SIMULTANEOUS POTENTIOMETRIC DETERMINATION OF PHARMACEUTICALLY POTENT ACECLOFENAC-PARACETAMOL COMBINATION DRUGS IN NON-AQUEOUS MEDIUM

P.P. Deohate[1*] and K.N. Puri[2]
[1]Department of Chemistry, Shri Radhakisan Laxminarayan Toshniwal College of Science, Akola, India
[2]Department of Chemistry, Shri Shivaji Science College, Amravati, India
*pradip222091@yahoo.co.in, knpuri2008@rediffmail.com

ABSTRACT

The simultaneous potentiometric determination of pharmaceutically potent aceclofenac-paracetamol combination drugs in non-aqueous medium using the solvent isopropanol and the titrant KOH in isopropanol has been established. The drug aceclofenac as well as the paracetamol are distinctly acidic in nature. These drug combinations are widely used in medicines and pharmaceuticals. Herein these drugs are simultaneously determined in their binary mixtures using a pair of glass and calomel electrodes by the non-aqueous differentiating potentiometric titration method. This method has been found to be precise for assay of double component combination drugs and results obtained are comparable with those obtained by Indian Pharmacopoeia (IP) method.

Keywords : *Aceclofenac-paracetamol, non-aqueous, potentiometric determination*

Introduction

The potentiometric determination in non-aqueous medium using different electrode pairs has been reported earlier[1-5]. For the determination of combination drugs, different methods have been suggested and these are mostly concerns with the separation of components followed by individual component estimation using suitable technique. In the pharmacopoeias, various methods are included for the determination of combination drugs[6-8]. In literature, the estimation of combination drugs barbitone-paracetamol[2], salicylamide-paracetamol[9,10], aspirin-paracetamol[11] by differentiating potentiometric titrations have been reported. Determination of nimesulide-tizanidine[12], nimesulide-chlorzoxazone[13], nimesulide-diclofenac sodium[14] etc. has been reported earlier in some communications. Two component mixture of drugs aceclofenac-paracetamol[15] and three component mixture of drugs aceclofenac-paracetamol-chlorzoxazone[16] have been determined earlier by spectrophotometric and chromatographic techniques. Determination of aceclofenac-paracetamol combination drug by differentiating potentiometric titration method using isopropanol was not found to be reported in literature. The drugs aceclofenac and paracetamol are distinctly acidic in nature and hence could not be titrated directly with aqueous alkali owing to their hydrolysis. The basic titrants are also superior to the alkoxide solvents which are more susceptible to the atmospheric moisture and CO_2.

Herein, the simple method for analysis of pharmaceutical drugs is reported which will help the analysis of raw materials and products for quick check of spurious drugs that are feared to penetrate the markets. In present work, potentiometric titrations in non-aqueous medium were carried out to estimate the aceclofenac and paracetamol in two component combination drugs without any separation using the solvent isopropanol and titrant KOH in isopropanol.

Material and Methods

The titrations were performed using a digital potentiometer (Equiptronics, EQ-602). Glass electrode was used as an indicator electrode whereas calomel electrode as a reference. Drugs and chemicals were weighed on Precisa-310-M (±0.001 g) balance. Chemicals and solvents used were AR grade. Solvents were purified and made anhydrous by standard methods[17]. Titrants were protected from atmospheric moisture and CO_2. Drugs selected for present investigation are included in pharmacopoeias[6-8], these are pharmaceutical in nature and obtained from pharmaceutical laboratories.

Ten tablets of the same batch of aceclofenac-paracetamol drugs were accurately weighed and powdered for the present study. Quantity of powder equivalent to about 100 mg of aceclofenac and 325 mg of paracetamol was accurately weighed. It was treated with 50 ml of isopropanol and stirred vigorously so as to dissolve the active component of the tablets, binding agents and fillers remained insoluble. Calcium carbonate, glucose, lactose, starch, gum etc. are common additives in the tablets and are mostly insoluble in isopropanol. Solutions were filtered, residues were washed twice and volumes of solutions were made to 100 ml with isopropanol. Using isopropanol, 10 ml aliquots of these solutions were diluted to 20 ml and potentiometrically titrated with 0.1 M solution of KOH in isopropanol using a pair of glass and calomel electrodes. Titrant was standardized by potentiometric titration using 0.1 M benzoic acid in isopropanol. End points were determined by plotting the graphs and later on amount of drugs present in titrated weights of tablet powder was calculated. Knowing the average weight of the tablet, amount of active components (drugs) present in one tablet was calculated. Same tablets were then analyzed by the method given in pharmacopoeias for the comparison of results.

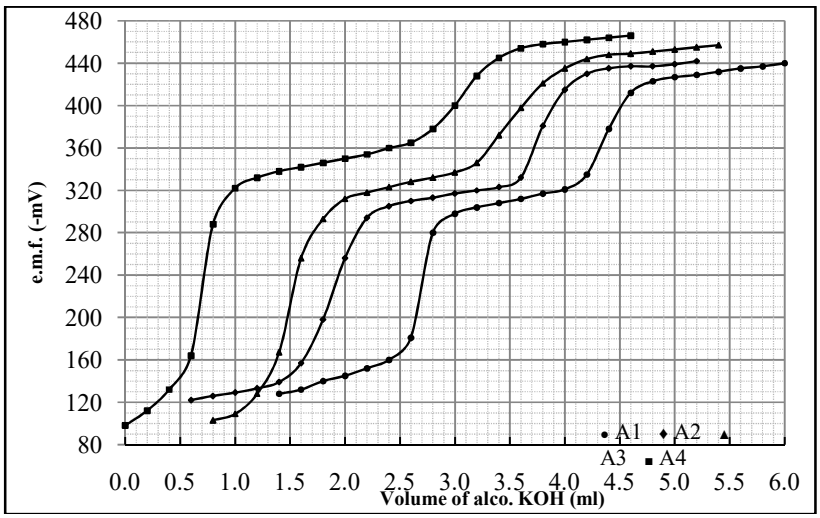
Results and Discussion

Ten tablets of drugs aceclofenac and paracetamol of the same batch were weighed accurately and powdered. Quantity of powder equivalent to about 100 mg of aceclofenac and 325 mg of paracetamol was accurately weighed. It was extracted with isopropanol and the volume was made to 100 ml. A 10 ml aliquot of this solution was diluted to 20 ml with isopropanol and titrated with KOH in isopropanol using potentiometer. Titrant was standardized using standard benzoic acid in isopropanol by potentiometric titration. Weight of aceclofenac and paracetamol drugs present in titrated amount of tablets was calculated. Same tablets were analyzed by IP method and results for four tablets of different brands are tabulated. It has been observed that, the given non-aqueous potentiometric titration method gives fairly accurate and comparable results to those obtained by IP method (**Table-1**). It is quite simple, precise and free from indicator error or interferences. In presence of aqueous alkali, acidic drugs get hydrolyzed but this is avoided in non-aqueous medium. In the procedure given in US Pharmacopoeia, alcoholic solution of the acidic drugs is to be titrated with aqueous alkali and such a titration must be performed quickly so as to minimize hydrolysis but present method has no such limitations. Calcium carbonate, sugars, gum etc. are most common additives present in the tablets, these are insoluble in isopropanol and do not affect the results. Solvent isopropanol can be used as a good differentiating solvent. Potentiometric breaks obtained are quite pronounced and prominent with minimum error using isopropanol as solvent (**Graph-1**). Near the end point, solvent isopropanol permitted a large change in the solvated proton concentration. Isopropanol can be purified and made anhydrous very easily, its dielectric constant is smaller. This method is simple than other methods where the components are separated and determined by spectrophotometric, chromatographic or other techniques.

Table-1 : Determination of aceclofenac-paracetamol combination drugs

Sample	Label Claim (mg)		Weight Found by IP method (mg)		Weight Found by present method (mg)	
	Aceclofenac	Paracetamol	Aceclofenac	Paracetamol	Aceclofenac	Paracetamol
A1	100	325	99.52	323.42	99.73	324.18
A2	100	325	99.60	324.14	99.93	324.72
A3	100	325	99.74	324.08	99.97	324.61
A4	100	325	99.89	323.89	100.01	324.77

Graph-1 : Determination of aceclofenac-paracetamol combination drugs



Conclusion

Simultaneous potentiometric determination of pharmaceutically potent aceclofenac-paracetamol combination drugs in non-aqueous medium is fast, simple, precise method and can be performed without the use of any sophisticated instrument in all common laboratories. Glass and calomel electrodes pair gave stable potentials and were attained quickly. Solvent isopropanol was found to be good one for titration of drugs in non-aqueous medium and gave quite satisfactory results. KOH in isopropanol was found to be better basic titrant to the alkoxide solvents that are susceptible to atmospheric moisture and CO_2.

Acknowledgement

Authors are most thankful to Principal, Shri Radhakisan Laxminarayan Toshniwal College of Science, Akola for providing sophisticated equipments and necessary laboratory facilities.

References

1. Rele, R. V. and Terse, R. H. (2011). A validated non-aqueous potentiometric titration method for the quantitative determination of azelnidipine from pharmaceutical preparation. J. Chem. Pharm. Res., 3(3): 1-5.
2. Rhodes, H. J., Denardo, J. J., Bode, D. W. and Blake, M. I. (1975). Differentiating nonaqueous titration of aspirin, acetaminophen and salicylamide mixtures. J. Pharm. Sci., 64(8): 1386-1388.
3. Wollish, E. G., Colarusso, R. J., Pifer, C. W. and Schmall, M. (1954). Determination of aspirin and acetophenetidine in presence of caffeine by nonaqueous titration. *Anal. Chem.,* 26(11): 1753-1754.
4. Elnemma, E. M. and Hamada, M. A. (1997). Plastic membrane electrodes for the potentiometric determination of codeine in pharmaceutical preparations. Microchimica. Acta., 126(1,2): 147-151.
5. Vyas, P. N. and Kharat, R. B. (1988). Potentiometric titration of paracetamol in nonaqueous medium. Indian J. Pharm. Sci., 50: 279-281.
6. Pharmacopoeia of India (2007). Directorate of Publications, New Delhi.
7. United States Pharmacopoeia XX and National Formulatory XV (1980). U. S. Pharmocopeal Convention, Rockville.
8. British Pharmacopoeia, Vol. I and II (2004). Her Majesty's stationary office, London.
9. Blake, M. I., Hunt, J. and Rhodes, H. J. (1974). Analysis of acetaminophen and barbiturate combinations by differentiating nonaqueous titration. J. Pharm. Sci., 63(1): 89-91.

10. Blake, M. I. and Shumaker, L. B. (1973). Differentiating nonaqueous titration of mixtures containing acetaminophen and salicylamide. J. Ass. Off. Anal. Chem., 56(3): 653-655.
11. Fogg, A. G., Sausins, P. J. and Smithson, J. R. (1970). Determination of paracetamol and aspirin in mixtures by non-aqueous potentiometric titrimetry or by ultraviolet spectrophotometry. Anal. Chimica. Acta., 49(2): 342-345.
12. Nimje, H., Wate, S. P., Dharkar, D. P. and Razdan, R. (2007). Simultaneous RPHPLC determination of nimesulide and tizanidine in tablets. Indian J. Pharm. Sci., 69(2): 281-283.
13. Zarapkar, S. S., Bhandari, N. P. and Halkar, U. P. (2000). Simultaneous determination of nimesulide and chlorzoxazone in pharmaceutical dosage by RPHPLC. Indian Drugs, 37: 467-475.
14. Nagoji, K. E., Vijaysrinivas, S., Kumar, K. M., Mathivanam, N., Kumar, S. M. and Rao, M. E. (2003). Simultaneous reverse phase HPLC estimation of nimesulide and diclofenac sodium. Indian J. Pharm. Sci., 65: 407-409.
15. Mahaparale, P. R., Sangshetti, J. N. and Kuchekar, B. S. (2007). Simultaneous spectrophotometric estimation of aceclofenac and paracetamol in tablet dosage form. Indian J. Pharm. Sci., 69(2): 289-292.
16. Shaikh, K. A. and Devkhile, A. B. (2008). Simultaneous determination of aceclofenac, paracetamol and chlorzoxazone by RP-HPLC in pharmaceutical dosage form. J. Chromatographic Sci., 46(7): 649-652.
17. Kucharsky, J. and Safarik, L. (1965). Titrations in Non-aqueous Solvents. Elsevier, New York.