock solutions of ibuprofen in different solvents were diluted to 20 ml and titrated separately with KOH in isopropyl alcohol. The results obtained are tabulated and it can be seen from that, the accuracy of result in determination of ibuprofen by using the solvent isopropyl alcohol is much more with minimum % error as compare to other solvents (Table 1). As compared to the solvent methanol, potentiometric breaks obtained using dimethyl formamide and acetone are smoother one. The potentiometric break obtained using

**Table 1.** Effect of solvent on potentiometric determination of ibuprofen

Solvent	Weight titrated (mg) ( $\pm 0.5\%$ )	Weight found (mg)	Error (%)
Acetone	4.144	4.081	-1.52
Methanol	4.144	4.001	-3.45
Dimethyl formamide	4.144	4.113	-0.74
Isopropyl alcohol	4.144	4.114	-0.72

isopropyl alcohol is much more pronounced and prominent with maximum potential difference near the equivalence point (Graph 1). The solvent isopropyl alcohol permitted a large change in the solvated proton concentration near the end point. The dielectric constant of isopropyl alcohol is also the smaller one as compared to acetone and dimethyl formamide. It can be purified and made anhydrous very easily as compared to other solvents.

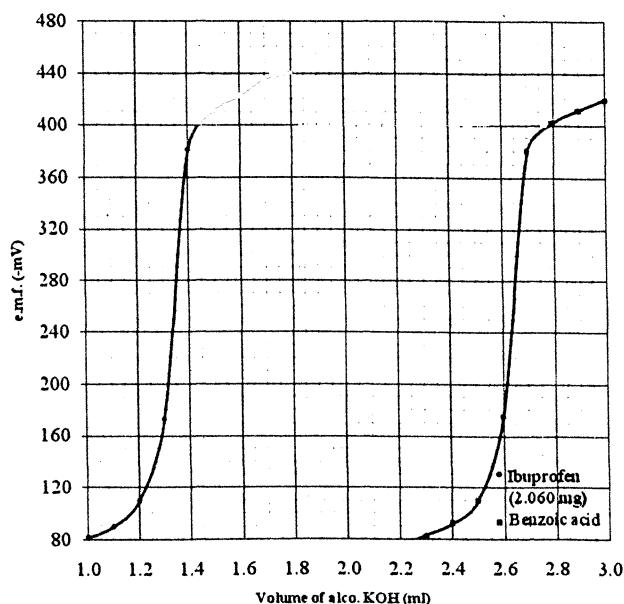
**Graph 1.** Effect of solvent on potentiometric determination of ibuprofen.

For the study of effect of concentration and to find out the suitable concentration range which gives best results, different volumes of the stock solution of ibuprofen were diluted to 20 ml with isopropyl alcohol and titrated separately with KOH in isopropyl alcohol. The results obtained are tabulated and it can be seen from that, the

potentiometric method gave an accuracy of  $\pm 1.0\%$  for the entire range of 4.120 to 18.54 mg. It is observed that the results obtained are quite satisfactory with much more accuracy than other methods. Both positive as well as negative errors are obtained (Table 2). This method is found to be better than the pharmacopoeias method of visual titration in respect of indicator error. The potentiometric breaks obtained are much more pronounced (Graph 2). Values of mean, mean deviation and standard deviation for the determination of effect of concentration of ibuprofen are 11.30, 5.15, 6.24 (for weight titrated);

**Table 2.** Effect of concentration on potentiometric determination of ibuprofen

Weight titrated (mg)	Weight found (mg)	Error (%)
2.060	2.088	+1.35
4.120	4.114	-0.14
6.180	6.203	+0.37
8.240	8.308	+0.82
10.300	10.239	-0.59
12.360	12.250	-0.88
14.420	14.370	-0.34
16.480	16.317	-0.98
18.540	18.453	-0.46
20.600	20.087	-2.49

**Graph 2.** Effect of concentration on potentiometric determination of ibuprofen.

11.24, 5.05, 6.11 (for weight found) and -0.334, 0.7472, 1.0618 (for % error) respectively. Confidence level of weight titrated and weight found in respect of ibuprofen is 0.0299 which is statistically non significant.

#### *Estimation of ibuprofen in single component tablets :*

Ten tablets of the same batch of ibuprofen were accurately weighed and powdered. The required quantity of powder was weighed accurately, it was extracted with isopropyl alcohol and the volume was made to 100 ml. An aliquot of 10 ml of this solution was diluted to 20 ml with isopropyl alcohol and titrated with KOH in isopropyl alcohol using potentiometer. The titrant was standardized by potentiometric titration with standard benzoic acid in isopropyl alcohol. The weight of ibuprofen present in one tablet was calculated. The same tablet powder was analyzed by I.P. method. The results obtained for four different samples of ibuprofen tablets are tabulated and it is observed that, the present potentiometric method gives results comparable to those obtained by I.P. method (Table 3). It is much better, accurate and simple method than other methods reported in the literature. Ibuprofen gets hydrolyzed in presence of aqueous alkali but this is avoided in non-aqueous medium. Commonly the additives present in the tablets are calcium carbonate, sugars, gum etc. These additives are insoluble in isopropyl alcohol and do not affect the results.

**Table 3.** Estimation of ibuprofen in single component tablets

Sample	Label claim (mg)	Weight found (mg)	
		I.P. method	Present method
A	200.0	198.22	197.899
B	200.0	191.87	192.250
C	400.0	400.79	401.446
D	400.0	394.12	389.615

#### **Experimental**

The potentiometric titrations were performed by a digital potentiometer (Equiptronics, EQ-602). Glass was used as an indicator electrode and calomel as a reference electrode. All weighing were made on Precisa-310M ( $\pm 0.001$  g) balance. The chemicals and solvents used were of A.R. grade. Solvents were purified and made anhydrous by standard methods<sup>8</sup>. Care was taken to protect the titrant from atmospheric moisture and carbon dioxide. The ibuprofen selected for present investigation was of phar-

maceutical in nature and is included in pharmacopoeias<sup>4,9</sup>. It was obtained from pharmaceutical laboratories.

#### *Effect of solvent and concentration on potentiometric determination of ibuprofen :*

To study the effect of solvent on potentiometric determination of ibuprofen, stock solutions of ibuprofen (2.072 mg/ml,  $\pm 0.5\%$ ) were prepared by dissolving it in acetone, methanol, dimethyl formamide and isopropyl alcohol. 2 ml of these solutions were diluted to 20 ml with same solvents and titrated separately with KOH in isopropyl alcohol using a pair of glass and calomel electrodes. For the study of effect of concentration, a stock solution of ibuprofen (2.06 mg/ml) was prepared by dissolving it in isopropyl alcohol. Different volumes (1 to 10 ml) of this stock solution were diluted to 20 ml with isopropyl alcohol and titrated separately with KOH in isopropyl alcohol. The titrant was added in the lots of 0.1 ml and the potential developed across the two electrodes was measured after each addition. Magnetic stirrer was used to stir the solution and a waiting period of about 1 to 2 min was allowed to get the potential stabilized. The addition of titrant was continued till 0.3 to 0.5 ml excess of it was added. Near the end point readings were recorded for each addition of 0.02 ml of the titrant. The end points were determined by plotting the graphs of potential developed against volume of the titrant.

#### *Estimation of ibuprofen in single component tablets :*

In this analysis, ten tablets of the same batch of ibuprofen were accurately weighed and powdered. The powder containing 100 mg of the drug was weighed accurately and treated with 50 ml of isopropyl alcohol and stirred vigorously so as to dissolve the active component of the tablet. Binding agents or filler remained insoluble. The additives commonly present in the tablets are calcium carbonate, glucose, lactose, starch, gum etc. which are mostly insoluble in isopropyl alcohol. The solution was filtered, residue was washed three to four times with small portions of isopropyl alcohol and the volume of solution was made to 100 ml with isopropyl alcohol. An aliquot of 10 ml of this solution was diluted to 20 ml with isopropyl alcohol and titrated with 0.1 *M* of solution of KOH in isopropyl alcohol by potentiometric method using the glass and calomel electrodes. The titrant was standardized by potentiometric titration with 0.1 *M* benzoic

acid in isopropyl alcohol. The end points were found out by plotting the graphs as described earlier; the amount of drug present in titrated weight of tablet powder was calculated. The amount of active component (drug) present in one tablet was calculated by knowing the average weight of the tablet. Later on the same tablet powder was analyzed by the method of pharmacopoeias and the results obtained were compared.

#### Conclusion :

The acidic pharmaceutical drug selected for this study was ibuprofen. It could be noted that being distinctly acidic could not be titrated directly with aqueous alkali due to its easy hydrolysis but the non-aqueous titration of ibuprofen gave satisfactory results. The solvent isopropyl alcohol is found to be more satisfactory for all the titrations. Potassium hydroxide in isopropyl alcohol was found to be better titrant. This basic titrant was also superior to the alkoxide solvents which are more susceptible to atmospheric moisture and carbondioxide. It gave better potentiometric breaks. The pair of calomel and glass electrode gave stable potentials which were quickly attained. The potentiometric breaks obtained with this electrode pair system were much larger. In the present research work, method for determination of acidic drug ibuprofen was developed. It is fast, simple and accurate which can be used even in common laboratories and do not involve use of any sophisticated instrument.

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