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Spectrophotometric Estimation of Tolterodine Tartarate In Bulk And Tablet Dosage Form

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ABSTRACT

A simple, precise and economical UV Spectrophotometric method has been developed for the estimation of Tolterodine tartarate in bulk and pharmaceutical dosage form. The method is based on measurement of absorption at maximum wavelength of 283.0 nm. Linearity for detector response was observed in the concentration range of 10-50 µg/ml. The accuracy of the method was assessed by recovery studies and was found to be 99.80%. The LOD and LOQ were found to be 0.1865 and 0.5621 respectively. The developed method was validated with respect to linearity, accuracy (recovery), precision, specificity and robustness and ruggedness. The results were validated statistically as per ICH Q2 R1 guideline and were found to be satisfactory. The proposed method was successfully applied for the determination of Tolterodine tartarate in commercial pharmaceutical dosage form.

Keywords: Tolterodine tartarate, UV Spectrophotometry, validation.

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INTRODUCTION

Tolterodine tartarate (TOL) is a competitive muscarinic receptor antagonist. Both urinary bladder contraction and salivation are mediated via cholinergic muscarinic receptors.

Chemically Tolterodine tartarate is 2-[(1R)-3-[bis(propan-2-yl)amino]-1-phenylpropyl]-4-methylphenol (Figure 1).

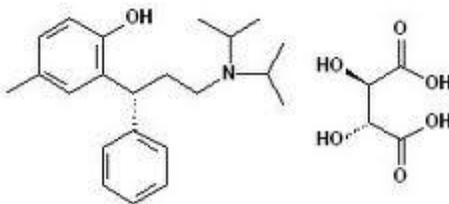


Figure 1: Structure of Tolterodine tartarate

The literature survey reveals that no UV spectrophotometric method has been reported for the estimation of Tolterodine tartarate. Hence, a simple, rapid, precise and accurate method for the estimation of Tolterodine tartarate in bulk and pharmaceutical formulation is developed and validated.

MATERIAL AND METHODS

Materials:

Tolterodine tartarate was generous gift sample. A Commercial Roliten tablets containing 2 mg of Tolterodine tartarate was purchased from local market and used within their shelf-life period. All chemicals and reagents used were of spectroscopic grade for UV Studies.

Instrumentation and Equipment:

A systronic UV-visible spectrophotometer, Model- 2201, with a fixed bandwidth (1.5 nm) and 1 mm quartz cell was used for spectral and absorbance measurements. In addition, Contech Precision balance, micropipette and sonicator were used.

Solubility Studies:

These studies were carried out with a view to find an ideal solvent in which the drug was completely soluble and stable. Various solvents like distilled water, methanol, 0.1 N HCl, 0.1 N NaOH, etc were tried for checking solubility of TOL. From solubility studies it was concluded that the drug was freely soluble in distilled water and soluble in methanol, from this distilled water was selected as solvent for further analysis.

Preparation of standard stock solution:

Standard stock solution of TOL was prepared by dissolving accurately weighed 25 mg of TOL in distilled water in 25 mL volumetric flask. Final volume was made up to 25 mL with distilled

water to get stock solution of each containing 1000 $\mu\text{g/mL}$ of TOL. Further from 1000 $\mu\text{g/mL}$, 1 mL was accurately pipetted out and diluted to 10 mL to get working standard solution of each containing 100 $\mu\text{g/mL}$ of TOL.

RESULTS AND DISCUSSION

Selection of analytical wavelength for analysis:

By appropriate dilution of standard stock solution of TOL in distilled water, solution containing 10 $\mu\text{g/mL}$ of TOL was scanned in the spectrum mode between the wavelength range of 200-300 nm. Wavelength of maximum absorption was determined for the drug. TOL showed maximum absorbance at 283 nm. Overlain spectrum of the drug is shown in Figure 2.

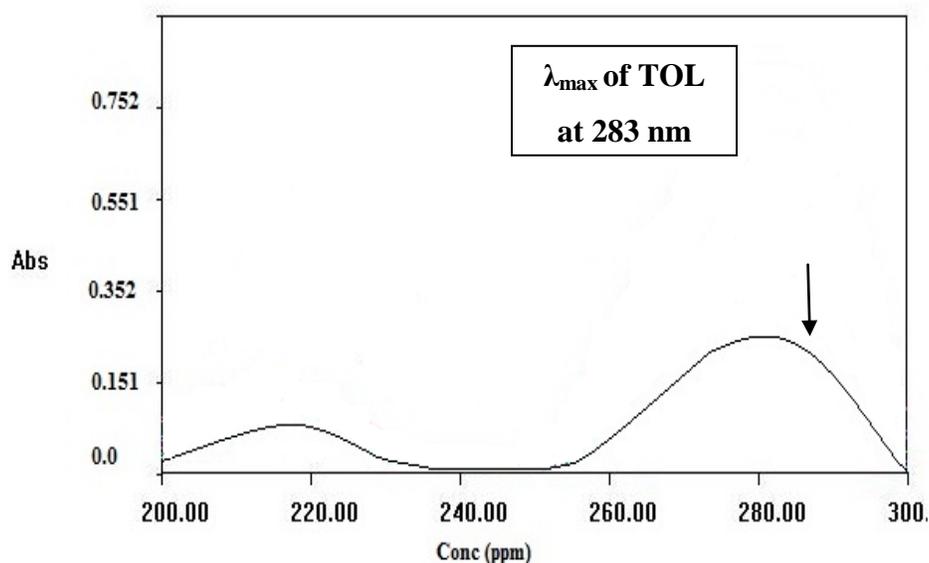


Figure 2: Absorption spectrum of TOL

Study of Beer- Lambert's range:

From the standard stock solution of 1000 $\mu\text{g/mL}$ of TOL, 1 ml was pipetted to get working standard solution of 100 $\mu\text{g/mL}$ of TOL. Hence from the working standard solution of 100 $\mu\text{g/mL}$ of TOL, further 1, 2, 3, 4 and 5 ml were pipetted to 10 ml volumetric flask to get the final concentration within the Beer's range *i.e.* 10, 20, 30, 40 and 50 $\mu\text{g/mL}$ respectively. Calibration data of drug at 283 nm is given in Table 1, whereas the calibration curves are shown in Figure.3

Table 1: Calibration data of TOL

Conc.($\mu\text{g/mL}$)	Absorbance(283nm)
10	0.185
20	0.371
30	0.553
40	0.727
50	0.914

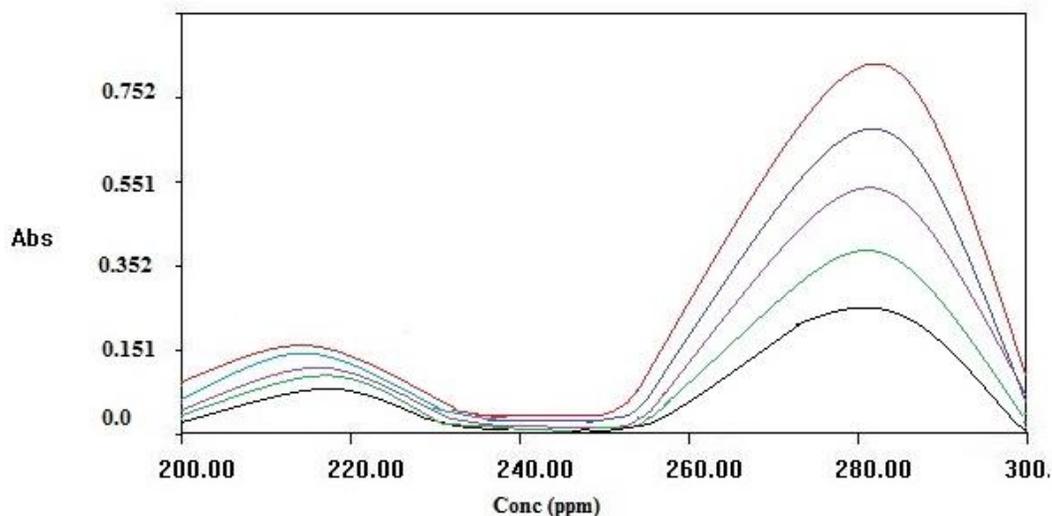


Figure 3: Overlain Spectra of TOL

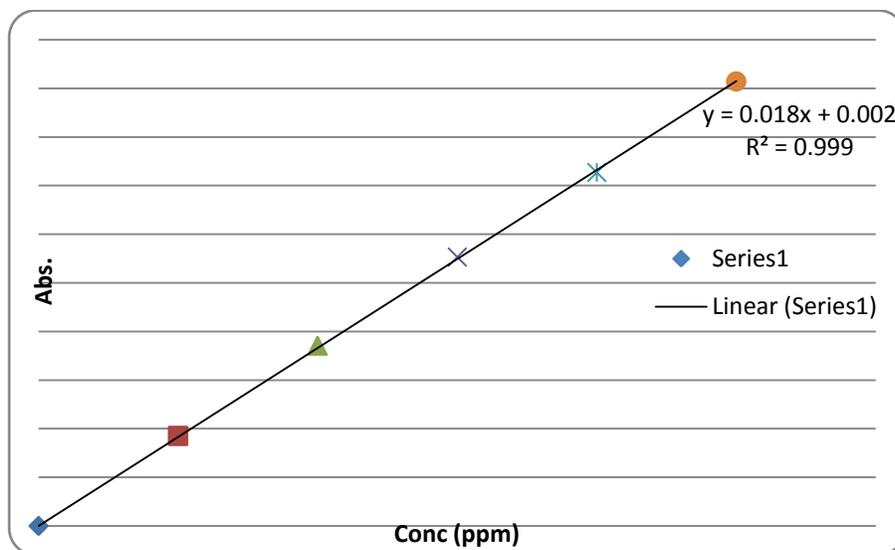


Figure 4: Calibration curve of TOL

Analysis of the marketed formulation:

For the estimation of drug in the commercial formulation, twenty tablets containing label claim of 2 mg of TOL was weighed and average weight was calculated. The tablets were crushed and powdered in glass mortar and the powder equivalent to 25 mg was transferred to 25 ml volumetric flask and ultrasonicated for 20 minutes and volume was made up to the mark with distilled water. The solution was then filtered through a Whatmann filter paper (No. 42). The filtrate was appropriately diluted further to obtain the final concentration within the Beer's range. The concentration of TOL was determined by measuring absorbance of sample solutions at 283 nm (λ_{max} of TOL). The procedure was repeated six times. The results of the analysis of the marketed formulations are given in Table 2.

Table 2: Results of Analysis

Sr.no.	Label claim (mg)	Amount of drug estimated (mg/tab)	% Recovery
1	2	1.994	99.73
2	2	1.996	98.43
3	2	1.966	98.30

* Average of six determinations

Validation of the developed method:

The developed method was validated as per ICH guidelines.

Accuracy

To check the accuracy of the proposed method, recovery studies were carried out according to ICH guidelines by applying the standard addition method to known amount of TOL corresponding to 80, 100 and 120% in pre-analyzed sample. The tablet sample solution of 2 µg/mL of TOL was prepared and the recovery studies were performed three times at each level. The results of the recovery studies and its statistical evaluation are summarized in Table 3.

Table 3: Results of Recovery studies

Level of Recovery (%)	Amt. taken (µg/mL)	Amt. of Std. added (µg/mL)	Abs. at 283 nm	Conc. from Std graph	Amount of TOL in formulation	% purity
80	20	16	0.693	36	2 µg/mL	98.63
100	20	20	0.731	40		99.80
120	20	24	0.856	44		98.73

Precision

Intermediate precision

The Intra and Inter-day precision was determined by analysis of the marketed formulation on the same day at different time intervals and on different days respectively. The results are given in Table 4.

Table 4: Results of Inter-day and Intra-day precision studies

Sr.no.	Precision	Absorbance	S.D.	% RSD
1.	Intraday	0.3530	0.0075	0.2963
2.	Interday	0.3591	0.0101	0.3920

* Average of six determinations

Specificity

Marketed formulations were analysed to determine the specificity of the optimized method in the presence of impurities and excipients. The specificity of the method was ascertained by analyzing standard drug and sample.

Table 5: Results of Specificity

Sr. no	Excipient conc. (%)	Drug conc. (μg)	Drug recovered (μg)	Drug recovered (%)	Mean recovered (%)	S.D.	%RSD
1	50	20	19.80	99.59			
2	100	20	19.99	99.94	99.76	0.257	0.249
3	150	20	19.95	99.75			

Robustness and Ruggedness

The evaluation of robustness should be considered during the development phase and depends on the type of procedure under study. It should show the reliability of an analysis with respect to deliberate variations in method parameters.

Table 6: Results of Robustness

Temperature ($^{\circ}\text{C}$)	Concentration ($\mu\text{g/ml}$)	Absorbance	S.D
30 $^{\circ}\text{C}$	20	0.364	0.004
25 $^{\circ}\text{C}$	20	0.387	0.005

* Average of six determinations

Table 7: Results of Ruggedness

Analyst	Concentration ($\mu\text{g/ml}$)	Absorbance	S.D
Analyst 1	20	0.356	0.002
Analyst 2	20	0.364	0.003

* Average of six determinations

Limit of detection (LOD) and limit of quantitation (LOQ)

The LOD and LOQ were separately determined based on calibration curve. The residual standard deviation of a regression line or the standard deviation of y-intercepts of regression lines were used to calculate the LOD and LOQ.

Table 8: LOD and LOQ of TOL

Parameter	Drug	S.D.
Limit of detection ($\mu\text{g/ml}$)	0.1865	0.1164
Limit of quantitation ($\mu\text{g/ml}$)	0.5621	0.0029

CONCLUSION

In present work, UV-Spectrophotometric method was developed and validated as per ICH guidelines for Tolterodine tartarate in bulk and tablet dosage form. The standard deviation (SD), % RSD and standard error (SE) calculated for all the methods were low, indicating high degree of precision. The results of the recovery studies exhibited high degree of accuracy of the proposed method. Hence, it can be concluded that the proposed method is accurate, precise, reproducible & economical and can be employed for routine quality control of Tolterodine tartarate in bulk drug and tablet dosage form.

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