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ESTIMATION OF TAMSULOSIN AND TOLTERODINE IN ITS PHARMACEUTICAL DOSAGE FORM BY SPECTROPHOTOMETRIC METHOD

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ABSTRACT: Two accurate and precise methods were developed for the estimation of Tamsulosin and Tolterodine in its pharmaceutical dosage form. First method is area under the curve method; the areas under the curve in the range of 230.5-220.5 nm (for TAM) and 289.0-279.0 nm (for TOL) were selected for the analysis. Second method is first order derivative spectroscopy by solving simultaneous equation, 221.5 nm (for TAM) and 234.0 nm (for TOL) were selected for the analysis. In both the methods linearity for detector response was observed in the concentration range of 5-25 µg/ml and 10-50 µg/ml for Tamsulosin and Tolterodine, respectively. The proposed methods were successfully applied for the simultaneous determination of both drugs in its commercial pharmaceutical preparation. The results of the analysis have been validated statistically and by recovery studies.

Keywords: Tamsulosin; Tolterodine; area under the curve method; derivative spectroscopy

INTRODUCTION

Chemically, Tamsulosin (TAM) is (-)-(R)-5-2-(2-(0-Ethoxyphenoxy)-ethyl)-amino)-propyl)-2-methoxy benzenesulphonamide. It is an α_1-adrenoceptor blocking agent and used in benign prostatic hyperplasia[1]. Tolterodine (TOL) is (+)-(R)-(α-(-2-Diisopropylamino)-ethyl))-benzyl)-p-cresol tartarate. It is a tertiary antimuscarinic agent and used in the management of urinary frequency, urgency and incontinence in detrusor instability[1]. Tamsulosin and Tolterodine combination is new and Capsules containing 0.4 mg TAM and 4 mg TOL given in Indian Drug Manufacturing Association-2008. Literature survey revealed that Tamsulosin is estimated by HPLC[2-4] and mass spectroscopy[5-6] while Tolterodine is estimated only by HPLC[7-8]. However, there is no analytical method reported for the estimation of TAM and TOL in a combined dosage formulation. Present work describes two methods for simultaneous estimation of TAM and TOL in capsule formulation

MATERIAL AND METHODS

Instrument A double-beam Shimadzu UV- Visible spectrophotometer, 1700 Pharmaspec, with spectral bandwidth of 2 nm, wavelength accuracy ± 0.5 nm and a pair of 1-cm matched quartz cells was used to measure absorbance of the resulting solution.

Materials: Cipla Pvt. Ltd., Mumbai, provided standard gift sample of Tamsulosin and Tolterodine. Combined dose Tamsulosin and Tolterodine capsules were prepared in the lab.

Solvent: Methanol was used as a solvent.

Stock solution: Standard stock solutions of TAM (100 µg/ml) and TOL (100 µg/ml) were prepared in Methanol and used for the analysis.

Procedure

Method A- Area Under the Curve Method

For the selection of analytical wavelength, solutions of TAM and TOL (20 µg/ml, each), were prepared separately by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm. From the overlain spectra of both drugs (Fig. 1), the areas under the curve in the range of 230.5-220.5 nm (for TAM) and 289.0-279.0 nm (for TOL) were selected for the

analysis. The calibration curves for TAM and TOL were prepared in the concentration range of 5-25 µg/ml and 10-50 µg/ml at their respective AUC range. The 'X' values of the drugs were determined for both the drugs at the selected AUC range. The 'X' value is the ratio of area under the curve at selected wavelength ranges with the concentration of component in mg/ml. These 'X' values were the mean of six independent determinations. A set of two simultaneous equations obtained by using mean 'X' values are given below.

A1 = 339.43 CTAM + 181.21 CTOL -------- (at $\lambda_{230.5\text{-}220.5}$ nm) --------(1)

A2 = 84.9 CTAM + 67.47 CTOL ---------- (at $\lambda_{289.0\text{-}279.0}$ nm) -------- (2)

Where A1 and A2 are the area under the curve of sample at the wavelength range 230.5-220.5 nm and 289.0-279.0 nm, respectively, 339.43 and 84.9 are the 'X' values of TAM at the wavelength range 230.5-220.5 nm and 289.0-279.0 nm, respectively. Similarly 181.21 and 67.47 are the 'X' values of TOL at the wavelength range 230.5-220.5 nm and 289.0-279.0 nm, respectively. CTAM is the concentration of TAM and CTOL is the concentration of the TOL. The mixture concentration was determined by using the equation (1) and (2).

Method B- First Order Derivative Spectroscopy

In this method solutions of TAM and TOL (20 µg/ml, each), were prepared separately by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm. The absorption spectra thus obtained were derivatized from first to fourth order. First order derivative spectra were selected for analysis of both drugs. From the overlain spectra of both drugs (Fig. 2), 221.5 nm (for TAM) and 234.0 nm (for TOL) were selected for the analysis. The calibration curves for TAM and TOL were plotted in the concentration range of 5-25 µg/ml and 10-50 µg/ml at their respective wavelength 221.5 nm and 234.0 nm, respectively. The absorptivity values of the drugs were determined at the selected wavelengths. These absorptrivity values are the mean of six determinations. Concentration of sample solution was determined by using following equations:

A1 = 0.62 CTAM - 1.475 CTOL ---------- (λmax at 221.5 nm)

A2 = -3.41 CTAM - 1.255 CTOL ---------- (λmax at 234.0 nm)

Where A1 and A2 are absorbance of the sample at 221.5 nm and 234.0 nm respectively, 0.62 and -3.41 are the absorptivity values of TAM at 221.5 nm and 234.0 nm respectively. Similarly -1.475 and -1.255 are the absorptivity value of TOL at 221.5 and 234.0 nm respectively. CTAM is the concentration of TAM and CTOL is the concentration of the TOL.

Application of the proposed method for the determination of TAM and TOL in its pharmaceutical formulation Twenty capsules were weighed and net content was calculated. Capsules powder equivalent to 25 mg of TOL was transferred to 100.0 ml volumetric flask and 10 mg standard Tamsulosin was added externally (to increase the intensity of the peak) volume made-up to the mark with Methanol. The solution was then filtered through a Whatmann filter paper (No. 41). From the filtrate, 4.0 ml solution was transferred to a 50.0 ml volumetric flask and diluted to the mark with same solvent to obtain 10 µg/ml of TAM and 20 µg/ml of TOL.

For Method-A, the concentration of both TAM and TOL were determined by measuring the areas under the curve in the range of 230.5-220.5 nm (for TAM) and 289.0-279.0 nm (for TOL) and values were substituted in the respective formulae to obtain concentrations.

In Method-B, the concentration of both OF and ST were determined by measuring the absorbance of the sample at 221.5 nm and 234.0 nm in first order spectrum mode. The results of the tablet analysis were calculated by solving simultaneous equation.

Validation

The methods were validated with respect to linearity, accuracy, precision and selectivity.

Accuracy To ascertain the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% & 120%). Percent recovery for TAM and TOL, by both the methods, was found in the range of 98.30 % to 100.13 %,

Linearity: The linearity of measurement was evaluated by analyzing different concentrations of the standard solution of TAM and TOL. For both the methods, the Beer-Lambert's concentration range was found to be from 5-25µg/ml and 10-50µg/ml for TAM and TOL, respectively.

Precision: The reproducibility of the proposed method was determined by performing tablet assay at different time intervals (morning, afternoon and evening) on same day (Intraday assay precision) and on three different days (Interday precision). Result of intraday and interday precision is expressed in % RSD. Percent RSD for Intraday assay precision was found to be 0.3041 (for TAM) and 0.2916 (for TOL) in area under the curve method; 0.3648 (for TAM) and 0.6933 (for TOL) in first order derivative spectroscopy method. Interday assay precision was found to be 0.4380 (for TAM) and 0.4212 (for TOL) in area under the curve method; 0.2906 (for TAM) and 0.5343 (for TOL) in first order derivative spectroscopy method.

RESULTS AND DISCUSSION

The methods discussed in the present work provide a convenient and accurate way for simultaneous estimation of TAM and TOL in its pharmaceutical dosage form. In area under the curve method, the areas under the curve in the range of 230.5-220.5 nm (for TAM) and 289.0-279.0 nm (for TOL) were selected for the analysis. In first order derivative spectroscopy method, 221.5 nm (for TAM) and 234.0 nm (for TOL) were selected for the analysis In both the methods linearity for detector response was observed in the concentration range of 5-25 µg/ml (for TAM) and 10-50 µg/ml (for TOL). 'X' values (Method-A) and absorptivity values (Method-B) were calculated for both the drugs at selected wavelengths and substituted in equations for determining concentration of TAM and TOL

in its capsule dosage form. Percent label claim for TAM and TOL in capsule analysis, by area under the curve method was found to be 99.24 ±0.5880 and 99.17 ±0.3754, respectively. Similarly percent label claim for TAM and TOL in capsule analysis, by first order derivative spectroscopy was found to be 98.66 ±0.5969 and 99.44 ±0.3696 respectively. Standard deviation and coefficient of variance for six determinations of tablet sample, by both the methods, was found to be less than ± 2.0 indicating the precision of both the methods. Accuracy of proposed methods was ascertained by recovery studies and the results are expressed as % recovery. Percent recovery for TAM and TOL, by both the methods, was found in the range of 98.30 % to 100.13 %, values of standard deviation and coefficient of variation were satisfactorily low indicating the accuracy of both the methods. Based on the results obtained, it is found that the proposed methods are accurate, precise & reproducible and can be employed for routine quality control of Tamsulosin and Tolterodine in combined dose formulation.

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Table 1. Optical Characteristics of Tamsulosin and Tolterodine

	Method-A		Method-B	
	TAM	**TOL**	**TAM**	**TOL**
Working λ	230.5-220.5 nm	289.0-279.0 nm	221.5 nm	234.0 nm
Linearity range (µg/ml)	5-25	10-50	5-25	10-50
Regression value				
1. Slope	0.3537	0.0627	0.0006	-0.0012
2. Intercept	-0.0819	0.0528	-0.0001	-0.0011
3. Correlation-coefficient	0.9993	0.9988	0.9992	0.9989

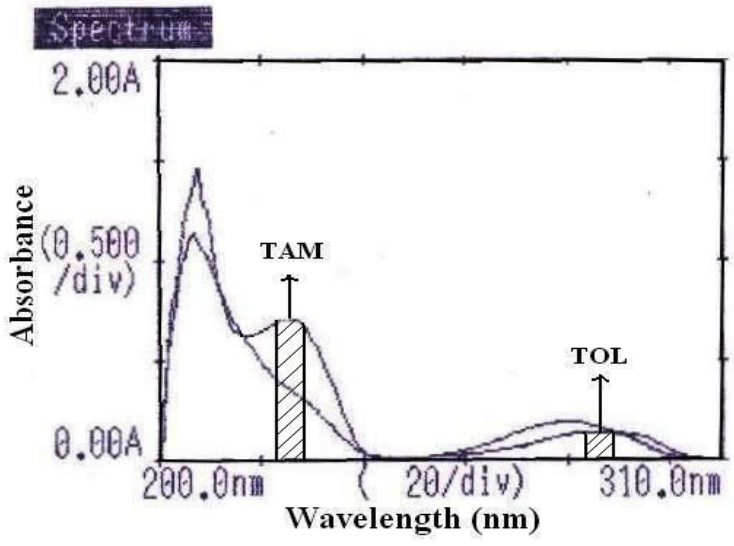

Fig.-1: Overlain Spectra of Tamsulosin (TAM) and Tolterodine (TOL) in Method- A

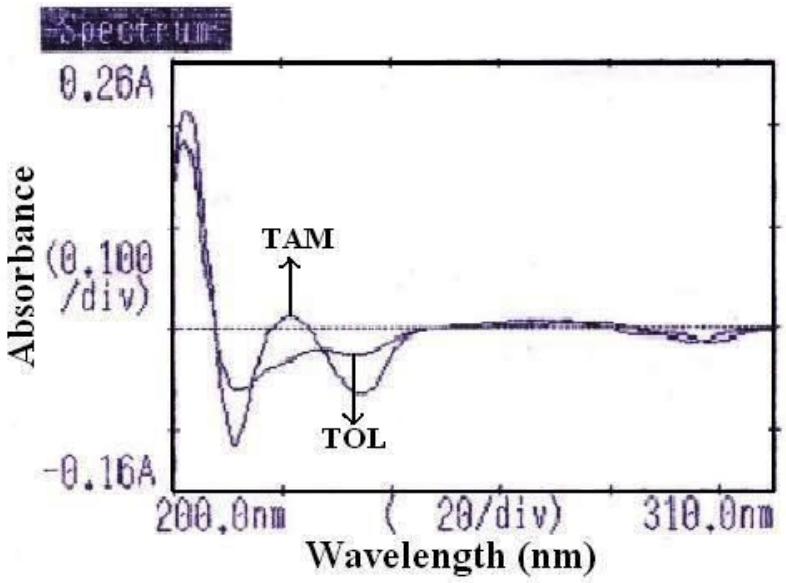

Fig.-1: Overlain Spectra of Tamsulosin (TAM) and Tolterodine (TOL) in Method- B

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