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Non-Aqueous Potentiometric Analysis of Drug Furosemide in Bulk and Single Component Pharmaceutical Tablets

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Abstract

Non-aqueous potentiometric analysis of drug furosemide in bulk and single component pharmaceutical tablets was performed by using the solvent isopropanol and titrant KOH in isopropanol. Effect of solvent and concentration on non-aqueous potentiometric analysis of drug furosemide and its estimation in bulk and single component drugs was studied using a glass and calomel electrode pair. The method of non-aqueous potentiometric titration was found to be simple, accurate and coherent. Results obtained are comparable to that of Indian Pharmacopoeia (I.P.) method.

Keywords: Non-aqueous, potentiometric, analysis, drug furosemide.

Introduction

Non-aqueous potentiometric analysis of various drugs using varied electrode pairs has been reported earlier in the literature[1-5]. Literature is enriched with number of methods of analysis of drug furosemide[6,7]. Its determination by potentiometric technique has been reported earlier by some researchers[8]. Spectrophotometry, spectrofluorometry, colorimetry, reversed phase liquid chromatography methods were also used for analysis of this drug[9-11]. Drug furosemide is distinctly acidic. It could not be titrated directly with aqueous alkali because of its easy hydrolysis. Basic titrant is superior to the alkoxide solvents which are more susceptible to carbondioxide and atmospheric moisture. The aim of present work is to find out basic, accurate method for analysis of commonly used pharmaceutical drugs which will be helpful in determining the raw materials and products for instant check of spurious drugs that are feared to penetrate the markets. In present communication, non-aqueous potentiometric analysis of drug furosemide in bulk and single component pharmaceutical tablets using solvent isopropanol and titrant KOH in isopropanol has been reported. Effect of solvent and concentration on potentiometric analysis of drug furosemide has also been studied.

Results and Discussion:

Effect of solvent and concentration on potentiometric analysis of drug furosemide.

Accuracy of results in determination of drug furosemide by using different solvents was checked by non-aqueous potentiometric titration method. Required volumes of stock solutions of drug furosemide in various solvents were diluted to 20 ml and separately titrated with KOH in isopropanol. It was found that, accuracy of result in analysis of drug furosemide by using solvent isopropanol is much more as compared to other solvents with minimum % error (**Table 1**). Potentiometric breaks obtained using solvents dimethyl formamide and acetone are smoother as compared to methanol whereas using isopropanol, potentiometric break obtained is much more pronounced and prominent with high potential difference near equivalence point (**Graph 1**). Dielectric constant of isopropanol is less than dimethyl formamide, methanol and acetone. It permitted a large change in the solvated proton concentration near the end point. Isopropanol can be purified and made anhydrous very easily as compared to other solvents.

To determine suitable concentration range that gives best results, different volumes of stock solution of drug furosemide were diluted to 20 ml with isopropanol and separately titrated with KOH in isopropanol. It was found that, potentiometric method gave an accuracy of ±0.5% for the range of 3.310 to 33.100 mg. Results obtained are much more accurate as compared to

other methods with both positive and negative errors (**Table 2**). Present method of analysis is found to be better in respect of indicator error than visual titration method given in pharmacopoeias. Potentiometric breaks obtained are much more pronounced (**Graph 2**). The mean, mean deviation and standard deviation values of study of effect of concentration on potentiometric analysis of drug furosemide are 18.205, 8.275, 10.021 for weight titrated, 18.207, 8.339, 10.085 for weight found and 0.167, 0.249, 0.314 for % error respectively.

Analysis of drug furosemide in single component pharmaceutical tablets

Drug furosemide containing 10 pharmaceutical tablets of the same batch were accurately weighed and powdered. Required quantity of powder was weighed accurately, it was extracted with isopropanol and volume was made to 100 ml. An aliquot of 10 ml of this solution was diluted with isopropanol to 20 ml and titrated with KOH in isopropanol using potentiometer. Titrant was standardized by potentiometric titration using standard benzoic acid in isopropanol. Weight of furosemide present in 1 tablet was calculated. Same tablet was analyzed by I.P. method. Results obtained for 3 different brands of pharmaceutical tablets are tabulated and it is observed that, present potentiometric method gives fairly comparable and accurate results to those obtained by I.P. method (**Table 3**). Present method is much better, accurate and simple than the methods reported in literature. It is free from indicator error or interferences. Drug furosemide gets hydrolyzed in presence of aqueous alkali but this is avoided in non-aqueous medium. Most common additives present in pharmaceutical tablets are calcium carbonate, sugars, gum etc. and as these are insoluble in isopropanol do not affect the results.

Table 1 : Effect of solvent on potentiometric analysis of drug furosemide.

Solvent	Weight Titrated (mg) (±0.5%)	Weight Found (mg)	Error (%)
Isopropanol	6.620	6.601	+ 0.28
Acetone	6.620	6.591	+ 0.43
Methanol	6.620	6.642	– 0.33
Dimethyl formamide	6.620	6.588	+ 0.48

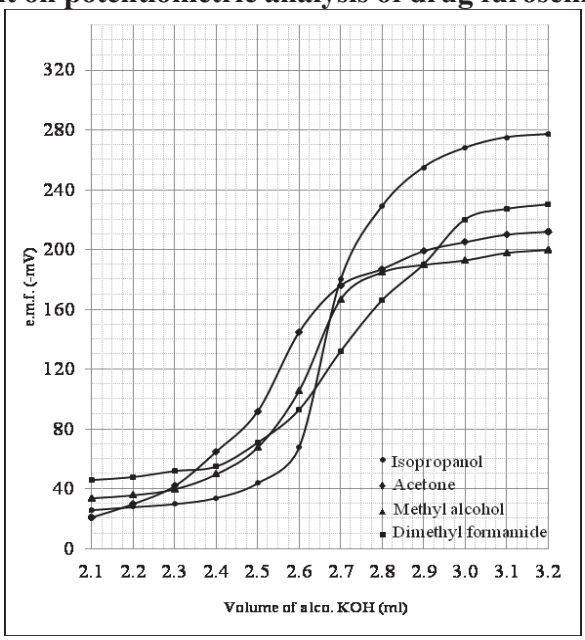
Table 2 : Effect of concentration on potentiometric analysis of drug furosemide.

Weight Titrated (mg)	Weight Found (mg)	Error (%)
3.310	3.320	+ 0.31
6.620	6.647	+ 0.42
9.930	9.666	+ 0.37
13.240	13.222	– 0.13
16.550	16.483	– 0.48
19.860	19.901	+ 0.21
23.170	23.204	+ 0.15
26.480	26.448	– 0.12
29.790	29.938	+ 0.50
33.100	33.245	+ 0.44

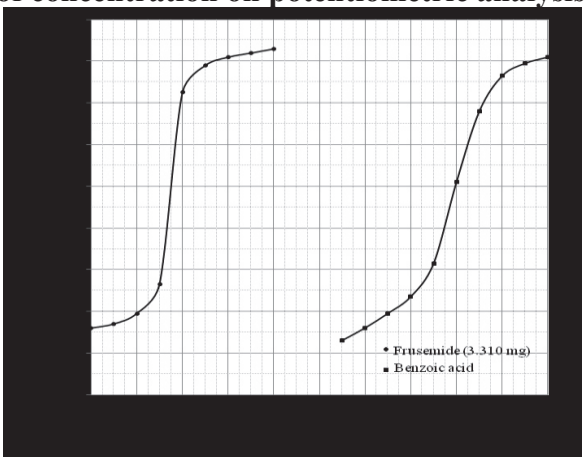
Table 3 : Analysis of drug furosemide in single component pharmaceutical tablets.

Sample	Label Claim (mg)	Weight Found (mg)	
		I.P. Method	Present Method
A	100.0	99.38	100.51
B	100.0	101.01	100.08
C	250.0	248.98	249.66

Graph 1 : Effect of solvent on potentiometric analysis of drug furosemide.



Graph 2 : Effect of concentration on potentiometric analysis of drug furosemide.



Experimental

All titrations were performed using potentiometer (Equiptronics, EQ-602). Glass electrode was used as an indicator whereas calomel as a reference electrode. Weighings were done using balance (Precisa-310M, ±0.001 g). Chemicals and solvents used were of A.R. grade. Solvents were purified and made anhydrous using standard methods[12,13]. Care was taken to protect titrant from carbon dioxide and atmospheric moisture. Drug furosemide used for this study was collected from pharmaceutical laboratories. It is of pharmaceutical in nature and included in pharmacopoeias[14-16].

Effect of solvent and concentration on potentiometric analysis of drug furosemide:

During study of effect of solvent on potentiometric analysis of drug furosemide, its stock solutions (3.310 mg/ml, ±0.5%) were prepared by dissolving it in solvents isopropanol, acetone, methanol and dimethyl formamide. Then 2 ml of these solutions were diluted to 20 ml with same solvents and separately titrated with KOH in isopropanol using a pair of glass and calomel electrodes. For study of effect of concentration, stock solution of furosemide (3.310 mg/ml) was prepared by dissolving it in isopropanol. Different volumes (1 to 10 ml) of stock solution were diluted to 20 ml with isopropanol and separately titrated with KOH in isopropanol by adding titrant in lots of 0.1 ml with stirring by magnetic stirrer. Potential developed across two electrodes was measured after each addition. Waiting period of about 1 to 2 minutes was allowed

to get potential stabilized. Addition was continued till 0.3 to 0.5 ml excess of titrant was added. At the end point readings were recorded for each addition of 0.02 ml of titrant. End points were found out by plotting graphs of potential developed against volume of titrant.

Analysis of drug furosemide in single component pharmaceutical tablets :

During this analysis, 10 tablets of drug furosemide of same batch were accurately weighed and powdered. Powder containing 100 mg of drug was weighed accurately, treated with 50 ml of isopropanol and vigorously stirred to dissolve active component of tablet. Most common additives present in pharmaceutical tablets are calcium carbonate, sugars, gum etc. which are mostly insoluble in isopropanol. Solution was filtered, residue was washed three to four times with small portions of isopropanol and volume of solution was made to 100 ml with isopropanol. An aliquot of 10 ml of this solution was diluted to 20 ml with isopropanol and titrated with 0.1 M of solution of KOH in isopropanol by potentiometric method using a pair of glass and calomel electrodes. Titrant was standardized by potentiometric titration with 0.1 M benzoic acid in isopropanol. End points were determined by plotting graphs as described earlier and amount of drug present in titrated weights of tablet powder was calculated. Amount of active component (drug) present in 1 tablet was calculated from average weight of tablet. Same tablets were then analyzed by method of pharmacopoeias and results obtained were compared.

Conclusion

Non-aqueous potentiometric titration of drug furosemide gave better results. Solvent isopropanol is found to be excellent for all titrations. Basic titrant, potassium hydroxide in isopropanol was superior to alkoxide solvents that are more susceptible to carbondioxide and atmospheric moisture. It gave better potentiometric breaks. Pair of calomel and glass electrodes gave stable potentials which were quickly attained. Potentiometric breaks obtained using this pair of electrodes were quite larger. In this study, method for analysis of acidic drug furosemide was developed. It is simple, accurate, coherent and can be used even in common laboratories without use of any sophisticated instrument.

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