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Spectrophotometric determination of losartan potassium through ion association reaction

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ABSTRACT

Simple, selective, sensitive, accurate and economical spectrophotometric methods (A and B) have been described for the determination of Losartan potassium in bulk drug and pharmaceutical formulations (tablets). The developed methods involve the formation of orange red / yellow colored chloroform extractable ion-association complex of Losartan potassium with BCG / BTB in acid medium, exhibiting absorption maxima at 430nm, and obeying Beer's law in the concentration range of 2.0 -10.0 for BCG and 2.5 – 12.5µg/ml respectively with good correlation. Statistical analysis of the results of the proposed methods reveals high accuracy and good precision. The proposed methods could be successfully extended to the commercial pharmaceutical formulations containing Losartan potassium.

Keywords: Losartan potassium, BCB, BTB, Ion association complex, Visible Spectrophotometry.

INTRODUCTION

Losartan potassium, chemically 2-n-butyl-4-chloro-5-hydroxymethyl-1-((2-(1H-tetrazol-5-yl)(biphenyl-4-yl)methyl) imidazole, potassium salt, is an oral drug which belongs to the class of angiotensin receptor blockers (ARBs)[1-3](Fig. 1.). It is prescribed for the treatment of hypertension. It is also used to lower the risk of strokes in patients with high blood pressure and an enlarged heart.

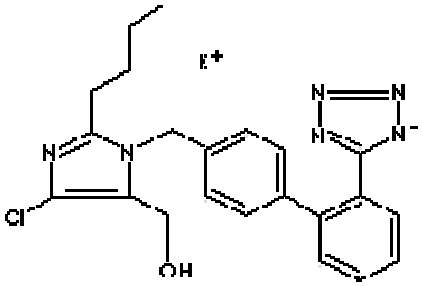


Fig.1. Chemical structure of Losartan potassium

Several methods have been described for the determination of Losartan potassium drug substance in tablets. These methods employ techniques such as capillary electrophoresis (CE)[4], high performance thin layer chromatography (HPTLC)[5], supercritical fluid chromatography (SFC)[6], high performance liquid chromatography (HPLC) with UV detection and fluorescence detection[7] mostly in biological fluids,

O.C.Lastra[8] et aldeveloped and validated an UV derivative spectrophotometric determination of Losartan potassium in tablets. Permender Rathee[9] et al developed two new stability indicating UV-Spectrophtometric methods for the simultaneous determination of losartan potassium and hydrochlorothiazide in bulk drug and in tablet dosage forms using 0.01N HCl as the solvent. Nafisur Rahman[10] developed kinetic spectrophotometric method for the determination of losartan potassium in pure and dosage forms. This method is based on oxidation of the losartan potassium with alkaline potassium permanganate at room temperature (25^{o}C). Anuja K. Kolsure[11]developed simple, economical, precise and accurate method for simultaneous determination of Atorvastatin and Losartan in combined tablet dosage forms. A first-derivative UV spectroscopic and HPLC method was developed by Ansari M[12] et al for the determination of losartan in the tablet dosage forms. T. Iwasa[13] et al developed a liquid chromatography electrospray ionization tandem mass spectrometric method for the simultaneous determination of losartan and its major active metabolite in human plasma by LC equipped with a reversed-phase C_{18} column and mass spectrometer with pneumatically-assisted nebulization.

MATERIALS AND METHODS

Instrument

A ELICO SL-159 UV–VIS spectrophotometer (India) with 1.0 cm quartz cells was used for all absorbance measurements under the following operating conditions. An Elico model L1-10 (India) pH meter was used for pH measurements.

Reagents and solutions

All chemicals were of analytical reagent grade or chemically pure grade and double distilled water was used throughout the study.

Bromocresol Green solution {[BCG 0.2%, Ranbaxy Fine Chemicals Ltd., New Delhi}: Prepared by dissolving 0.2 g of the reagent (BCG) in 100 ml of water, and filtering it to remove the insoluble residue.

Bromothymol Blue solution {[BTB 0.2%, Ranbaxy Fine Chemicals Ltd., New Delhi}: Prepared by dissolving 0.5 g of the reagent (BTB) in 100 ml of water, and filtering it to remove the insoluble residue.

Buffer solution, pH 3.0: Prepared by mixing 50mL of 0.2 M Glycine acetate solution with 11.4 ml of 0.2 M HCl solution and diluted to 200mL with doubly distilled water. The pH of the solution was adjusted to an appropriate value with the aid of a pH meter.

Preparation of Standard stock solution

A stock standard solution containing 1000µg/ml of Losartan potassium was prepared freshly by dissolving 100 mg of Losartan potassium in 100 ml double distilled water. Final working standard solution of Losartan potassiumof 40 µg/ml for Method A and 50 µg/ml for Method B was prepared by diluting 4.0 ml & 5.0 ml solution of the above solution to 100 ml with double distilled water.

Preparation of marketed sample solution

Ten tablets were weighed, finely powdered and mixed thoroughly. An accurately weighed amount of powder equivalent to 50 mg of drug was transferred into a 50 ml volumetric flask and was dissolved with double distilled water and shaked for 10 min. Then an aliquot portion of this solution was diluted to 100.0 ml with distilled water to get sample solutions 40 µg/ml for **BCG** and 50µg/ml for **BTB** and analyzed as given in the above proposed assay procedures.

Proposed Procedures for Methods A & B:

Aliquots of working standard solution of Losartan potassium (**40**µg/ml**for Method A and 50**µg/ml **for Method B**) ranging from 0.5 – 2.5 ml were transferred into a series of 125ml separating funnels. To these 2.0 ml of acidic dye **(BCG/ BTB**) was added. The total volume of aqueous phase was adjusted to 10.0mL with Glycine buffer solution of

pH - 3.0 and 10.0ml of chloroform was added. The contents were shaken for 2 minutes. The two phases were allowed to separate and the absorbance of the yellow colored chromogen was measured at 430 nm against reagent blank(set zero) and the amount of Losartan potassium present in the sample solution was computed from its calibration curve **(Fig.2 & 3)**.

RESULTS AND DISCUSSION

Absorption Spectra

The absorption spectra were scanned on a spectrophotometer in the wave length region of 340 to 900 nm against similar reagent blank or distilled water. The absorption spectrums of each proposed method were recorded against distilled water and are represented in **Fig. 2&3** for BCG and BTB. The absorption curves of the colored species in each method show characteristic absorption maxima at 430 nm for both the dyes where as the blank in each method has low or no absorption in this region.

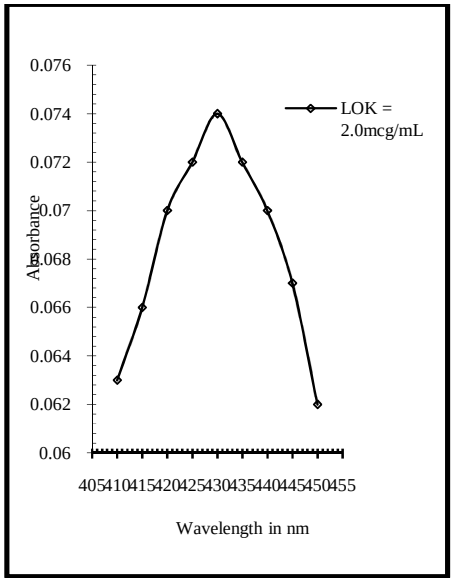


Fig.2. Absorption spectrum of LOK with BCG

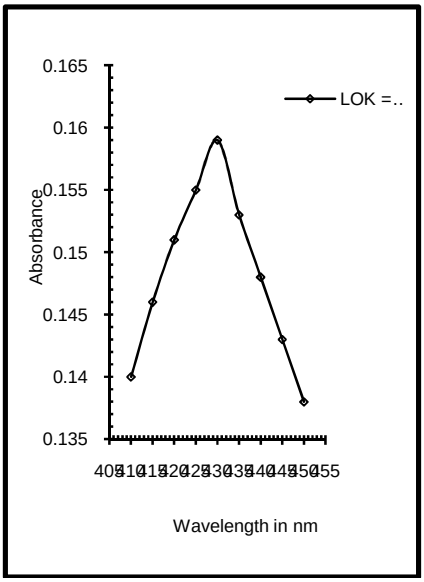


Fig.3. Absorption spectrum of LOK with BTB

Table: 1. OPTIMUM CONDITIONS ESTABLISHED IN METHODS WITH BCG & BTB

Parameter	Optimum range	Conditions in procedure	Remarks
λ_{max} (nm) BCG	410 - 440	430	
λ_{max} (nm) BTB	410 - 440	430	
Effect of buffer (3.0) on color development.	0.5-2.0mL for BCG & BTB	BCG & BTB	Variation of concentration or pH beyond the upper and lower limits resulted in low absorbance values.
Choice of organic solvent for extraction of the colored complex.	Chloroform for BCG & BTB	Chloroform for BCG & BTB	Chloroform was preferred for its selective extraction of the colored drug-dye complex from the aqueous phase.
Effect of shaking time on extraction.	1- 5 min	2 min	Constant absorbance values were obtained for shaking periods between 1-5 min.
Effect of temperature on the colored species.	Laboratory temperature ($28+30^0$C)	Laboratory temperature	At low temperature (< 20^0C) the extraction of colored species was found to be improper. At high temperature (> 35^0C) the stability of the colored species was found to be less.
Stability of the colored species in organic solvent.	1 - 60 min 1 - 60 min	15 min 15 min	

Optimization the developed procedures

A number of preliminary experiments for the proposed methods were established for rapid and quantitative formation of colored ion-pair complex to achieve the maximum stability and sensitivity. Optimum condition was

fixed by varying one parameter at a time while keeping other parameters constant and observing its effect on the absorbance at 430 nm for both BCG and BTB. The following experiments were conducted for this purpose and the conditions so obtained were incorporated in recommended procedures. The optimum conditions established for methods were described in **Table. 1.**

Validation of the proposed methods

Validation of the proposed spectrophotometric methods was done according to ICH guidelines.

Linearity

Beer's law plots of the above proposed methods A&B were developed at five concentration levels ranging from 2.5µg/ml to 12.5µg/ml for Losartan potassium. The calibration curves were constructed by plotting the absorbances of coloured ion-pair complexes against various concentrations of Losartan potassium. The regression equations derived using the least-squares method for the calibration curves of Losartan potassium were Y=0.031x+0.001 (R^2=0.9995) for Method A(BCG) and 0.036x+0.003 (R2=0.9998) for Method B(BTB) respectively. The results showed an excellent correlation between absorbance and concentration of drugs within the concentration range indicated above (Table.2) for both the methods proposed.

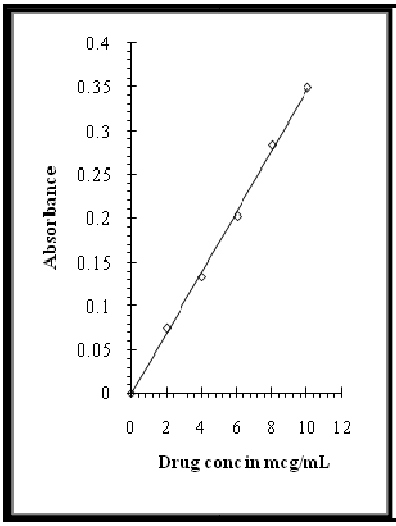


Fig.4: Beers law spectrum of LOK with BCG

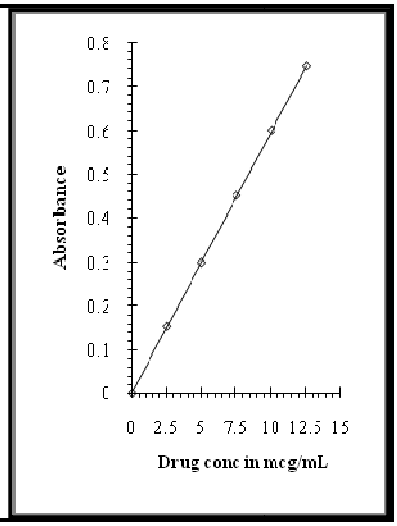


Fig.5: Beers law spectrum of LOK with BTB

Sensitivity (LOD and LOQ)

The limit of detection (LOD) is defined as the lowest concentration of an analyte that an analytical process can reliably differentiate from back-ground levels. The limit of quantification (LOQ) is defined as the lowest concentration of the standard curve that can be measured with an acceptable accuracy, precision and variability. In this study, LOD and LOQ were based on the standard deviation of the response and the slope of the corresponding curve. The values of LOD and LOQ for Method A (BCG) and Method B(BTB) are given in Table 2**.**

Precision

The precision of the method was established by intraday variation studies. In the intraday studies, six recurring estimations of standard solutions were made and the absorbances of the drug are determined and the percent relative standard deviation (% RSD) and percent range of error (at 0.05 and 0.01 confidence limits) were calculated for each proposed methods and the results are given in Table 2.

Accuracy (Recovery)

Recovery experiments were performed by applying the standard-addition technique. The recovery was assessed by determining the agreement between the measured standard concentration and added known concentration to the sample. The test was done by spiking the pre-analyzed tablet powder with pure losartan potassium at three different levels [50, 100 and 150% of the content present in the tablet powder (taken)] and the total was found by the

proposed method. Each test was repeated six times. In all the cases, the recovery percentage values ranged between 99.63 and 100.02%. Closeness of the results to 100% showed the fairly good accuracy of the proposed methods.

Table: 2. STATISTICAL DATAOF QUANTITATIVE PARAMETERS FOR THE PROPOSED METHODS

Name of the Parameter	BCG	BTB
Maximum Wavelength λ_{max}	430	430
Beer's Law Limits mcg/mL	2.0-10.0	2.5-12.5
Optimum Photometric Range mcg/mL	3.0 -9.0	3.0 -9.5
Sandell's Sensitivity(µg/cm^2/0.001 Absorbance)	0.0300	0.0167
Molar Absorptivity lt/mole/cm	1.532x10^4	2.768x10^4
Slope (b)	0.0247	0.05944
Intercept(a)	0.0077	0.0046
Correlation Coefficient (r)	0.9953	0.9999
Limit of Detection (LOD) mcg/mL	0.0964	0.00892
Limit of Quantification (LOQ) mcg/mL	0.321	0.0297
Standard Deviation on Slope(S_b)	0.00137	0.0003063
Standard Deviation on Intercept(S_a)	0.00795	0.0001767
Standard Error on Estimation(S_e)	0.00872	0.002422

Ruggedness

The ruggedness of the developed methods was expressed as RSD% of the same procedures applied under different laboratory conditions by the same instrument on different days for same standard and tablet dosage forms of losartan potassium. The results showed no statistical differences between the different conditions and instruments suggesting that the developed methods were rugged.

Analysis of pharmaceutical preparations

Commercially available Losartan potassium tablets were subjected to analysis by the proposed methods. Results obtained by the proposed methods [Method A(BCG) and Method B(BTB)] (Table. 3) for Losartan potassium were successful to the determination of the active drug in pharmaceutical formulations without any interference from the excipients present in the tablets. The results were compared statistically with those obtained by a (UV reference method) by applying Student's t-test for accuracy and F-test for precision(Table 3). At the 95% confidence level, the calculated t- and F-values did not exceed the tabulated values (t = 2.262 and F = 5.05) suggesting that the proposed methods are accurate and precise.

Table: 3. DETERMINATION OF LOSARTAN POTASSIUM [LOK] IN DOSAGE FORMS

Method	Pharmaceutical Formulation	Labeled Amount (mg)	Proposed Method			reference method [9]±S.D	% Recovery by proposed method**
			Amount found* (mg)±S.D	t value	F Value		
BCG	**Tablet-I**	25	24.92 ± 0.12	0.692	2.25	24.97±0.18	99.79±0.32
BTB	**Tablet-I**	25	24.91 ± 0.16	0.203	1.26		99.75±0.56

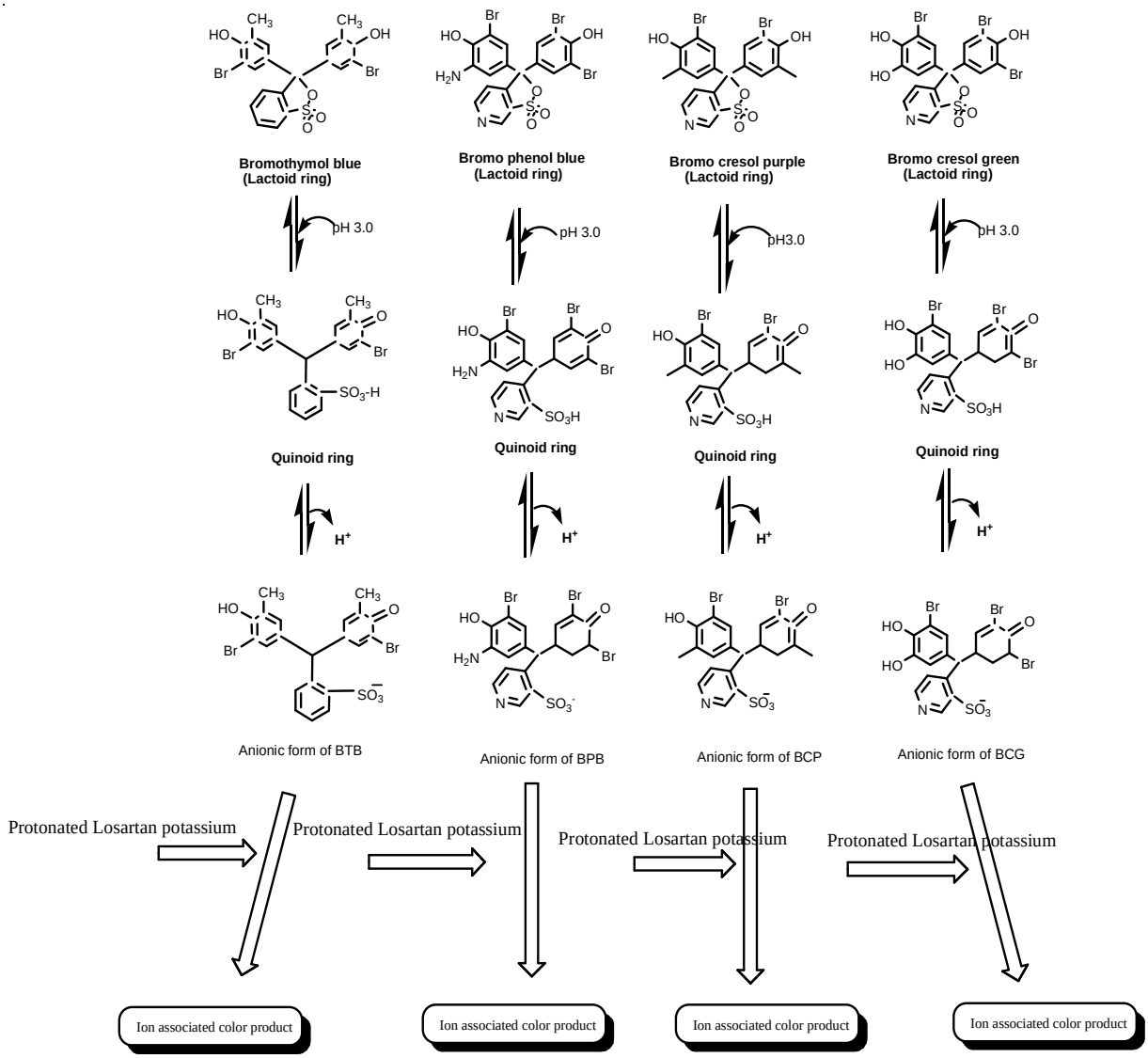
**Average ± standard deviation of six determinants the t and F- values refer to comparison of the proposed method. Theoretical values at 95 % confidence limits t = 2.365 and F = 4.88.*

*** Average of five determinations.*

DISCUSSION

Nature of the color Species: An attempt has been made to indicate the nature of colored species in each proposed method for losartan potassium tentatively based on analogy of reactive functional moiety in drug and reagents.

For BCG and BTB Methods: As losartan potassium possesses secondary amine group involves in ion association complex formation with acid dyes BCG and BTB which is extractable into chloroform from the aqueous phase. The protonated nitrogen moiety (positive charge) of losartan potassium is expected to attract the oppositely charged part (negative charge) of dye and behave as a single unit being held together by electrostatic attraction. Based on analogy the structures of ion association complexes are shown in **Scheme-1** given below.



CONCLUSION

From the literature survey it is understood that very few spectrophotometric methods were available for the determination of losartan potassium in pure and dosage forms by exploiting its functional groups. The present work describes the author's attempts in developing new visible spectrophotometric methods for the determination of losartan potassium using some acidic dyes. The methods developed by the author involves the formation of ion association complex reaction of the cited drug with some acid dyes such as Bromocresol Green[BCG] and Bromothymol Blue [BTB], in acidic medium (pH-3.0). These methods have been successfully applied to the determination of losartan potassium in pure and dosage forms. This procedure did not require sample pretreatment or any time-consuming step prior to drug assay.

The reagents provide simple and sensitive methods for the spectrophotometric determination of losartan potassium in pure and pharmaceutical formulations. The proposed methods does not involve any stringent reaction conditions and offers the advantages of high stability (more than 24hours).The statistical analysis of the results by t and F- tests showed that, there is no significant difference in accuracy and precision between the proposed methods and reference method. The proposed methods can be successfully applied for routine analysis of losartan potassium in quality control and research laboratories.

REFERENCES

[1] A. Chiu, D. Mc Call, W. Price, P. Wong, J. Carini, J. Duncia, S. Yoo, A. Johnson, P. Timmermans, *J. Pharmacol. Exp. Ther*., **1990,** 252, 711-718.
[3] P. Wong, W. Price, A. Chiu, J. Duncia, D. Carini, R.Wexler, A. Johnson, P. Timmermans, *J. Pharmacol. Exp.Ther*,.**1990**, 256,211-217.
[3] C.L. Furteck, M.W. Lo, *J.Chromatogr*.,**1992,** 573,295- 301.
[4] R.C.Williams,V.L.Alasandro,V.L. Fasone, R.J. Boucher,J.F. Edwards, *J.Pharm.Biomed.Anal*.,**1996**, 14,539-1546.
[5] K.E. McCarthy, Q. Wang, E.W. Tsai, R.E. Gilbert, D.P.Ip, M.A. Brooks, *J. Pharm. Biomed. Anal.*, **1998,**17, 671-677.
[6] A.Soldner,H.Spahn-Langguth,E.Mutschler, *J.Pharm.Biomed. Anal*.,**1998**, 16, 863-873.
[7] D. Farthing, D. Sica, I. Fakhry, A. Pedro, T.W. Gehr, *J.Chromatogr*.,**1997**, 704,374-378.
[8] C. Olga,Lastra ,G. Igor,Lemus, Hugo J. Sa´nchez, Renato F. Pe´rezFacultad de CienciasQuı´micas y, Casilla, Santiago,*Farmace´uticas, Universidad de Chile.*,**2007**,233,657.
[9] R.Permender, R. Sushila, R. Dharmender, C. Hema, *Eurasina journal of analytical chemistry*,**2009,**l4,1.
[10] N.Rahman, M.RazaSiddiqui and Sd.Najmul Hejaz Azmi, *Journal of the Chinese Chemical Society*, **2006**, *53*, 735-743.
[11] K. AnujaKolsure, S. SnehalIngale, A.SumitAbnawe, R.AnuruddhaChabukswar, P. Vishnu Choudhari, S. Bhanudas Kuchekar, *Journal of Pharmacy Research*, **2010,** 3, 9.
[12] M. Ansari, M. Kazemipour, F.Khosravi, M. Baradaran..*Chem Pharm Bull*.,**2004,** 52, 1166-70.
[13] T. Iwasa, T. Takano, K. Hara, T. Kamei, *J. Chromatogr.B.*,**1999,** 734, 325-330.