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Development and Validation of Ultraviolet-Spectrophotometric Method for the Determination of Tamsulosin

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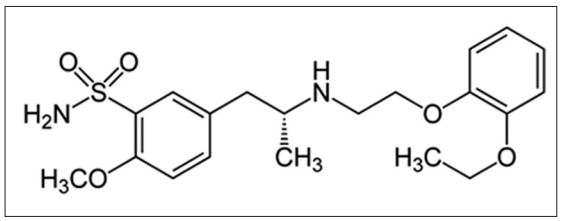
ABSTRACT

A simple, specific, and economical ultraviolet-spectrophotometric method has been developed for the determination of tamsulosin in pharmaceutical and biological fluid samples. Tamsulosin undergoes diazotization when treated with the sodium nitrite and hydrochloric acid. The excess of nitrous acid during the diazotization is removed by the addition of urea solution. The diazonium cation reacts with the coupling reagent, β-naphthol by electrophilic substitution at the o-position of the coupling agent to produce an orange azo product. This orange product shows maximum absorbance at 475 nm. The calibration curve is linear over the concentration range of 25-150 μg/ml of tamsulosin. The optical characteristics of the proposed method such as molar absorptivity, Sandell's sensitivity, slope, and intercept were 1.5574 L.mole^{-1}cm^{-1}, 0.0025 μg.cm^{-2}, 0.00394, and 0.011905 for tamsulosin, respectively. The developed method was found to be simple, specific, robust, accurate, and precise for the determination of tamsulosin.

Key words: *Tamsulosin, Sodium nitrite, Hydrochloric acid, β-naphthol and ultraviolet-spectrophotometric method.*

1. INTRODUCTION

Tamsulosin is chemically (R)-5-(2-{[2-(2-ethoxyphenoxy) ethyl] amino} propel)-2-methoxy benzene-1-sulfonamide (Scheme 1). This medication is used in men to treat the symptoms of an enlarged prostate. It is known as an alpha 1 adrenoceptor blocker, used in the symptomatic treatment of benign prostatic hyperplasia (BPH) [1] (Figure 1). Tamsulosin is used to treat men who are having problems of urinating because of BPH. It is not approved for the treatment of high blood pressure, which can provide relief in some cases within 48 h. Tamsulosin also assists the passage of kidney stones by the same mechanism of muscle relaxation via alpha antagonism. Spectrophotometric methods provide simple, rapid, sensitive, and accurate procedure for determination of drugs [2,3].



Scheme 1: Structure of tamsulosin.

Literature survey revealed that tamsulosin is estimated by high-performance liquid chromatography (LC) [4-7], mass spectroscopy (MS) [8,9], high-performance thin layer chromatography [10], and LC-electrospray ionization-MS/MS [11,12] methods in pharmaceutical dosage forms.

However, the above mentioned methods are very complex, and expensive equipment is involved. Hence,

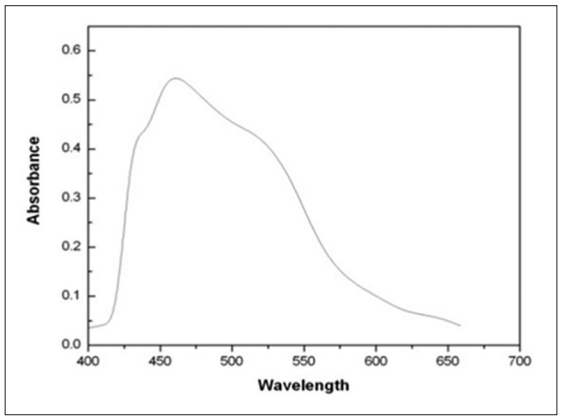


Figure 1: Absorption spectrum of diazotized tamsulosin treated with β-naphthol.

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in the present investigation a simple, cost effective, selective, accurate, and rapid spectrophotometric method has been developed for the determination of tamsulosin in bulk, in pharmaceutical formulations and in biological fluid samples.

2. EXPERIMENTAL

2.1. Instrumentation

A Shimadzu ultraviolet-visible double-beam spectrophotometer (model 2450) with 1 cm matched quartz cells was used for all the spectral measurements.

2.2. Chemicals and Reagents

All the chemicals used were of analytical grade. Double distilled water was used for all the experimental studies. 0.1 N sodium nitrite, 1% β-naphthol, 1% urea solution, 0.5 N sodium carbonate, methanol, and 0.1 N hydrochloric acid were used.

2.3. Assay Procedure

1.0 ml of tamsulosin solution (100 μg/ml) is transferred into a 10 ml volumetric flask. To this, 2.0 ml of 0.1 N hydrochloric acid and 1.0 ml of cold 0.1 N sodium nitrite solutions are added. The resultant solution is well mixed and then allowed to stand for 5 min at 0-5°C temperature for diazotization. To this solution 1 ml of 1% urea solution is added and shaken frequently for nitrogen gas to escape. Then 1.0 ml of 0.5 N sodium carbonates and 1 ml of 1% β-naphthol solution are added and the volume is made up to the mark with methanol. The absorbance of the orange color formed is measured in the wavelength range of 400-650 nm, against the reagent blank. The spectrum is given in Figure 2.

The maximum absorbance of the orange colored solution is measured at 475 nm against the reagent blank. Calibration graph is obtained by plotting absorbance values against the concentration of tamsulosin solution. The calibration curve is found to be linear over a concentration range of 25-150 μg/ml of tamsulosin (Figure 2). The amount of tamsulosin present in the sample is estimated from the calibration graph.

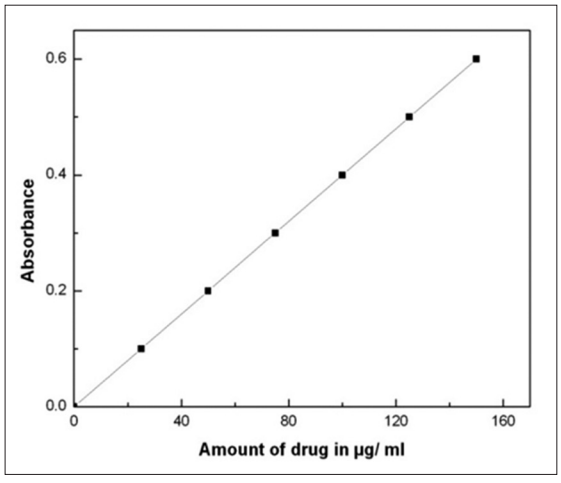

Figure 2: Calibration curve of tamsulosin.

3. RESULTS AND DISCUSSION

3.1. Effect of Concentration of Hydrochloric Acid

The stability of the colored species depends on the concentration of hydrochloric acid. The effect of hydrochloric acid on the absorbance is studied by varying the volume of hydrochloric acid (0.1 N) and measuring the absorbance at 475 nm. The data are presented in Table 1.

The data in Table 1 shows that 2.0 ml of hydrochloric acid produces maximum absorbance and hence the same concentration is maintained throughout the experimental work.

3.2. Effect of Concentration of Sodium Nitrite on the Coupling Reaction

In a series of 10 ml volumetric flasks containing 1.0 ml of (100 μg/ml) tamsulosin, 2.0 ml of 0.1 N hydrochloric acid, 1.0 ml of 1% urea solution, 1.0 ml of 0.5 N sodium carbonate solution, and 1.0 ml of 1% β-naphthol are taken, and varying amounts of sodium nitrite are added. The contents are made up to the mark and set aside for 5 min for completion of the reaction. The absorbance of the resultant solutions is measured at 475 nm and the data are presented in Table 2.

The data in Table 2 indicate that 1.0 ml of sodium nitrite is necessary for achieving maximum absorbance and hence maintained throughout the experimental studies.

3.3. Effect of Concentration of β-naphthol

In a series of 10 ml volumetric flasks containing 1.0 ml of (100 mg/ml) tamsulosin, 2.0 ml of 0.1 N hydrochloric

Table 1: Effect of concentration of hydrochloric acid solution on absorbance.

Volume of HCl (ml)	Absorbance at 475 nm
1.0	0.582
1.5	0.860
2.0	1.074
2.5	1.071

Table 2: Effect of concentration of sodium nitrite.

Volume of sodium nitrite (ml)	Absorbance at 475 nm
0.5	0.989
1.0	1.053
1.5	1.051
2.0	1.051

acid, 1.0 ml of 0.1 N sodium nitrite solution, 1.0 ml of 1% urea solution, and 1.0 ml of 0.5 N sodium carbonate solution are taken, and varying amounts of β-naphthol are added. The contents are made up to the mark and set aside for 5 min for completion of the reaction. The absorbance of the resultant solutions is measured at 475 nm and the data are presented in Table 3.

The data in Table 3 indicate that 1.0 ml of 1% β-naphthol is necessary for achieving maximum absorbance and hence maintained throughout the experimental studies.

3.4. Method Validation

3.4.1. Linearity

The method was validated as per ICH guidelines. The following validation characteristics were addressed; linearity, accuracy, precision specificity, limit of detection, limit of quantification, and robustness.

The optical characteristics such as Beer's law limits, molar absorptivity, and Sandell's sensitivity are persecuted in Table 4. The regression analysis was made for the slope (a), intercept (b), correlation coefficient (r), and the results are summarized in Table 4.

The low values of % relative standard deviation indicate that the developed method is precise and accurate for the determination of tamsulosin.

Table 3: Effect of concentration of β-naphthol.

Volume of beta-naphthol (ml)	Absorbance at 475 nm
0.5	0.723
1.0	1.025
1.5	1.022
2.0	1.020

Table 4: Optical characteristics of proposed methods.

Parameters	Value
λ_{max} (nm)	475
Beer's law limit (μg ml^{-1})	25-150
Molar absorptivity (L.$mole^{-1}$ cm^{-1})	1.5576
Sandell's sensitivity (μg.cm^{-2}/0.001 A.U)	0.0025
Slope (b)	0.00394
Intercept (a)	0.011905
Regressing (or) correlation coefficient (r)	0.994033
%RSD	0.25
LOD	0.76087
LOQ	2.5336

LOD: Limit of detection, LOQ: Limit of quantification, RSD: Relative standard deviation

3.4.2. Robustness and ruggedness

In the study of robustness, some parameters like concentrations of the drug and reagents and shaking time were interchanged. Even after that the results were unaffected by small deliberate and shaking time.

The method of ruggedness was expressed as the percentage of relative standard deviation for the proposed method developed by two analysts in two different instruments in two different days. The results proved that there is no statistical difference between the above said two analysts and instruments in different days (Table 5) which conclude the developed analytical method was robust and rugged.

3.4.3. Effect of interferences

To study the selectivity of the proposed analytical method, the effect of the excipients viz. glucose, sucrose, lactose, dextrose, talc, and starch which frequently come with the drug tamsulosin in its dosage forms was studied. The results showed that there is no interference from the degradation which indicates a high selectivity of the proposed method in determining tamsulosin in its dosage form. These results are recorded in Table 6.

Table 5: Evaluation of interday and intraday accuracy.

Taken (μg/ml)	Found	Recover (%)	±SD	%RSD
Interday				
10	9.99	99.98	0.998	0.0521
11	10.98	99.88	0.0099	0.0912
12	11.98	99.83	0.0055	0.0402
13	12.95	99.76	0.0053	0.0328
Intraday				
10	9.987	99.87	0.9987	0.0530
11	10.975	99.77	0.0095	0.0902
12	11.958	99.65	0.0045	0.0464
13	12.975	99.80	0.0052	0.0428

RSD: Relative standard deviation, SD: Standard deviation

Table 6: Determination of tamsulosin in presence of excipients.

Excipients	Amount taken (mg/ml)	*Found (mg/ml)	Recovery (%)	±SD
Glucose	5	4.98	99.6	0.01
Sucrose	10	9.98	99.8	0.01
Lactose	15	14.96	99.7	0.01
Dextrose	20	19.84	99.2	0.66
Talc	25	24.97	99.8	0.02
Starch	30	34.98	99.7	0.02

SD: Standard deviation

Table 7: Assay of tamsulosin in pharmaceutical formulations.

Tablets	Labeled amount (mg/ml)	Amount found (mg/ml)	Recovery (%)	±SD
1	100	99.8	99.83	0.057
2	200	199.7	99.90	0.100
3	300	299.5	99.83	0.529

SD: Standard deviation

Table 8: Method accuracy from recovery assay.

Sample	Added (mg/ml)	*Found (mg/ml)	Recovery (%)	±SD
Serum samples	0.8	0.78	98.54	0.007
	1	0.98	98.55	0.005
	1.2	1.19	99.55	0.004
	1.4	0.39	99.61	0.004
Urine samples	2	1.98	99.26	0.006
	2.2	2.19	99.81	0.001
	2.4	2.39	99.88	0.002
	2.6	2.59	99.88	0.002

SD: Standard deviation

3.4.4. Assay in pharmaceutical formulations and in serum and urine samples

The developed method is applied for the determination of tamsulosin in its pharmaceutical formulation and the results were presented in Table 7.

Blood and urine samples were collected from donors and centrifuged at 3000 rpm per min. for nearly 10 min. The resulted solutions were filtered and preserved in the absence of light at a temperature of 4°C. From these solutions, various concentrations of the drug tamsulosin were analyzed with the help of proposed analytical method and these results were recorded in Table 8. These results indicate that the proposed method can be successfully applied to recover tamsulosin in biological samples, viz. urine and serum.

4. CONCLUSION

The proposed method is found to be simple, precise, accurate, time saving, reproducible, and can be conveniently adopted for routine analysis of estimation of tamsulosin in bulk drug samples and pharmaceutical formulations.

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***Bibliographical Sketch**

Prof. P. Venkateswarlu has more than 30 years of teaching and research experience in the Department of Chemistry, S. V. University, Tirupati. He guided 15 PhD students. He has more than 115 publications in internationally reputed journals which are indexed in Science Citation Index. He is the reviewer for many Elsevier journals.