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Non-aqueous potentiometric determination of pharmaceutically potent drug diphenhydramine hydrochloride

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Abstract : The non-aqueous potentiometric determination of pharmaceutically potent drug diphenhydramine hydrochloride by performing the titrations using isopropyl alcohol as the solvent and KOH in isopropyl alcohol as the titrant has been carried out. The effect of solvent and concentration on potentiometric determination of this drug has been studied followed by its estimation in single component tablets. A pair of glass and calomel electrode was used to do the titrations. The method was found to be precise for assay of diphenhydramine hydrochloride and results obtained are comparable with those obtained by Indian Pharmacopoeia (I.P.) method.

Keywords : Non-aqueous, potentiometric determination, diphenhydramine hydrochloride.

Introduction

The potentiometric determination in non-aqueous media using different electrode pairs has been reported earlier[1]. Literature is enriched with various methods for the determination of drug diphenhydramine hydrochloride[2]. Its estimation by conductometry has been reported earlier by few workers[3]. It has been also determined by spectrophotometric method[4] and analyzed by liquid chromatography[5]. Diphenhydramine hydrochloride is distinctly acidic and due to its easy hydrolysis it could not be titrated directly with aqueous alkali. Basic titrant is superior to the alkoxide solvents which are more susceptible to the atmospheric moisture and carbondi-oxide. The aim of present work is to find out the simple procedure for analysis of common drugs that will help in determination of raw materials and products for quick check of spurious drugs which are feared to penetrate the markets. The non-aqueous potentiometric determination of drug diphenhydramine hydrochloride by performing the titrations using isopropyl alcohol as the solvent and KOH in isopropyl alcohol as the titrant has been reported in this communication. The effect of solvent, concentration and the estimation of this drug in single component tablets have been also studied.

Results and discussion

Effect of solvent and concentration on potentiometric determination of diphenhydramine hydrochloride :

In the study of effect of solvent, the accuracy of results in determination of drug diphenhydramine hydrochloride by using different solvents was checked by potentiometric titration method. The required volumes of the stock solutions of this drug 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 diphenhydramine hydrochloride by using the solvent isopropyl alcohol is much more with minimum % error as compare to other solvents (Table 1). As compared to the solvent dimethyl formamide, methanol and acetone the potentiometric break obtained using isopropyl alcohol is much more pronounced and prominent with maxi-

Table 1. Effect of solvent on potentiometric determination of diphenhydramine hydrochloride

Solvent	Weight titrated (mg) (±0.5%)	Weight found (mg)	Error (%)
Acetone	5.8364	5.6169	-3.76
Methanol	5.8364	5.8843	+0.82
Dimethyl formamide	5.8364	5.7506	-1.46
Isopropyl alcohol	5.8364	5.7952	-0.70

mum potential difference near the equivalence point (Fig. 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 smaller as compared to dimethyl formamide, methanol and acetone. It can be purified and made anhydrous very easily as compared to other solvents.

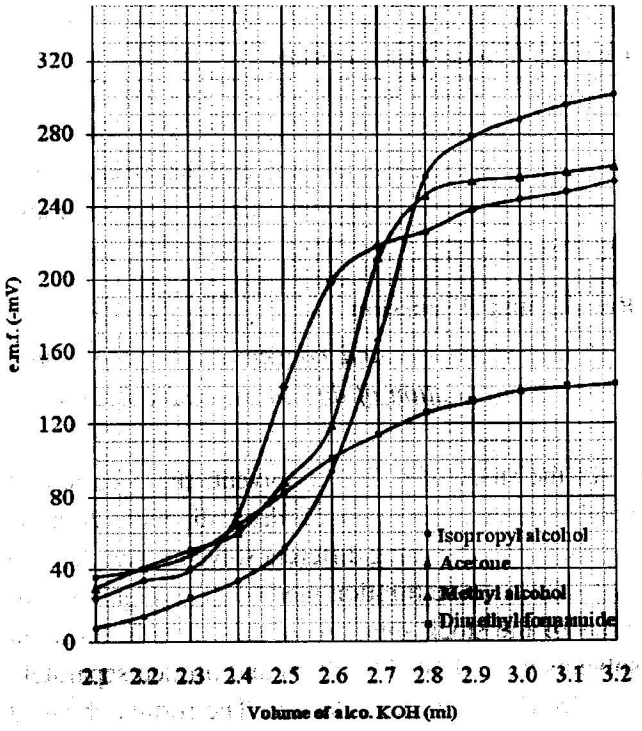

Fig. 1. Effect of solvent on potentiometric determination of diphenhydramine hydrochloride.

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 diphenhydramine hydrochloride 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 +1.7% for the range of 2.92 to 11.68 mg and -0.9% for the range of 14.60 to 29.20 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 (Fig. 2). Values of mean, mean deviation and standard deviation for the determination of effect of concentration of diphenhydramine hydrochloride are 16.06, 7.30, 8.84 (for weight titrated); 15.97, 7.14, 8.69 (for weight found) and 0.155, 0.838, 0.958 (for % error) respectively.

Table 2. Effect of concentration on potentiometric determination of diphenhydramine hydrochloride

Weight titrated (mg)	Weight found (mg)	Error (%)
2.920	3.005	+1.03
5.840	5.900	+1.03
8.760	8.906	+1.67
11.680	11.800	+1.08
14.600	14.584	-0.10
17.520	17.078	-0.23
20.440	20.373	-0.32
23.360	23.156	-0.87
26.280	26.051	-0.87
29.200	28.945	-0.87

Estimation of diphenhydramine hydrochloride in single component tablets :

Ten tablets of the same batch of diphenhydramine hydrochloride 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 diphenhydramine hy-

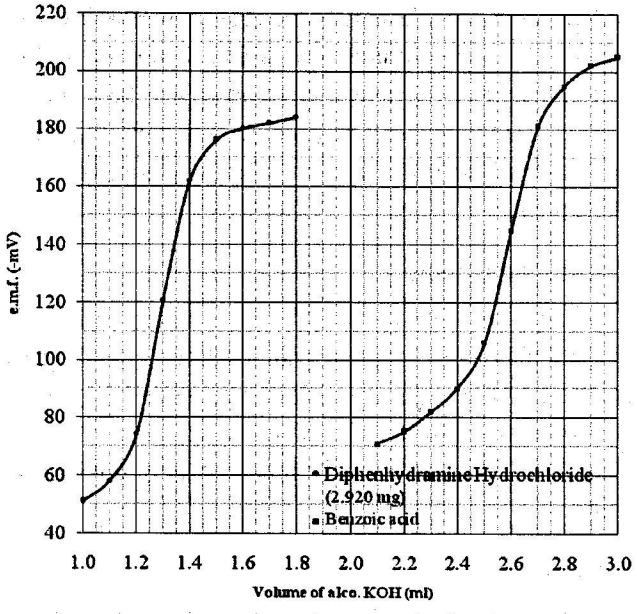

Fig. 2. Effect of concentration on potentiometric determination of diphenhydramine hydrochloride.

drochloride present in one tablet was calculated. The same tablet powder was analyzed by I.P. method. The results obtained for four different samples of 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. Diphenhydramine hydrochloride 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 diphenhydramine hydrochloride in single component tablets

Sample	Label claim	Weight found (mg)	
	(mg)	I.P. method	Present method
A	100.0	101.98	100.89
B	100.0	102.04	101.08
C	100.0	100.96	100.55
D	100.0	101.46	100.94

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 (±0.001 g) balance. The chemicals and solvents used were of A.R. grade. Solvents were purified and made anhydrous by standard methods[6]. Care was taken to protect the titrant from atmospheric moisture and carbon dioxide. The diphenhydramine hydrochloride selected for present investigation was of pharmaceutical in nature and is included in pharmacopoeias[7,8]. It was obtained from pharmaceutical laboratories.

Effect of solvent and concentration on potentiometric determination of diphenhydramine hydrochloride :

To study the effect of solvent on potentiometric determination of diphenhydramine hydrochloride, its stock solutions (2.918 mg/ml, ±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 diphenhydramine hydrochloride (2.920 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 diphenhydramine hydrochloride in single component tablets :

In this analysis, ten tablets of the same batch of diphenhydramine hydrochloride 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 diphenhydramine hydrochloride. 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 diphenhydramine hydrochloride 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 diphenhydramine hydrochloride 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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