15. Non-Aqueous Potentiometric Analysis of Drug Paracetamol in Bulk and Single Component Pharmaceuticals

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Abstract

Non-aqueous potentiometric analysis of drug paracetamol in bulk and single component pharmaceuticals have been carried out using isopropyl alcohol as the solvent and KOH in isopropyl alcohol as the titrant. Effect of solvent and concentration on potentiometric analysis of drug paracetamol as well as its analysis in bulk and single component pharmaceuticals has been studied by using platinum-calomel electrode pair. Method was found to be simple, efficient, precise and gave results comparable to those obtained by Indian Pharmacopoeia (I.P.) method.

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

Introduction

In past years, scientific literature is enriched with progressive findings about the methods of determination of pharmaceutical compounds. Various methods are reported in literature for determination of paracetamol[1-3]. Determination of paracetamol by spectrophotometric and colorimetric methods has been carried out by many workers[4-8]. Literature is enriched with potentiometric determination of paracetamol[9-12]. Investigation of paracetamol by R.P.-H.P.L.C. and H. P. L. C. technique[13-15] was performed earlier. Some workers used solid phase extraction, gas chromatography and mass spectrometry technique for analysis of paracetamol[16]. Potentiometric determination of paracetamol in combination with aceclofenac, mefenamic acid, diphenhydramine hydrochloride has been carried out earlier[17-19]. However, determination of

paracetamol in isopropyl alcohol by potentiometric titration using platinum-calomel electrode pair was not carried out so far.

Paracetamol is distinctly acidic and it could not be titrated directly with aqueous alkali owing to its easy hydrolysis. Basic titrant is also superior to alkoxide solvents which are more susceptible to atmospheric moisture and carbondioxide. Purpose of present work is to find out simple analysis method for common pharmaceutical drugs. It will help to analyze raw materials and products for quick check of spurious drugs that are feared to penetrate the markets. In this communication, non-aqueous potentiometric analysis of drug paracetamol in bulk and single component pharmaceuticals using isopropyl alcohol as solvent and KOH in isopropyl alcohol as titrant has been reported with use of platinum-calomel electrode pair. Study of effect of solvent and concentration on potentiometric analysis of drug paracetamol has also been attempted.

Results and Discussion

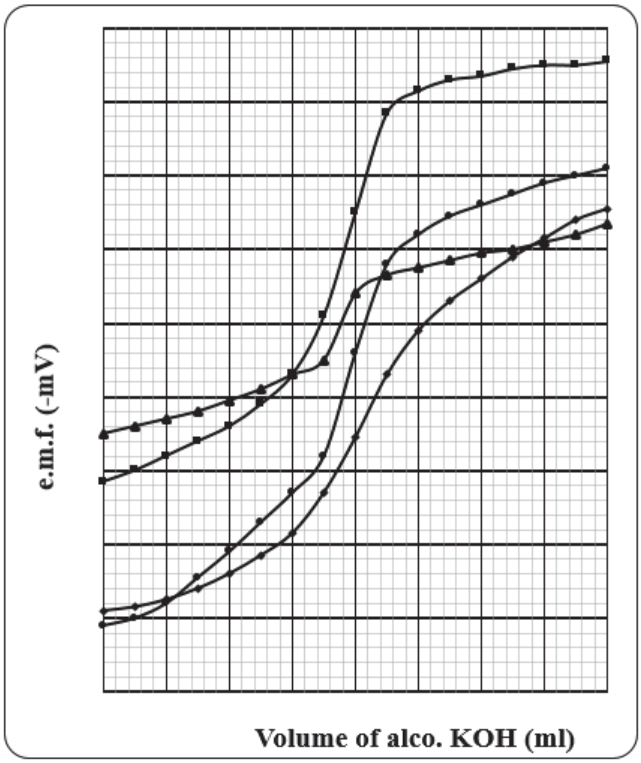
Effect of Solvent and Concentration on Potentiometric Analysis of Drug Paracetamol

Herein the study of effect of solvent, accuracy of results in analysis of drug paracetamol using different solvents was checked by non-aqueous potentiometric titration. Required volumes of stock solutions of drug paracetamol in different solvents were diluted to 20 ml and then titrated separately with KOH in isopropyl alcohol. From results, it can be seen that accuracy of result in analysis of drug paracetamol using solvent isopropyl alcohol is much more with minimum % error as compare to other solvents (**Table-1)**. Potentiometric breaks obtained using solvents dimethyl formamide, acetone are smoother as compared to methanol whereas potentiometric break obtained using isopropyl alcohol is much more pronounced and prominent with maximum potential difference near the equivalence point (**Graph-1**). Dielectric constant of isopropyl alcohol is smaller than dimethyl formamide, methanol and acetone. It permitted large change in solvated proton concentration near end point. Compared to other solvents, isopropyl alcohol can be purified and made anhydrous easily and fastly.

Table - 1 : Effect of Solvent on Potentiometric Analysis of Drug Paracetamol

Solvent	Weight Titrated (mg) (±0.5%)	Weight Found (mg)	Error (%)
Acetone	30.200	30.654	+ 1.50
Dimethyl formamide	30.200	30.890	+ 2.28
Methanol	30.200	29.594	– 2.00
Isopropyl alcohol	30.200	30.420	+ 0.72

Graph-1 : Effect of Solvent on Potentiometric Analysis of Drug Paracetamol

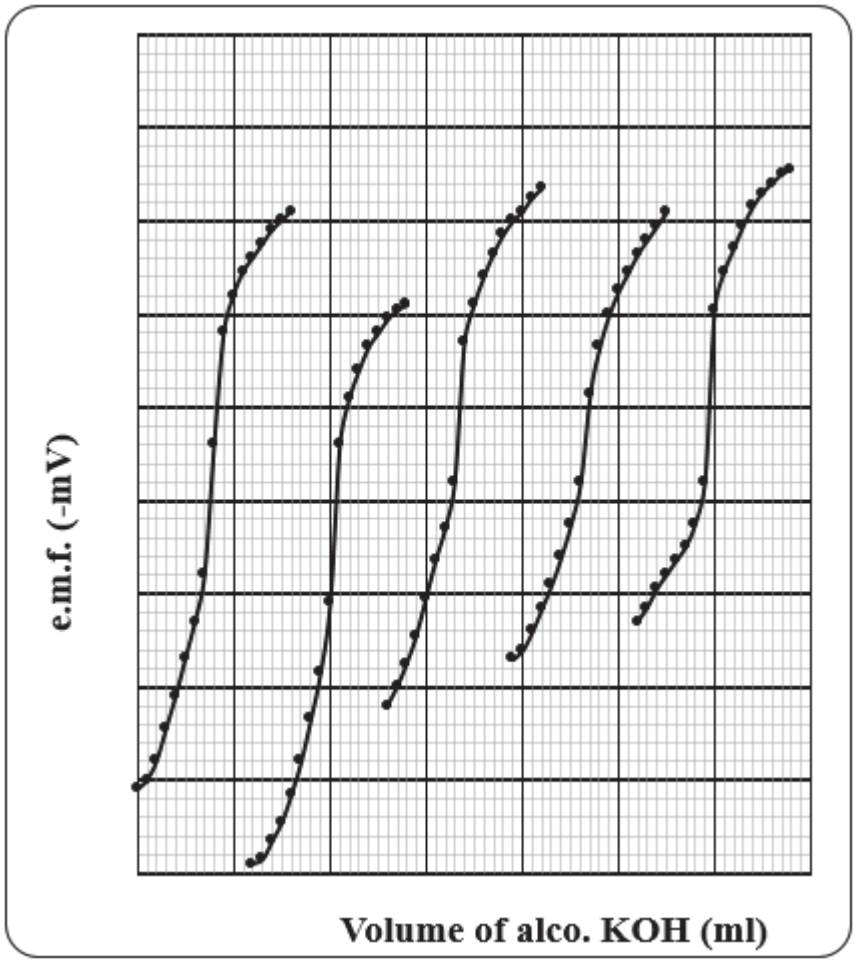


To study of effect of concentration and to find out suitable concentration range that gives best results, different volumes of stock solution of drug paracetamol were diluted to 20 ml with isopropyl alcohol and titrated separately with KOH in isopropyl alcohol. From results, it can be seen that potentiometric method gave an accuracy of ±0.7% for entire range of 30.420 to 152.100 mg. Results obtained are good and much more accurate than other methods with both positive as well as negative errors (**Table-2)**. This 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**).

Table-2 : Effect of Concentration on Potentiometric Analysis of Drug Paracetamol

Weight Titrated (mg)	Weight Found (mg)	Error (%)
30.200	30.420	+ 0.72
60.400	60.132	– 0.44
90.600	90.786	+ 0.20
120.800	121.440	+ 0.52
151.000	152.100	+ 0.72

Graph-2 : Effect of Concentration on Potentiometric Analysis of Drug Paracetamol



Analysis of Drug Paracetamol in Single Component Pharmaceuticals

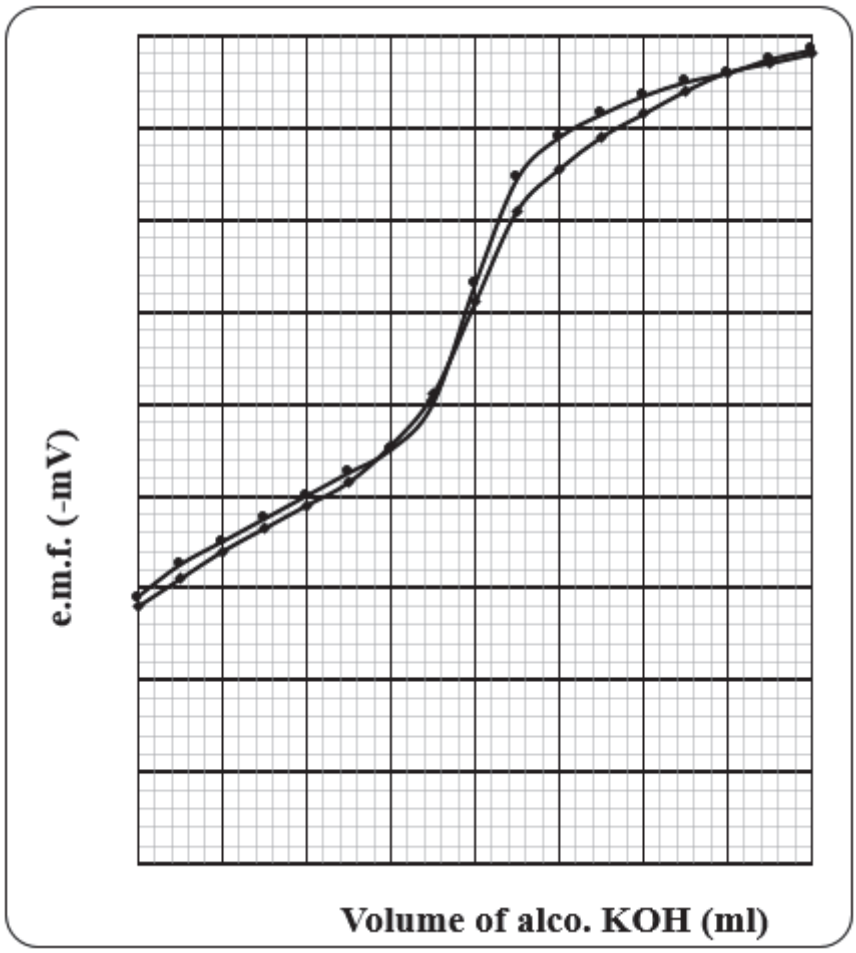
Drug paracetamol containing ten pharmaceutical tablets of same batch were accurately weighed and powdered. Required quantity of powder was weighed accurately, it was extracted with isopropyl alcohol and volume was made to 100 ml. An aliquot of 10 ml of this solution was diluted with isopropyl alcohol to 20 ml and titrated with KOH in isopropyl alcohol using potentiometer. Titrant was standardized by performing potentiometric titration using standard benzoic acid in isopropyl alcohol. Weight of drug paracetamol present in one tablet was calculated. Same tablet was analyzed by I.P. method. Results obtained for two different brands of pharmaceutical tablets are tabulated and it is observed that, present potentiometric method gives fairly accurate and comparable results to those obtained by I.P. method (**Table-3)**. This method is better, accurate and simple than methods reported in literature. It is free from indicator error or

interferences. Potentiometric breaks obtained are more pronounced (**Graph-3**). Paracetamol 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 isopropyl alcohol do not affect results.

Table-3 : Analysis of Drug Paracetamol in Single Component Pharmaceuticals

Sample	Label Claim (mg)	Weight Found (mg)	
		I.P. Method	Present Method
A1	500	494.750	495.200
A2	500	492.295	492.800

Graph- 3 : Analysis of Drug Paracetamol in Single Component Pharmaceuticals



Experimental

Titrations were carried out using digital pH-meter (Systronics, MK-VI). Platinum was used as an indicator and calomel as a reference electrode. Weighing were made on Precisa-310M (Adair Dutt) (±0.001 g) balance. Chemicals and solvents of A.R. grade were used. All solvents were purified and made anhydrous by standard methods[20,21]. Care was taken to protect titrant from atmospheric moisture and carbon dioxide. Drug paracetamol used for present study was obtained from pharmaceutical laboratories and it is included in pharmacopoeias[22-24].

Effect of solvent and concentration on potentiometric analysis of drug paracetamol

To study effect of solvent on potentiometric analysis of drug paracetamol, its stock solutions (15.100 mg/ml, ±0.5%) were prepared by dissolving it in solvents acetone, dimethyl formamide, methanol and isopropyl alcohol. Then 2 ml of these solutions were diluted to 20 ml with same solvents and separately titrated with KOH in isopropyl alcohol using platinum-calomel electrode pair. For study of effect of concentration, stock solution of drug paracetamol (15.100 mg/ml) was prepared by dissolving it in isopropyl alcohol. Different volumes (2 to 10 ml) of stock solution were diluted to 20 ml with isopropyl alcohol and separately titrated with KOH in isopropyl alcohol by adding titrant in lots of 0.1 ml with continuous stirring using 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. Near 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 Paracetamol in Single Component Pharmaceuticals

In this analysis, drug paracetamol containing ten tablets of same batch were accurately weighed and powdered. Powder containing 500 mg of drug was weighed accurately, treated with 50 ml of isopropyl alcohol 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 isopropyl alcohol. Solution was filtered, residue was washed three to four times with small portions of isopropyl alcohol and 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 platinum-calomel electrode pair. Titrant was standardized by

potentiometric titration with 0.1 M benzoic acid in isopropyl alcohol. End points were determined by plotting graphs as described earlier; amount of drug present in titrated weights of tablet powder was calculated. Amount of active component (drug) present in one tablet was calculated from average weight of tablet. Same tablets were then analyzed by method of pharmacopoeias and results obtained were compared.

Conclusion

Pharmaceutical drug selected for present study was paracetamol. Being distinctly acidic it could not be titrated directly with aqueous alkali owing to its easy hydrolysis but non-aqueous titration of paracetamol gave better results. Solvent isopropyl alcohol is found to be excellent for all titrations. Basic titrant, potassium hydroxide in isopropyl alcohol was superior to alkoxide solvents that are more susceptible to atmospheric moisture and carbondioxide. It gave better potentiometric breaks. Platinum-calomel electrode pair gave stable potentials which were quickly attained. Potentiometric breaks obtained using these electrode pair systems were quite larger. In present work, method for analysis of acidic drug paracetamol was developed. It is simple, efficient and precise. It can be used even in common laboratories without use of any sophisticated instrument.

Acknowledgement

Authors are thankful to Dr. V. D. Nanoty, Principal, Shri Radhakisan Laxminarayan Toshniwal College of Science, and Akola for providing required facilities.

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