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Research Article

SENSITIVE SPECTROPHOTOMETRIC ASSAY OF MUSCARINIC RECEPTOR ANTAGONIST TOLTERODINE TARTRATE IN BULK DRUG AND PHARMACEUTICAL FORMULATIONS

RAGAA EL-SHEIKH[1], WAFAA S HASSAN[2], AYMAN A GOUDA[1]*, MARWA M EL-GABRY[1]

[1]Department of Chemistry, Faculty of Science, Zagazig University, Zagazig, 44519, Egypt. [2]Department of Analytical Chemistry, Faculty of Pharmacy, Zagazig University, Zagazig, Egypt. Email: aymangouda77@gmail.com

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ABSTRACT

Objective: Simple, sensitive, and accurate spectrophotometric methods have been developed for the assay of tolterodine tartrate (TOL) in bulk drug and pharmaceutical formulations.

Methods: The proposed methods are based on oxidation reaction of TOL with a known excess of cerium(IV) ammonium sulfate as an oxidizing agent in acid medium followed by determination of unreacted oxidant by adding a fixed amount of dye, e.g., amaranth (AM), rhodamine 6G (Rh6G), and indigo carmine (IC) followed by measuring the absorbance at 520, 530, and 610 nm, respectively. The effect of experimental conditions was studied and optimized.

Results: The Beer's law was obeyed in the concentration ranges of 1.0-10, 1.0-12, and 0.5-9.0 µg/mL using AM, Rh6G, and IC dyes, respectively, with a correlation coefficient ≥0.9995. The calculated molar absorptivity values are 1.868×10^4, 1.008×10^4, and 1.623×10^4 L/mol/cm using AM, Rh6G, and IC dyes, respectively. The limits of detection and quantification were reported. Intraday and interday accuracy and precision of the methods have been evaluated. No interference was observed from the additives.

Conclusion: The proposed methods were successfully applied to the assay of TOL in tablets preparations, and the results were statistically compared with those of the reported method by applying Student's t-test and F-test. The reliability of the methods was further ascertained by performing recovery studies using the standard addition method.

Keywords: Tolterodine tartrate, Spectrophotometry, Cerium(IV) ammonium sulfate, Dyes, Tablets.

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INTRODUCTION

Tolterodine tartrate (TOL) is a competitive muscarinic receptor antagonist used for the treatment of urinary incontinence (incontinence in detrusor instability) and other overactive bladder symptoms, such as urgency and high micturition frequency. TOL is chemically designated as (R)-N,N-diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-phenylpropanamine L-hydrogen tartrate (Fig. 1). Tolterodine acts on M1, M2, M3, M4, and M5 subtypes of muscarinic receptors whereas modern antimuscarinic treatments for overactive bladder only act on M3 receptors making them more selective [1].

Several methods including high performance liquid chromatographic[2-9],electrochemical[10,11]spectrofluorimetric[12], and spectrophotometric [13-25] methods have been reported for the determination of TOL in pure drug and pharmaceutical formulations. However, these previously reported spectrophotometric methods suffer from one or other disadvantage such as poor sensitivity, depending on critical experimental variables; few methods require a rigid pH control and tedious and time-consuming liquid–liquid extraction step and use of expensive reagent or large amounts of organic solvents. For these reasons, it was worthwhile to develop a new, simple, cost-effective, selective, and sensitive spectrophotometric method for the determination of TOL in pure form and pharmaceutical formulations.

This work aims to develop new, simple, rapid, sensitive, accurate, precise, cost-effective, and validated spectrophotometric method for the estimation of TOL in pure and dosage forms. The method is based on the oxidation of TOL with slight excess of cerium(IV) ammonium sulfate (CAS) in acidic medium. The unconsumed of oxidant is then estimated by adding a fixed amount of amaranth (AM), rhodamine 6G (Rh6G), and indigo carmine (IC) dyes to form colored species which absorbs maximally at 520, 530, and 610 nm, respectively. The proposed methods have been demonstrated to be superior to the reported methods with respect to simplicity, speed, sensitivity, being accurate and precise, cost-effectiveness, and eco-friendliness and can be adopted by the pharmaceutical laboratories for industrial quality control.

MATERIAL AND METHODS

Apparatus

All absorption spectra were made using Varian UV–Vis spectrophotometer (Cary 100 Conc., Australia) equipped with 10 mm quartz cell was used for absorbance measurements. This spectrophotometer has a wavelength accuracy of ±0.2 nm with a scanning speed of 200 nm/min and a bandwidth of 2.0 nm in the wavelength range of 200-900 nm.

Materials and reagents

All chemicals, solvents and reagents used in this work were of analytical reagent or pharmaceutical grade, and all solutions were prepared fresh daily. Bidistilled water was used throughout the work.

Working standard of TOL was kindly supplied by the ADWIA Pharmaceuticals Community, El Obour City, Egypt, with a purity of 99.60±0.90%. All pharmaceutical preparations were obtained from commercial sources in the local markets. Incont tablets manufactured by ADWIA Pharmaceuticals Community, El Obour City, Egypt, Terodine tablets manufactured by Pharaonia Pharmaceuticals Company, Alexandria, Egypt, and Detrusitol tablets manufactured by Pharmacia and Upjohn Company labeled to contain (2.0 mg TOL per tablet) were obtained from commercial sources.

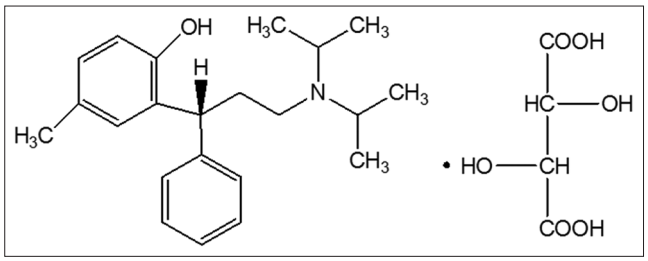
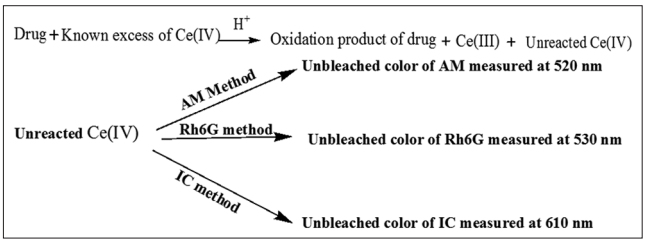


Fig. 1: The chemical structure of tolterodine tartrate



Scheme 1: The suggested reaction pathway for the proposed spectrophotometric methods using cerium(IV) ammonium sulfate and dyes

Standard solution

A stock standard solution (100 µg/mL) of TOL was prepared by dissolving 10 mg of pure TOL in methanol further diluted to 100 mL with the same solvent in a 100 mL measuring flask. The standard solution was found stable for at least 1 week without alteration when kept in an amber colored bottle and stored in a refrigerator when not in use.

Reagents

CAS (5.0×10^{-3} mol/L)

A stock solution of 5.0×10^{-3} mol/L CAS (E-Merck, Darmstadt, Germany) was freshly prepared by dissolving 316.2 mg of ($CeN_4H_{20}S_4O_{18}$, M.Wt.=632.55 g/mol) in the least amount of H_2SO_4 (2.0 mol/L) then completed to the mark in a 100 mL calibrated flask with the same acid and kept in a dark bottle and a refrigerator when not in use.

Sulfuric acid (H_2SO_4) (2.0 mol/L)

A stock solution of 2.0 mol/L H_2SO_4 was prepared by adding 10.8 mL of concentrated acid (Merck, Darmstadt, Germany, 98%, Sp. Gr. 1.84) to bidistilled water, cooled to room temperature, transfers to 100 mL with measuring flask, diluted to the mark and standardized as recorded [26].

Dyes (1000 µg/mL)

A stock solutions (1000 µg/mL) AM, Rh6G and IC were first prepared by dissolving accurately weighed 112 mg of each dye (Sigma-Aldrich, 90% dye content) in bidistilled water and diluting to volume in a 100 mL calibrated flask. The solution was then diluted 5.0-fold to get the working concentration of 200 µg/mL of each dye.

Recommended procedures

Different aliquots (0.1-1.0 mL), (0.1-1.2 mL), and (0.05-0.9 mL) of a standard 100 µg/mL TOL solution using AM, Rh6G, and IC methods, respectively, were transferred into a series of 10 mL calibrated flasks followed by adding 1.0 mL of 2.0 mol/L H_2SO_4 and 2.0 mL of (5.0×10^{-3} mol/L) CAS solution for all dyes. The flasks were stoppered and the contents were mixed well and the flasks were kept in boiled water bath for 5.0 minutes with occasional shaking. Finally, the solution was cooled and 1.0 mL of (200 µg/mL) dye solution was added to each flask and mixed well, and then the volume was diluted to the mark with bidistilled water. The decrease in color intensity of dye was measured after 5.0 minute against reagent blank solution treated similarly omitting TOL drug at their corresponding λ_{max}520, 530, and 610 nm for AM, Rh6G, and IC, respectively. The concentration of unknown was determined in each case from calibration graph which obtained by plotting the concentration of TOL against the decrease in absorbance of dye at the corresponding λ_{max}.

Procedure for tablet formulations

The contents of 20 tablets were weighed accurately and ground into a fine powder. An accurate weight of the powdered tablets equivalent to 10 mg TOL was dissolved in methanol with shaking for 5.0 minutes and filtered using a Whatman No. 42 filter paper. The filtrate was diluted to the mark with methanol in a 100 mL measuring flask to give 100 µg/mL stock solution of TOL for analysis by the proposed methods. A convenient aliquot was then subjected to analysis by the spectrophotometric procedures described above. Determine the nominal content of the tablets using the corresponding regression equation of the appropriate calibration graph.

RESULTS AND DISCUSSION

Absorption spectra and chemistry of the reaction

Many dyes are irreversibly destroyed to colorless species by oxidizing agents in acid medium [26]. CAS because of its high oxidation potential and excellent solution stability has been widely used as an effective analytical reagent in spectrophotometric methods for the determination of many pharmaceutical compounds [27-31]. The analytical reactions involved two steps; the first one was concerned with oxidation of TOL with a known excess of CAS in acidic medium at room temperature (25°C±2°C). The second step involved the determination of the residual CAS via its reaction with a fixed amount of AM, Rh6G or IC dyes and measuring the absorbance at the respective λ_{max}. The tentative reaction scheme of spectrophotometric methods is shown in Scheme 1. In all methods, the absorbance increased linearly with increasing concentration of TOL. The latter methods make use of the bleaching action of oxidant on dyes, the discoloration being caused by the oxidative destruction of the dye.

Optimization of the reaction conditions

Effect of acid type and concentration

To investigate the effect of acid concentration, different types of acids were examined (HCl, H_2SO_4, H_3PO_4, HNO_3, and CH_3COOH) to achieve maximum yield of redox reactions. Better results were suitable in sulfuric acid (H_2SO_4) (2.0 mol/L) with CAS as oxidant. The effect of H_2SO_4 concentration on the reaction between TOL and CAS was studied by varying the volume of H_2SO_4 (2.0 mol/L H_2SO_4) from 0.25 to 3.0 mL, keeping the concentration of oxidant and TOL fixed. The results indicated that, at 1.0-2.0 mL of H_2SO_4 (2.0 mol/L), there were almost same absorbance values were obtained in the presence of TOL (Fig. 2.). At the acid volumes <1.0 mL, reaction led to go slower and incomplete. Therefore, 1.0 mL of H_2SO_4 (2.0 mol/L) was the optimum volume for subsequent studies for TOL.

Effect of oxidant concentration

To investigate the optimum concentration of CAS, different volumes of oxidant were treated in the range of 0.25-3.0 mL with a fixed concentration dyes in optimum acidic medium and the absorbance was measured at optimum wavelength. The results indicate that the maximum and constant absorbance was achieved with 2.0 mL of CAS (5.0×10^{-3} mol/L) solution was taken as the optimum concentration for all measurements (Fig. 3).

Effect of dye concentration

The effect of dye concentration on the intensity of the color developed was carried out to obtain the optimum concentration of dyes that produces the maximum and reproducible color intensity by reducing the residual of CAS. The effect dye concentration was studied using different volumes (0.25-3.0 mL) of the studied dyes (200 µg/mL) AM, Rh6G, and IC. It was observed that maximum color intensity of the oxidation products was achieved with 1.0 mL of AM, Rh6G, and IC dye solution (Fig. 4). The color was found to be stable up to 12 hr.

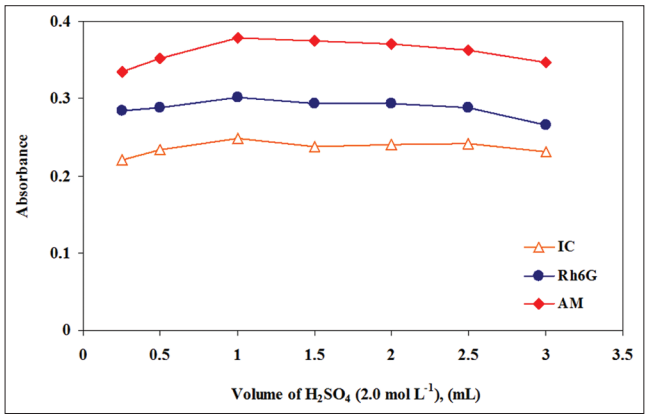


Fig. 2: Effect of volume of H_2SO_4 (2.0 mol/L) of the absorbance of oxidation product: Tolterodine tartrate (8.0 µg/mL); cerium(IV) ammonium sulfate (5.0×10^{-3} mol/L) and dyes (200 µg/mL)

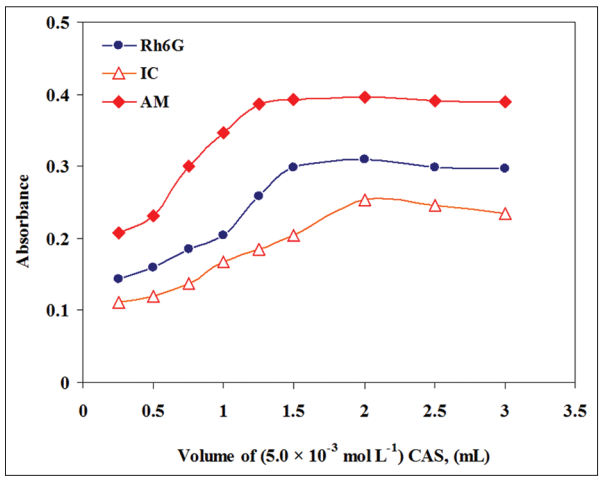


Fig. 3: Effect of volume of cerium(IV) ammonium sulfate oxidant on the absorbance of the reaction product: Tolterodine tartrate (8.0 µg/mL); dyes (200 µg/mL) in optimum acidic medium

Effect of temperature and mixing time

The effect of temperature was studied by heating a series of sample and blank solutions at different temperatures ranging from 25°C to 100°C in water bath. It was found that raising the temperature accelerate the oxidation process and give reproducible results, so maximum color intensity was obtained in boiling water bath. The effect of mixing time required completing oxidation of TOL and for reducing the excess oxidant was studied by measuring the absorbance of sample solution against blank solution prepared similarly at various time intervals 2.0-20 minutes. It was found that the contact times gave constant and reproducible absorbance values at 5.0 minutes in boiling water bath (Fig. 5). After oxidation process, 5.0 minutes in standing time was found necessary for the complete bleaching of the dye color by the residual CAS and the absorbance of the unreacted dye was stable for at least 12 hr, thereafter.

Effect of sequence of addition

After optimizing all other experimental variables, further experiments were performed to ascertain the influence of sequence of addition of reactants on the color development by measuring the absorbance. The optimum sequence of addition was TOL–H_2SO_4–CAS–dye. Other sequences gave lower absorbance values under the same experimental conditions.

Method validation

The proposed methods have been validated for linearity, sensitivity, precision, accuracy, selectivity, and recovery.

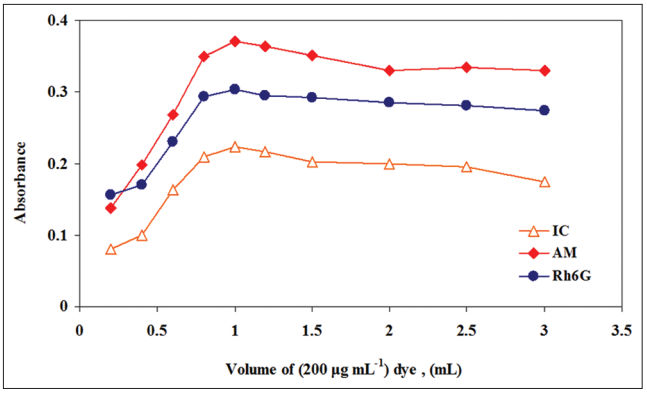


Fig. 4: Effect of volume of dyes on the absorbance of the reaction product: Tolterodine tartrate (8.0 µg/mL); cerium(IV) ammonium sulfate (5.0×10^{-3} mol/L) in optimum acidic medium

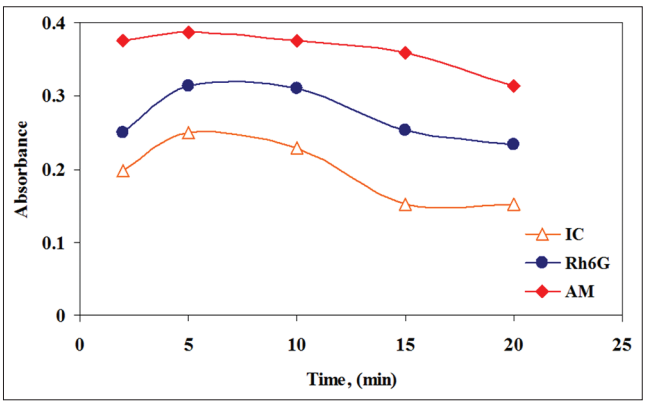


Fig. 5: Effect of time on the absorbance of the reaction product: Tolterodine tartrate (8.0 µg/mL); cerium(IV) ammonium sulfate (5.0×10^{-3} mol/L) and dyes (200 µg/mL) in optimum acidic medium

Linearity and sensitivity

Under the optimum conditions a linear correlation was found between absorbance at λ_{max} and the concentration of TOL in the ranges of 1.0-10, 1.0-12, and 0.5-9.0 µg/mL using AM, Rh6G, and IC methods, respectively. The calibration graph is described by the equation:

$$A=a+bC \quad (1)$$

Where A=Absorbance, a=Intercept, b=Slope, and C=Concentration in µg/mL, obtained by the method of least squares. Correlation coefficient, intercept and slope of the calibration data are summarized in Table 1. For accurate determination, Ringbom concentration range [32] was calculated by plotting log concentration of drug in µg/mL against transmittance % from which the linear portion of the curve gives an accurate range of micro determination of TOL and represented in Table 1. Sensitivity parameters such as apparent molar absorptivity and Sandell's sensitivity values, as well as the limits of detection and quantification (LOD and LOQ), were calculated as per the current ICH guidelines [33] and illustrated in Table 1. The high molar absorptivity and lower Sandell's sensitivity values reflects the good and high sensitivity of the proposed methods. The validity of the proposed methods was evaluated by statistical analysis [33] between the results achieved from the proposed methods and that of the reported method. Regarding the calculated Student's t-test and variance ratio F-test (Table 1), there is no significant difference between the proposed and reported method [25] regarding accuracy and precision.

The LOD and LOQ were calculated according to the same guidelines using the formulas [33,34]:

$$LOD=3.3\sigma/s \text{ and } LOQ=10\sigma/s \quad (2)$$

Where σ is the standard deviation of five reagent blank determinations, and s is the slope of the calibration curve.

Accuracy and precision

To evaluate the precision of the proposed methods, solutions containing three different concentrations of TOL were prepared and analyzed in six replicates. The analytical results obtained from this investigation are summarized in Table 2. Lower values of the relative standard deviation (RSD%) and percentage relative error (RE %) indicate the precision and accuracy of the proposed methods. The percentage RE is calculated using the following equation:

$$\%RE=\left[\frac{\text{Found}-\text{taken}}{\text{taken}}\right]\times 100 \quad (3)$$

The assay procedure was repeated 6 times, and percentage RSD % values were obtained within the same day to evaluate repeatability (intraday precision) and over five different days to evaluate intermediate precision (interday precision).

For the same concentrations, drugs inter- and intraday accuracy of the methods was also evaluated. The percentage recovery values with respect to found concentrations of each drug were evaluated to ascertain the accuracy of the methods. The recovery values close to 100% as compiled in Table 2 shows that the proposed methods are very accurate.

Table 1: Analytical and regression parameters of proposed oxidation spectrophotometric methods for determination of TOL

Parameters	AM	Rh6G	IC
Beer's law limits (µg/mL)	1.0-10	1.0-12	0.5-9.0
Ringboom limits (µg/mL)	2.0-8.0	2.0-10	2.0-8.0
Molar absorptivity (×10^4 L/mol/cm)	1.8681	1.0077	1.6232
Sandell sensitivity (ng/cm^2)	25.46	47.20	29.30
Regression equation[a]			
Intercept (a)	0.0016	0.0004	0.0004
Standard deviation of intercept (S_a)	0.007	0.008	0.005
Slope (b)	0.0386	0.0208	0.0332
Standard deviation of slope (S_b)	0.009	0.011	0.007
Correlation coefficient (r)	0.9997	0.9995	0.9997
Recovery±SD[b]	99.40±0.88	99.30±1.20	99.70±1.10
RSD%	0.89	1.21	1.10
RE%	0.93	1.27	1.16
Limit of detection (µg/mL)	0.27	0.30	0.14
Limit of quantification (µg/mL)	0.90	1.0	0.47
Calculated t value[c]	0.36	0.45	0.16
Calculated F value[c]	1.05	1.78	1.49

[a]A=a + bC, where C is the concentration in µg/mL, A is the absorbance units, a is the intercept, b is the slope. [b]Mean±SD. [c]The theoretical values of t and F are 2.57 and 5.05, respectively, at confidence limit at 95% confidence level and 5° of freedom (p=0.05). SD: Standard deviation, TOL: Tolterodine tartrate, AM: Amaranth, Rh6G: Rhodamine 6G, IC: Indigo carmine, RSD: Relative standard deviation, RE: Relative error

Robustness and ruggedness

Robustness was examined by evaluating the influence of small variation of method variables, including acid volume and reaction time on the performance of the proposed methods. In these experiments, one parameter was changed whereas the others were kept unchanged, and the recovery percentage was calculated each time. The analysis was performed with altered conditions by taking three different concentrations of TOL, and it was found that small variation of method variables did not significantly affect the procedures as shown by the RSD values in the range of 1.10-2.70%. This provided an indication for the reliability of the proposed methods during its routine application for the analysis of TOL, and so the proposed spectrophotometric methods are considered robust. Ruggedness was expressed as the RSD and was also tested by applying the proposed methods to the assay of TOL using the same operational conditions but using three different instruments as well as three different analysts. The inter-analysts RSD were in the ranges 0.90-2.30%, whereas the inter-instruments RSD ranged from 0.75% to 2.40% suggesting that the developed methods were rugged. The results are shown in Table 3.

Recovery studies

To ascertain the accuracy, reliability, and validity of the proposed methods, recovery experiment was performed through standard addition technique. This study was performed by spiking three different levels of pure drugs (50, 100, and 150% of the level present in

Table 2: Results of intra- and interday accuracy and precision study for TOL obtained by the proposed CAS method

Method	Taken (µg/mL)	Recovery %	Precision RSD %[a]	Accuracy RE %	Confidence limit[b]
Intraday					
AM	3.0	99.50	0.80	−0.50	2.985±0.025
	6.0	99.00	0.90	−1.0	5.94±0.056
	9.0	99.70	1.50	−0.30	8.973±0.141
Rh6G	3.0	99.20	1.0	−0.80	2.976±0.031
	6.0	99.70	1.15	−0.30	5.982±0.072
	9.0	98.50	1.40	−1.50	8.865±0.13
IC	2.0	99.00	0.80	−1.0	1.98±0.017
	4.0	99.70	0.65	−0.30	3.988±0.027
	6.0	100.50	1.80	0.50	6.03±0.114
Interday					
AM	3.0	99.30	0.90	−0.70	3.972±0.038
	6.0	99.40	1.10	−0.60	5.964±0.069
	9.0	99.10	1.30	−0.90	8.919±0.122
Rh6G	3.0	99.00	0.50	−1.0	2.97±0.016
	6.0	99.80	1.0	−0.20	5.988±0.063
	9.0	101.0	1.70	0.50	9.09±0.162
IC	2.0	100.0	0.90	1.0	2.0±0.019
	4.0	99.30	1.50	−0.70	3.972±0.063
	6.0	99.60	1.90	−0.40	5.976±0.119

[a]RSD%, percentage relative standard deviation, RE%, percentage relative error. [b]Mean±standard error. TOL: Tolterodine tartrate, AM: Amaranth, Rh6G: Rhodamine 6G, IC: Indigo carmine, CAS: Cerium(IV) ammonium sulfate

the tablet) to a fixed amount of drugs in tablet powder (pre-analyzed) and the total concentration was found by the proposed methods. The determination with each level was repeated 3 times, and the percent recovery of the added standard was calculated from:

$$\%\text{Recovery}=\frac{[C_F - C_T]}{C_P}\times 100 \quad (4)$$

Where C_F is the total concentration of the analyte found, C_T is a concentration of the analyte present in the tablet preparation; C_P is a concentration of analyte (pure drug) added to tablets preparations. The results of this study presented in Table 4 revealed that the accuracy of the proposed methods was unaffected by the various excipients present in tablets which did not interfere in the assay.

Application of pharmaceutical formulations

The proposed methods were applied to the determination of TOL in pharmaceutical formulations (tablets). The results in Table 5 showed that the methods are successful for the determination of TOL and that the excipients in the dosage forms do not interfere. A statistical

Table 3: Results of method robustness and ruggedness

Methods	Nominal amount concentration (µg/mL)	RSD%			
		Variable alerted[a]			
		Robustness		Ruggedness	
		Acid volume (n=3)	Reaction time (n=3)	Different analysts (n=3)	Different instruments (n=3)
AM	3.0	1.40	1.10	0.90	1.20
	6.0	1.90	1.60	1.40	1.70
	9.0	2.20	1.90	1.80	2.25
Rh6G	3.0	1.30	1.20	1.10	0.75
	6.0	1.50	1.80	1.60	1.50
	9.0	2.30	2.50	2.30	1.90
IC	2.0	1.70	1.30	1.30	1.20
	4.0	2.0	1.70	1.80	1.90
	6.0	2.40	2.70	2.10	2.40

[a]Volume of (2.0 mol/L) H_2SO_4 is (1.0±0.2 mL) and reaction time is (5.0±2.0 minutes) (after adding CAS) were used. AM: Amaranth, Rh6G: Rhodamine 6G, IC: Indigo carmine, CAS: Cerium(IV) ammonium sulfate, RSD: Relative standard deviation

Table 4: Results of recovery experiments by standard addition method for the determination of TOL in tablets using the proposed methods

Samples	Taken drug in tablet (µg/mL)	Pure drug added (µg/mL)	AM		Rh6G		IC	
			Total found (µg/mL)	Recovery[a] (%) ± SD	Total found (µg/mL)	Recovery[a] (%) ± SD	Total found (µg/mL)	Recovery[a] (%) ± SD
Incont tablets	2.0	2.0	3.976	99.40±0.90	3.96	99.00±1.20	3.94	98.50±0.85
	2.0	4.0	5.94	99.00±1.10	5.94	99.30±0.90	5.982	99.70±0.90
	2.0	6.0	8.08	101.0±1.60	7.96	99.50±1.50	8.064	100.80±1.20
Terodine tablets	2.0	2.0	4.02	100.50±0.70	3.952	98.80±0.70	4.012	100.30±0.60
	2.0	4.0	5.952	99.20±0.90	6.06	101.0±1.50	5.976	99.60±1.10
	2.0	6.0	8.12	101.50±1.40	7.952	99.40±1.60	8.056	100.70±1.40
Detrusitol tablets	2.0	2.0	3.96	99.00±1.0	3.964	99.10±0.70	3.98	99.50±0.80
	2.0	4.0	5.988	99.80±1.40	5.976	99.60±0.90	6.0	100.0±0.90
	2.0	6.0	8.072	100.90±1.70	7.992	99.90±1.30	8.12	101.50±1.70

[a]Average of six determinations. AM: Amaranth, Rh6G: Rhodamine 6G, IC: Indigo carmine, SD: Standard deviation, TOL: Tolterodine tartrate

Table 5: Results of analysis of tablets by the proposed methods for the determination of TOL and statistical comparison with the reported method [25]

Samples	Recovery[a] (%) ± SD			Reported method [25]
	AM	Rh6G	IC	
Incont tablets	99.80±1.06	99.27±0.70	99.70±0.90	99.60±0.80
t value[b]	0.34	0.69	0.19	
F value[b]	1.86	1.31	1.27	
Terodine tablets	100.40±1.40	99.83±1.10	100.20±1.35	99.70±1.15
t value[b]	0.86	0.18	0.63	
F value[b]	1.48	1.09	1.38	
Detrusitol tablets	99.90±0.70	99.50±0.50	99.10±0.80	99.30±0.60
t value[b]	1.46	0.57	0.45	
F value[b]	1.36	1.44	1.78	

[a]Average of six determinations. [b]The theoretical values of t and F are 2.571 and 5.05, respectively, at confidence limit at 95% confidence level and 5° of freedom (p=0.05). AM: Amaranth, Rh6G: Rhodamine 6G, IC: Indigo carmine, SD: Standard deviation, TOL: Tolterodine tartrate

Table 6: Comparison between the proposed and report spectrophotometric methods for determination of TOL

Method	Wavelength (nm)	Beer's law (µg/mL)	Molar absorptivity (L/mol/cm)	Detection limit (µg/mL)	References
UV-spectrophotometry (NaOH, 0.1 N)	280	40-180	NA	0.715	[13]
UV-spectrophotometry	280	10-90	NA	NA	[14]
Eosin	545	1.0-10	0.1	NA	[15]
N-bromosuccinimide	520	5.0-35	NA	0.03	[16]
Chloramine-T	540	2.0-14	NA	0.09	
Phosphomolybdic acid	840	10-60	NA	0.02	
Gold (III) chloride	540	10-90	5.43×10^3	0.25	[17]
Para chloranilic acid	500	20-380	811.9	3.5	[18]
2,3-dichloro-5,6-dicyano- 1,4-benzoquinone	460	18-230	836.7	2.3	
3-methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH)/$FeCl_3$	650	5.0-25	106217.3	NA	[19]
4-amino phenazone/potassium ferricyanide	540	4.0-12	350755	NA	[20]
Excess of cerium(IV)/methylene blue	660	5.0-18	NA	1.45	[21]
N-bromosuccinimide (NBS)/indigo carmine	610	38-80	NA	12	
Tropaeolin OOO	503	1.0-30	1.1954×10^4	0.08	[22]
Potassium permanganate/methylene blue	600	12-60	NA	3.6	[23]
Residual permanganate	540	5.0-50	NA	2.2	
Ferric chloride/2,2-bipyridyl	530	5.0-25	1.724×10^4	NA	[24]
3-methyl-2-benzothiazolinone hydrazone (MBTH)/ ceric ammonium sulphate	555	10-50	9.5×10^4	NA	[25]
Ferric chloride/1,10-phenanthroline	520	2.5-12.5	2.682×10^4	NA	
CAS/AM	520	1.0-10	1.8681×10^4	0.27	Proposed work
CAS/Rh6G	530	1.0-12	1.0077×10^4	0.30	
CAS/IC	610	0.5-9.0	1.6232×10^4	0.14	

NA: Not available, TOL: Tolterodine tartrate, UV: Ultra violet

comparison of the results obtained from the assay of TOL by the proposed methods and the reported method [25] for the same batch of material is presented in Table 5. The results agree well with the label claim and also were in agreement with the results obtained by the reported method [25]. When the results were statistically compared with those of the reported methods by applying the Student's t-test for accuracy and F-test for precision, the calculated t value and F value at 95% confidence level did not exceed the tabulated values for 5° of freedom [34]. Hence, no significant difference between the proposed methods and the reported methods at the 95% confidence level with respect to accuracy and precision.

CONCLUSION

New, simple, rapid, and cost-effective spectrophotometric methods have been developed for the determination of TOL in bulk drug and in tablets using CAS as oxidizing agents and dyes and validated as per the current ICH guidelines. The present spectrophotometric methods are characterized compared with other previously reported methods (Table 6) by simplicity, high selectivity, and sensitivity, low-cost and are free from tedious and time-consuming extraction steps and use of organic solvents unlike many of the previous reported methods for TOL. The assay methods have some additional advantages involve less stringent control of experimental parameters such as the stability of the colored system, accuracy, reproducibility, time of analysis, temperature independence, and cheaper chemicals. These advantages encourage the application of the proposed methods in routine quality control analysis of TOL in pure and dosage forms.

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