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SPECTROPHOTOMETRIC DETERMINATION OF TOLTERODINE THROUGH ION ASSOCIATION COMPLEX REACTION IN BULK AND ITS PHARMACEUTICAL PREPARATIONS

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ABSTRACT

Two spectrophotometric methods A and B have been developed for the determination of Tolterodine in bulk and dosage forms. The methods are found to be simple, sensitive, rapid and accurate. These methods are based on the formation of chloroform soluble ion-associates in the presence of acidic dyes namely Bromo Phenol Blue, BPB (Method A) and Bromo Cresol Purple, BCP (Method B) exhibiting λ_{max} at 422 and 418 nm respectively. These methods obey Beer's law in the concentration range of 2.0-10.0 µg/mL and 2.0-10.0 µg/ml. The molar absorptivities are found to be $1.42x10^4$ and $9.61x10^3$ L/mol. cm for methods A and B. These methods are found to be suitable for the assay of Tolterodine in pharmaceutical formulations.

KEYWORDS: Tolterodine, BPB, BCP, Spectrophotometry.

INTRODUCTION

Tolterodine (TTD) is chemically (R)-2-[3-[bis(1-methylethyl)-amino]1-phenylpropyl]-4-methylphenol [R-(R*,R*)]- 2,3dihydroxybutanedioate (1:1) is a selective muscarinic receptor antagonist and thus prevents the frequent urinations. It was the first drug used for the treatment of overactive bladder (OAB)[1,2] and it was listed in Merck index and considered to exist in two isomeric forms R and S[3]. Tolterodine tartrate has been determined using various methods which include advanced techniques such as capillary chromatography[4,5], gas chromatography[5,6], liquid chromatography–mass spectrometry[7-12], and few spectro photometric was developed based on UV[13], charge transfer complexation[14] and other spectrophotometric methods.[15-18] The present manuscript describes two simple, sensitive, accurate and rapid spectrophotometric methods for the determination of TTD.

EXPERIMENTAL

Instruments

Spectral measurements have been made on Elico SL-159 model, 2nm high resolution, double beam Spectrophotometer with 1cm and length quartz coated optics; Wavelength range190-800 nm. All the chemicals and reagents were of analytical grade and the freshly prepared solutions were always used in the investigations.

Chemicals and Reagents

Aqueous solutions of (0.2%, $3.203x10^{-3}$M) Bromo Phenol Blue (BPB), (0.2%, $7.16x10^{-4}$M) Bromo Cresol Purple (BCP) and 0.1M HCl were prepared by dissolving 8.6 mL of Conc. HCl in 1 liter flask in distilled water.. Chloroform was used in both methods A&B.

Preparation of standard drug solution: The stock solution of 1% drug was freshly prepared by transferring accurately weighed 100mg of Tolterodine into 100mL volumetric flask and dissolved in double distilled water, and then made up to the mark. Then working standard solutions 100µg.mL^{-1} was prepared by transferring 10.0 mL of the stock solutions into 100mL standard flask and made up to the mark.

Recommended procedures for the Methods A & B: 6.0 ml of 0.1 M HCl solution and 5.0 ml of 0.2% dye solution were added successively into series of aliquots of standard drug solution (0.5-2.5 ml) into 125 mL separating funnels. The total volume of aqueous phase in each separating funnel was adjusted to 15 mL with distilled water and organic layer to 10 ml with $CHCl_3$. The contents were shaken for 2 minutes. The two phases were allowed to separate and absorbance of the separated chloroform layer was measured at λ_{max} 422 nm (Method A) & 418 nm (Method B) against a similar reagent blank. The amount of TTD present was deduced from the appropriate calibration curves (Figures 1and2).

RESULTS AND DISCUSSION

Table 1: Optical and regression characteristics of the proposed methods for Tolterodine

Name of the Parameter	Method A	Method B
Maximum wavelength (λ_{max})	422	418
Beer's law limits µg.mL^{-1}	2.0-10.0	2.0-10.0
Sandell's sensitivity(µg/cm^2 / 0.001 Absorbance)	1.42E-02	9.61E-03
Molar absorptivity (L/mole/cm)	2.29E+04	3.64E+04
Slope (b)	7.01E-02	1.02E-02
Intercept(a)	3.01E-03	3.10E-03
Standard deviation on slope(S_b)	3.77E-04	2.75E-04

Standard deviation on intercept(S_a)	2.50E-03	1.83E-03
Standard error on estimation(S_e)	2.21E-02	2.18E-02
Correlation coefficient (r)	0.9999	0.9999
Limit of detection (LOD) µg.mL^{-1}	0.1072	0.0536
Limit of quantification (LOQ) µg.mL^{-1}	0.3574	0.1788

Table 2: Assay of Tolterodine in pharmaceutical formulations

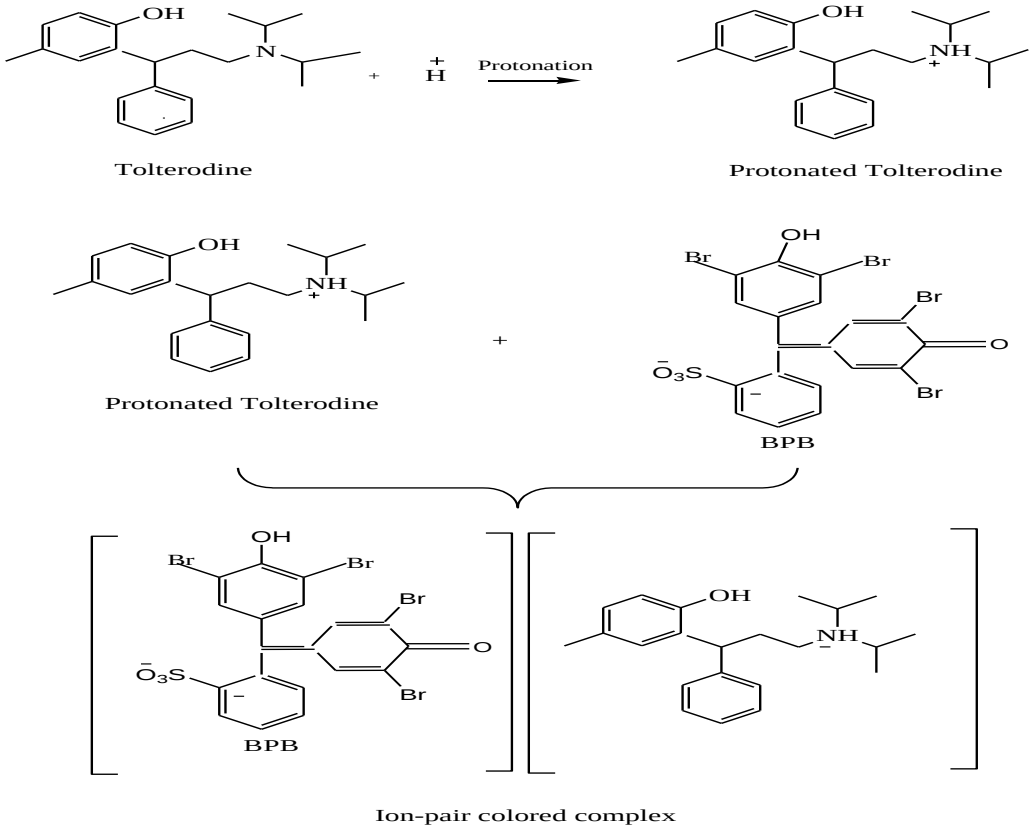
Formulations*	Amount taken (mg)	Amount found by proposed methods**		Reference method	Percentage recovery by proposed methods***	
		Method A	Method B		Method A	Method B
Tablet	10	9.986±0.05 F=3.24 t=0.19	9.989±0.06 F=2.25 t=0.12	9.994±0.09	99.19±0.21	99.50±0.13

****Average of six determinations considered**

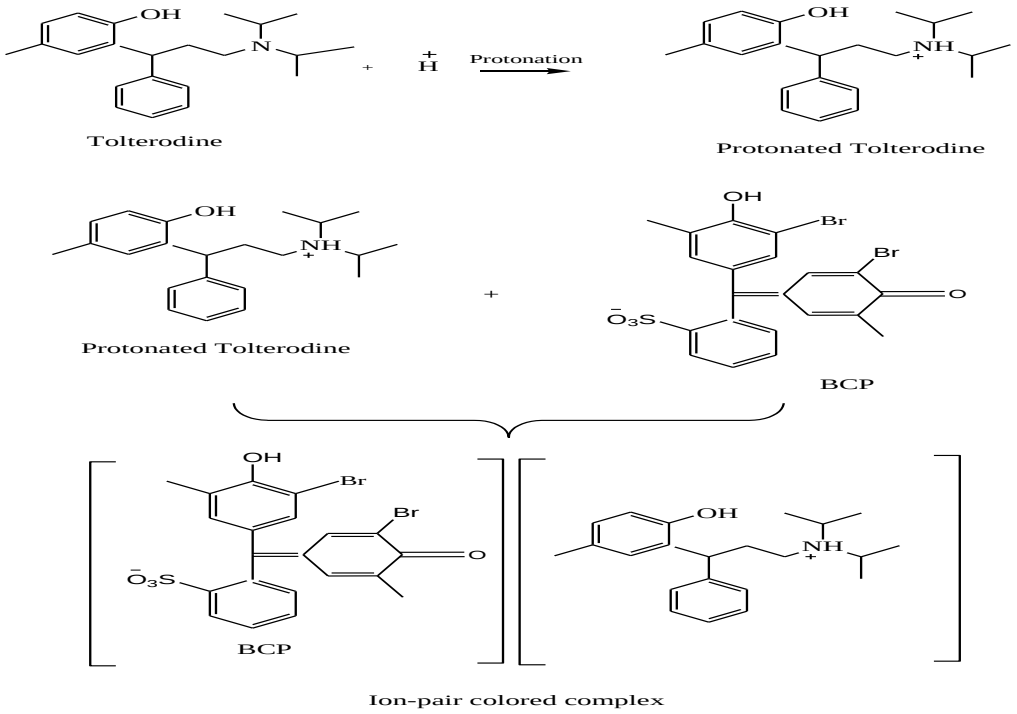
Reaction mechanism

Based on the analogy, the probable reaction mechanisms are given below.

Method-A: BPB



Method-B: BCP



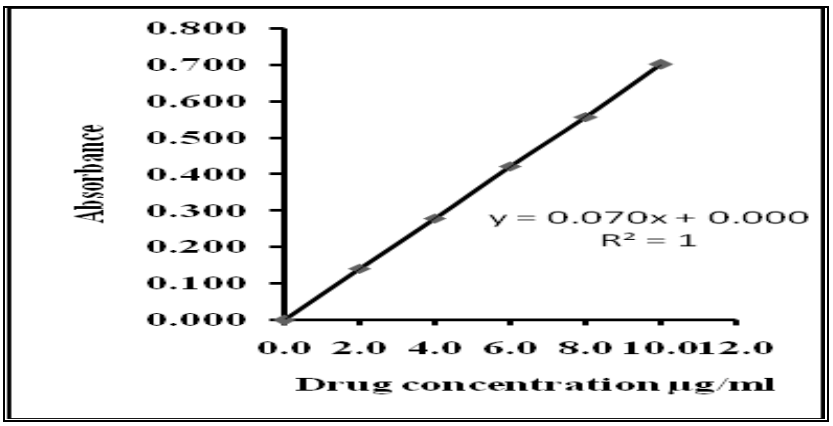


Fig. 1 Beer's Law plot of TTD with BPB (Method-A)

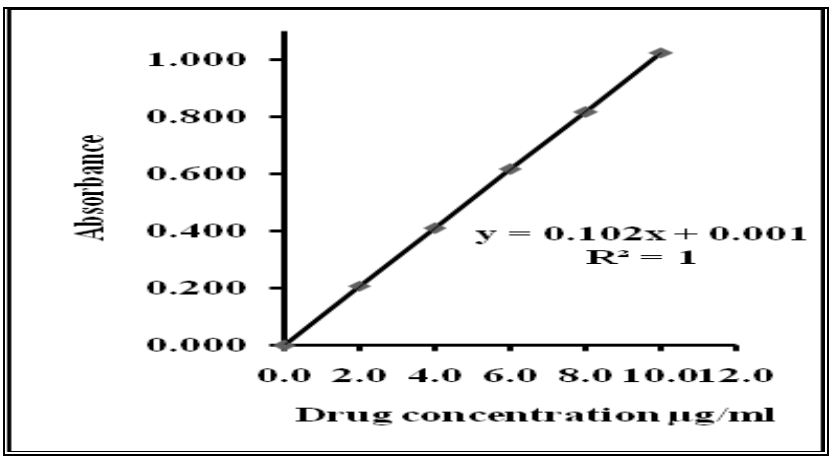


Fig. 2 Beer's Law plot of TTD with BCP (Method-B)

In present methods A&B, the stable anionic components produced by the two dyes BPB and BCP in aqueous medium interact with the protonated nitrogen of the drug in acidic medium to form ion associated complexes the complex thus formed is more stable due to electrostatic interactions. Ion-pair extractive spectrophotometry has attracted considerable attention for quantitative analysis of many pharmaceutically active compounds. The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar absorptivity, % relative standard deviation and regression characteristics like standard deviation of slope (Sb), standard deviation of intercept (Sa), standard error of estimation (S), and detection limit were calculated for the formulation TTD of was successfully analyzed by the proposed methods. The values obtained by the proposed methods are presented in **Table 1.** The Beer's law was obeyed in the concentration ranges. The values obtained for the determination of Tolterodine in tablet sample 1 by the proposed and U.V methods are compared in **Table 2.** To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the previously analyzed pharmaceutical preparation and the mixtures were analyzed by the proposed methods. The statistical analysis in terms of t-test and F-test indicates that the reported methods are not significantly different from that of literature method in terms of accuracy and precision (**Table 2).**

CONCLUSION

The methods reported here are found to be simple, sensitive, accurate and precise. The present methods involve the formation of highly stable colored species which makes it easier for the determination of TTD from pharmaceutical dosage forms in a routine manner. Further statistical parameters and the recovery study data clearly indicate the reproducibility and accuracy of the methods.

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