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Extractive Spectrophotometric Estimation of Tolterodine Tartrate Using Acid Dye Technique in both Bulk and Tablet Dosage Form

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ABSTRACT

For the estimation of tolterodine tartrate a new simple and accurate visible spectrophotometric method was developed. The proposed method was based on the formation of yellow-orange colored complex results from complete mixing of tolterodine tartrate, methyl orange and chloroform, which shows the maximum absorption at the wave length 417 nm. The linear relationship between the absorbance and the concentration of tolterodine tartrate was in the range of 20 – 120 µg/ml with a correlation coefficient = 0.997. This new method has offered a determination of tolterodine tartrate drug without any interference with excipients indirectly with a high accuracy for the analytical results. The method was found to be simple, economic, accurate and reproducible and can be used for routine analysis of tolterodine tartrate in bulk and in pharmaceutical formulation.

Keywords: Tolterodine tartrate, methyl orange, tolterodine tartrate tablets, colorimetry.

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INTRODUCTION

Tolterodine tartrate chemically is 2-((IR)-3-(bis (propan-2-yl) amino)-1-phenylpropyl)-4-methyl phenol. It is anti- muscarinic drug, it get metabolized in liver. Tolterodine tartrate and its active metabolites shows competitive antagonism at muscarinic receptors which results in bladder contraction inhibition, detrusor pressure decrease and incomplete bladder emptying. Literature shows that there are very less number of analytical methods developed for the analysis of this drug which includes UV Visible methods, HPLC, LC methods etc. In the methods which are reported earlier the reagents used are costly hence a new method was developed for the estimation of the drug in pure and in pharmaceutical dosage form which is accurate, simple and precise. In this visible method methyl orange dye was used as coloring agent. The method was validated by certain parameters like linearity, accuracy as per ICH guidelines.

Chemical structure

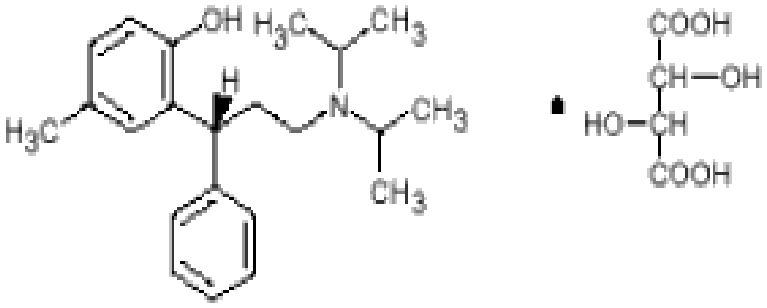

Figure 1 Chemical structure of tolterodine tartrate

MATERIALS AND METHODS

Apparatus

Shimadzu UV -1800 UV-Visible spectrophotometer was employed with spectral band length of 1nm attach with computer loaded with shimadzu UV PC software (UV Probe) version 2.31 and using a pair of 10mm matched glass cuvettes. Analytical balance systronics, Ph METER ELICO.

Drugs

Working standard tolterodine tartrate (99.75%) was procured from Aurabindo labs, Hyderabad, India. Roliten (Ranbaxy) was taken for study which contains tolterodine tartrate- 2mg were purchased from local pharmacy.

Chemicals and reagents

The solvent used was water (double distilled), chloroform (AR grade) manufactured by merk and methyl orange (AR grade) manufactured by fisher.

Standard stock solution of tolterodine tartrate

A stock solution of tolterodine tartrate was prepared by accurately weighed 25 mg of drug and transfer into 25ml volumetric flask and dissolved in 10ml of water initially and then make up to the mark i.e. to 25ml with distilled water to get 1mg/ml stock solution. This solution was further diluted stepwise with the same solvent to obtain working standard solution concentration of 100µg/ml.

Procedure for method development

A liquots of standard tolterodine tartrate solution (100µg/ml) such as 0.2,0.4,0.6,0.8,1.0 and 1.2ml were taken individually in a series of 25ml separating funnel, to get a concentration of 20,40,60,80,100 and 120µg/ml respectively. To this, add 5ml of methyl orange and 10ml of chloroform successively and then shake the separating funnel thoroughly for 10 minutes for the complete mixing of the solutions which gives a yellow-orange coloured complex. Then, the separating funnel was kept aside for 30 minutes to get an efficient separation. After that, the separated aqueous layer was collected and the colour intensity was measured at 417nm against reagent blank.

The calibration graph was constructed by plotting the drug concentration versus optical density. Regression equation was calculated and R^2 = 0.997. The amount of tolterodine tartrate in sample was estimated from corresponding regression equation.

Estimation of pharmaceutical formulation

An accurately weighed twenty tablets were triturated in motor and pestle and from that a powder equivalent to 10mg of ROLITEN (containing 2mg of tolterodine tartrate) was weighed and transferred to 10ml standard volumetric flask containing 5ml of water, shake well and final volume was made with remaining quality of water to obtain solution of TT (1000µg/ml). The mixture was then filtered through whatman 41 filter paper. Further dilution were made with water to obtain required concentration 100µg/ml. The filtrate was taken and used for the preparation of required test concentration in the same way as in the construction of calibration. The obtained color intensity was measured at 417nm and the amount was estimated using corresponding regression equation. The results were shown in table 1.

Validation

The methods were validated according to ICH guidelines (Q2R1) to study linearity, accuracy and precision.

Linearity

In order to find out the linearity range of the proposed visible method, studied were carried out by plotting absorbance of analyte against their respective concentrations.

A good linear relationship (r2=0.997) was observed between the concentration of TT and the corresponding absorbance. The regression equation observed was Y=0.0075x+0.007 (in which y represents absorbance and x represents concentration of TT). The results from linearity includes intercept, slope and regression coefficient were recorded in table 2.

Precision

Intraday and interday variation studies were carried out to demonstrate the precision. A concentration of 40µg/ml was prepared for six times and analyzed three times in a day in intra-day variation study. In case of inter-day variation study the procedure is same as intra-day but the sample analyzed three times for three consecutive days. The optical density values were reported in the precision table 3.

Accuracy

Solutions of different concentrations involves 50%, 100% and 150% were prepared to perform the accuracy study for the developed method. In these solution preparation the amount of pure drug added was varied that is 2mg, 4mg and 6mg in order to get 50%, 100% and 150% respectively whereas the amount of formulation (ROLITEN-2mg) was constant. The solutions were diluted to get the required concentrations in the range and the prepared dilutions was observed six times. The percentage recovery was calculated and reported in the accuracy table 4.

RESULTS AND DISCUSSION

The structure of tolterodine tartrate contains a tertiary amine. When an ionized form of amine added to methyl orange (ionized) an ion pair (salt) was produced which may be extracted into chloroform (organic solvent) from the excess of indicator. The absorbance is measured at indicator λmax. In this developed method, the coloring agent used was methyl orange and the ion pair complex was yellow orange in colour. The maximum colour intensity was showed at 417nm, the linearity ranges from 20-120ìg/ml and least square method was used for the calculation of regression equation which is used for the estimation of drug in formulation. The % amount was found to be 99.34% which indicates that the drug is good. The proposed method was accurate as the accuracy recoveries were found in between 98.6 to 101.25 and the method was found to be precise as the system and method precision results were found to be less than 2%. This method was economic for the estimation of TT and was validated as per ICH guidelines.

Table 1: Result of marketed formulation analysis

Formulation name	Labeled amount(mg)	Test conc.(µg/ml)	Mean amount found(mg)	%mean	%rsd
ROLITEN	2mg	60	1.98	99.34	0.75

Table 2: Linearity parameters

S.No.	Parameter	Value
1	Linearity(µg/ml)	20 - 120µg/ml
2	Linearity equation	Y= 0.0075x+0.007
3	Slope	0.0075
4	Intercept	0.007
5	Correlation coefficient	0.997

Table 3: Precision data for the developed method

S.No.	Test conc taken	Intra-day precision %RSD(n=6)	Inter-day precision %RSD(n=6)	
			Day-1	Day-2
1	40	0.829	0.795	0.801
2	40	0.730	0.573	0.673
3	40	0.612	0.664	0.543

Table 4: The Accuracy table

S.No.	Labeled amount(mg)	Spiked level	Amount of API added(mg)	Amount found (mg)(n=6)	%recovery (n=6)	Mean(n=6)
1	2	50%	2	1.95	98	98.36
2	2	100%	4	3.94	98.5	98.36
3	2	150%	6	5.92	98.6	98.36

Table 5: Optical characteristics of tolteridone tartrate visible method

S.No.	Optical characteristics	Results
1	λmax (nm)	417nm
2	Beer's law limit(µg/ml)	20-120(µg/ml)
3	Molar extinction coefficient(L/Mol.cm)	0.0701
4	Correlation coefficient	0.997
5	Regression equation	Y=0.0075x+0.007
6	Slope(a)	0.0075
7	Intercept(b)	0.007

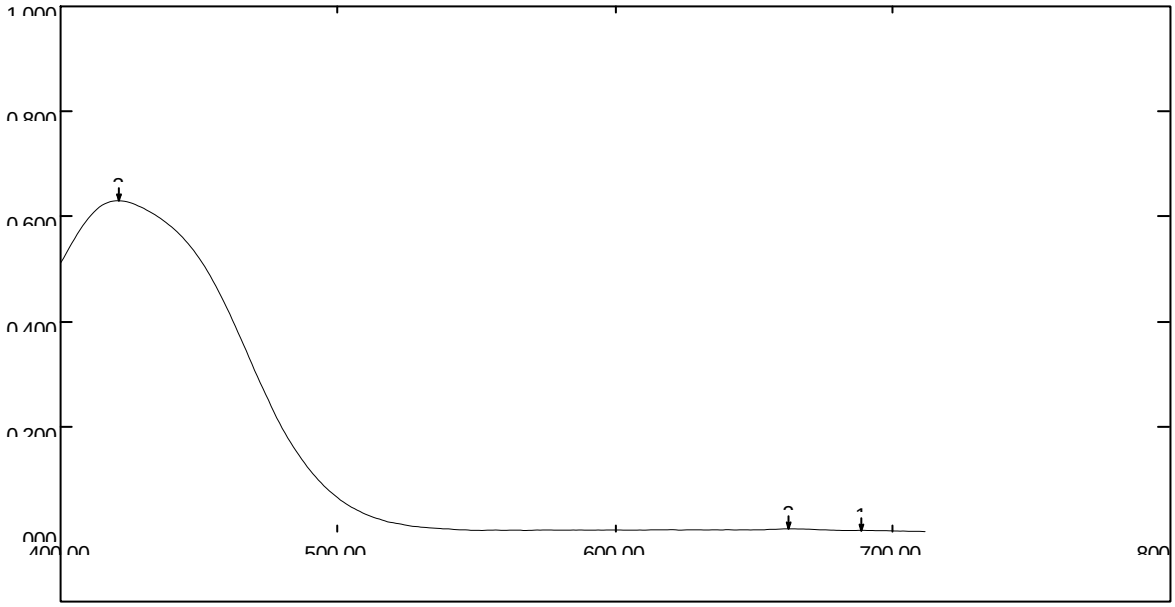

Figure 2. Spectrum of tolterodine tartrate

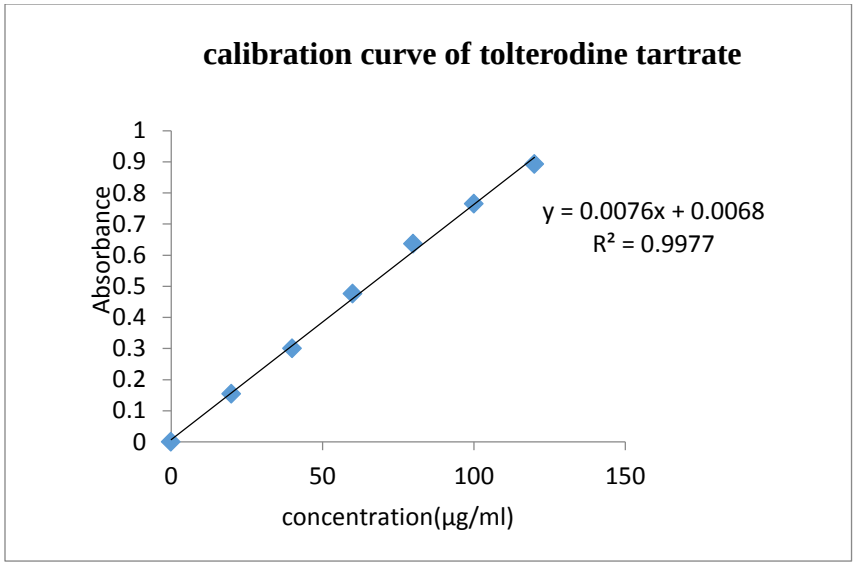

Figure 3: Calibration curve of tolterodine tartrate

CONCLUSION

The Extractive visible spectrophotometric method for the quantity estimation of tolterodine tartrate have been developed and validated based on current ICH guidelines. The procedure is based on well-established complex formation reaction and use cheaper and readily available chemicals. The method has been demonstrated to be free from rigid experimental conditions. These merits besides, the use of simple and inexpensive chemicals and instruments, recommend the use of the method in routine quality control laboratories.

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