

SIMULTANEOUS NON-AQUEOUS POTENTIOMETRIC DETERMINATION OF PHARMACEUTICALLY POTENT IBUPROFEN-DIPHENHYDRAMINE HYDROCHLORIDE AND PARACETAMOL-DIPHENHYDRAMINE HYDROCHLORIDE COMBINATION DRUGS

Deohate, P.P.

Department of Chemistry, Shri Radhakisan Laxminarayan Toshniwal College of Science,
Akola-444001, India
pradip222091@yahoo.co.in

ABSTRACT

The simultaneous non-aqueous potentiometric determination of pharmaceutically potent combination drugs by using isopropyl alcohol as the solvent and KOH in isopropyl alcohol as the titrant has been established. The two acidic combination drugs ibuprofen-diphenhydramine hydrochloride and paracetamol-diphenhydramine hydrochloride were determined simultaneously in their binary mixtures by the non-aqueous differentiating potentiometric titration methods. These drug combinations are widely used in medicines. Titrations were carried out using a pair of glass and calomel electrodes. The method was found to be precise for assay of double component tablets and results obtained are comparable with those obtained by Indian Pharmacopoeia (I.P.) method.

Keywords: Non-aqueous, potentiometric determination, combination drugs

INTRODUCTION

The non-aqueous potentiometric determination has been reported earlier using the pairs of different electrode¹⁻⁵. Different methods were suggested for the estimation of two or more drugs in combination and deals mostly with the separation of components followed by determination of individual component using suitable technique. For the determination of drugs in combination various methods were included in the pharmacopoeias⁶⁻⁸. Differentiating potentiometric titrations of mixtures like paracetamol-barbitone², paracetamol-salicylamide^{9,10}, paracetamol-aspirin¹¹ etc. have also been reported in literature. The literature is enriched with determination of nimesulide-tizanidine¹², nimesulide-chlorzoxazone¹³, nimesulide-diclofenac sodium¹⁴ etc. Binary mixture of ibuprofen-paracetamol¹⁵ as well as ternary mixture of ibuprofen-paracetamol-chlorzoxazone¹⁶ has also been determined by spectrophotometric and chromatographic technique. Determination of combination of ibuprofen-diphenhydramine hydrochloride and paracetamol-diphenhydramine hydrochloride drugs by differentiating potentiometric method using acetone or isopropyl alcohol was not reported in literature so far. As these drugs are distinctly acidic, could not be titrated directly with aqueous alkali due to their hydrolysis. The basic titrant is also superior to the alkoxide solvents which are more susceptible to the atmospheric

moisture and carbon dioxide. The aim of the present work is to find out simple analysis procedure for common drugs which will help the analysis of raw materials and products for quick check of spurious drugs that are feared to penetrate the markets. In this communication, study non-aqueous titrations were carried out to determine one component in presence of other without any prior separation. Determination of ibuprofen and diphenhydramine hydrochloride as well as paracetamol and diphenhydramine hydrochloride in two component tablets has been carried out using isopropyl alcohol as the solvent and KOH in isopropyl alcohol as the titrant by potentiometric titration method.

MATERIAL AND METHODS

The potentiometric titrations were carried out by using a digital potentiometer (Equiptronics, EQ-602). Glass and calomel electrodes were used as indicator and reference electrode respectively. Weighing of all the drugs and chemicals was made on Precisa-310-M (± 0.001 g) balance. The chemicals and solvents of AR grade were used. All solvents were purified and made anhydrous by standard methods¹⁷. Care was taken to protect the titrant from atmospheric moisture and carbon dioxide. The drugs selected for present investigation were obtained from pharmaceutical laboratories. These drugs are of pharmaceutical nature and are included in pharmacopoeias⁶⁻⁸. During this analysis, ibuprofen-diphenhydramine hydrochloride and paracetamol-diphenhydramine

hydrochloride drugs containing ten tablets of the same batch were accurately weighed and powdered. The quantity of powder equivalent to about 200 mg of ibuprofen/paracetamol and 25 mg of diphenhydramine hydrochloride was accurately weighed and treated with 50 ml of isopropyl alcohol and stirred vigorously so as to dissolve the active component of the tablets. Binding agents or filler remained insoluble. The additives commonly present in the tablets i.e. calcium carbonate, glucose, lactose, starch, gum etc. are mostly insoluble in acetone and isopropyl alcohol. The solutions were filtered, residues were washed three to four times with small portions of isopropyl alcohol and volumes of solutions were made to 100 ml with isopropyl alcohol. The aliquots of 10 ml of these solutions were diluted with isopropyl alcohol to 20 ml and titrated with 0.1 M solution of KOH in isopropyl alcohol using glass and calomel electrodes by potentiometric method. The titrant was standardized with 0.1 M benzoic acid in isopropyl alcohol by performing potentiometric titration. The end points were found out by plotting the graphs and then amount of drugs present in titrated weights of tablet powder was calculated. The amount of active components (drugs) present in one tablet was calculated by knowing the average weight of the tablet. The same tablets were later on analyzed by the method of pharmacopoeias and the results obtained were compared.

RESULTS AND DISCUSSION

Ibuprofen and diphenhydramine hydrochloride drugs containing ten tablets of the same batch were accurately weighed and powdered. The quantity of powder equivalent to about 200 mg of ibuprofen/paracetamol and 25 mg of diphenhydramine hydrochloride was accurately weighed, it was extracted with isopropyl alcohol and the volume was made to 100 ml. An aliquot of 10 ml of this solution was diluted with isopropyl alcohol to 20 ml and using potentiometer titrated with KOH in isopropyl alcohol. Similarly, the powder of tablets of the same batch having the drugs paracetamol and diphenhydramine hydrochloride was extracted with isopropyl alcohol and using potentiometer titrated with KOH in isopropyl alcohol. The titrant was standardized by performing potentiometric titration using standard benzoic acid in isopropyl alcohol. The weight of drugs ibuprofen and diphenhydramine hydrochloride as well as paracetamol and diphenhydramine hydrochloride present in titrated

amount of tablets was calculated. The same tablets were analyzed by I.P. method. The results obtained for two different brands of tablets are tabulated and it is observed that, the present potentiometric method gives fairly accurate and comparable results to those obtained by I.P. method. (**Table 1**) (**Table 2**). It is simple, precise and free from indicator error or interferences. The acidic drugs get hydrolyzed in presence of aqueous alkali but this is avoided in non-aqueous medium. However, in US Pharmacopoeia procedure alcoholic solution of the acidic drugs is titrated with aqueous alkali. Such a titration must be performed quickly so as to minimize hydrolysis. The present method has no such limitations. The most common additives present in the tablets are calcium carbonate, sugars, gum etc. and as these are insoluble in isopropyl alcohol do not affect the results. The solvent isopropyl alcohol can be used as a good differentiating solvent. Using the solvent isopropyl alcohol, potentiometric breaks obtained are quite pronounced and prominent with minimum error (**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 smaller. It can be purified and made anhydrous very easily. This method is simple than the other methods where the components are separated and estimated by chromatographic, spectrophotometric or other techniques.

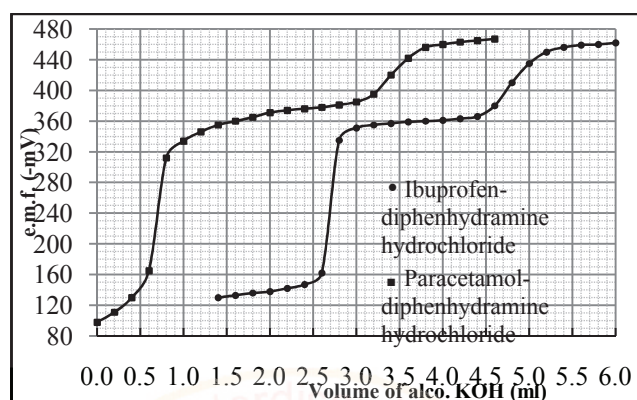
Table 1: Determination of ibuprofen-diphenhydramine hydrochloride (DPHH) in tablets

Sample	Label Claim (mg)		Weight Found by I.P. method (mg)		Weight Found by present method (mg)	
	Ibuprofen	DPHH	Ibuprofen	DPHH	Ibuprofen	DPHH
A	200.0	25.0	201.16	25.06	201.45	25.08
B	200.0	25.0	197.67	24.55	198.63	24.79
C	200.0	25.0	198.11	24.78	198.92	24.93

Table 2: Determination of paracetamol-diphenhydramine hydrochloride (DPHH) in tablets

Sample	Label Claim (mg)		Weight Found by I.P. method (mg)		Weight Found by present method (mg)	
	Paracetamol	DPHH	Paracetamol	DPHH	Paracetamol	DPHH
A	200.0	25.0	196.44	24.53	197.78	24.66
B	200.0	25.0	198.51	24.61	198.72	24.84
C	200.0	25.0	197.40	24.72	197.68	25.01

Graph 1 : Determination of ibuprofen-diphenhydramine hydrochloride and paracetamol-diphenhydramine hydrochloride in tablets



CONCLUSION

The simultaneous non-aqueous potentiometric determination of pharmaceutically potent ibuprofen-diphenhydramine hydrochloride and paracetamol-diphenhydramine hydrochloride combination drugs is fast, simple, precise method and can be used even in common laboratories without the use of any sophisticated instrument. The pair of glass and calomel electrodes gave stable potentials which were attained quickly. The solvent isopropyl alcohol is found to be more

satisfactory for non-aqueous titration of drugs and gave satisfactory results. The potassium hydroxide in solvent isopropyl alcohol was found to be better basic titrant to the alkoxide solvents which are more susceptible to atmospheric moisture and carbon dioxide.

ACKNOWLEDGEMENT

Thanks are due to **Dr. V. D. Nanoty**, Principal, Shri Radhakisan Laxminarayan Toshniwal College of Science, Akola for providing necessary facilities.

REFERENCES

1. R. V. Rele and R. H. Terse (2011). A validated non-aqueous potentiometric titration method for the quantitative determination of azelnidipine from pharmaceutical preparation, *J. Chem. Pharm. Res.*, 3(3), 1.
2. H. J. Rhodes, J. J. Denardo, D. W. Bode and M. I. Blake (1975). Differentiating nonaqueous titration of aspirin, acetaminophen and salicylamide mixtures, *J. Pharm. Sci.*, 64(8), 1386.
3. E. G. Wollish, R. J. Colarusso, C. W. Pifer and M. Schmall (1954). Determination of aspirin and Pharmacopoeia, Her Majesty's stationary office, London, Vol. I and II (2004).
4. E. M. Elnemma and M. A. Hamada (1997). Plastic membrane electrodes for the potentiometric determination of codeine in pharmaceutical preparations, *Microchimica Acta.*, 126(1,2), 147.
5. P. N. Vyas and R. B. Kharat (1988). Potentiometric titration of paracetamol in nonaqueous medium, *Indian J. Pharm. Sci.*, 50, 279.
6. Pharmacopoeia of India, Directorate of Publications, New Delhi (2007).
7. United States Pharmacopoeia XX and National Formulary XV, U. S. Pharmacopoeial Convention, Rockville (1980).
8. British Pharmacopoeia, J. Hunt and H. J. Rhodes (1974). Analysis of acetaminophen and barbiturate combinations by differentiating nonaqueous titration, *J. Pharm. Sci.*, 63(1), 89.
9. M. I. acetophenetidine in presence of caffeine by nonaqueous titration, *Anal. Chem.*, 26(11), 1753.
10. M. I. Blake and L. B. Shumaker (1973). Differentiating nonaqueous titration of mixtures

- containing acetaminophen and salicylamide, *J. Ass. Off. Anal. Chem.*, 56(3), 653.
11. A. G. Fogg, P. J. Sausins and J. R. Smithson (1970). Determination of paracetamol and aspirin in mixtures by non-aqueous potentiometric titrimetry or by ultraviolet spectrophotometry, *Anal. Chimica. Acta.*, 49(2), 342.
12. H. Nimje, S. P. Wate, D. P. Dharkar and R. Razdan (2007). Simultaneous RPHPLC determination of nimesulide and tizanidine in tablets, *Indian J. Pharm. Sci.*, 69(2), 281.
13. S. S. Zarapkar, N. P. Bhandari and U. P. Halkar (2000). Simultaneous determination of nimesulide and chlorzoxazone in pharmaceutical dosage by RPHPLC, *Indian Drugs*, 37, 467.
14. K. E. Nagoji, S. Vijaysrinivas, K. M. Kumar, N. Mathivanam, S. M. Kumar and M. E. Rao (2003). Simultaneous reverse phase HPLC estimation of nimesulide and diclofenac sodium, *Indian J. Pharm. Sci.*, 65, 407.
15. M. M. Sena, C. B. Freitas, L. C. Silva, C. N. Perez and Y. O. De-Paula (2007). Simultaneous spectrophotometric determination of paracetamol and ibuprofen in pharmaceutical formulations by multivariate calibration, *Quimica Nova*, 30(1), 75.
16. R. A. Sodhi, J. L. Chawla and R. T. San (1996). Simultaneous determination of paracetamol, ibuprofen and chlorzoxazone by HPLC, HPTLC and GC methods, *Indian Drugs*, 33(6), 280.
17. J. Kucharsky and L. Safarik (1965). Titrations in non aqueous solvents, Elsevier, New York.

