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A SIMPLE VISIBLE SPECTROPHOTMETRIC DETERMINATION OF TAMSULOSIN HYDROCHLORIDE USING OXIDATIVE COUPLING REACTION

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ABSTRACT

A direct, simple and sensitive visible spectrophotometric method is described for the assay of Tamsulosin hydrochloride in pure and solid dosage forms. The method involves oxidative coupling of tamsulosin with brucine in presence of sodium meta periodate and purple red colored species is formed and exhibits absorption maxima at 520nm. The proposed method is applied to commercial available tablets and the results are statistically compared with those obtained by the UV reference method and validated by recovery studies. The results are found satisfactory and reproducible. The method is applied successfully for the estimation of the tamsulosin hydrochloride in the presence of other ingredients that are usually present in dosage forms. The method offers the advantages of rapidity, simplicity and sensitivity and normal cost and can be easily applied to resource-poor settings without the need for expensive instrumentation and reagents.

INTRODUCTION

Tamsulosin hydrochloride (TAM) (Fig.1), 5-[(2R)-2-[2-(2-ethoxyphenoxy) ethylamino] propyl]-2-methoxybenzenesulfonamide hydrochloride is a new type of highly selective α_{1A} adrenergic receptor antagonist for treatment of benign prostatic hyperplasia (BPH) [1]. The drug exits in two enantiomeric forms, but only R-isomer is the pharmaceutically active component. It works by blocking α-receptors that are found in the muscle of the prostate gland, which causes the muscle in the prostate to relax. This allows urine to flow freely post the prostate and relieves the urinary symptoms. The drug is extensively metabolized by cytochrome P450 enzymes in the liver and the most frequently prescribed medication for the treatment of lower urinary tract symptoms associated with BPH. Compared to other α-antagonists, TAM has greater specificity for α-1-receptors in the human prostate and does not affect receptors on blood vessels. The drug is official in European Pharmacopoeia [2].

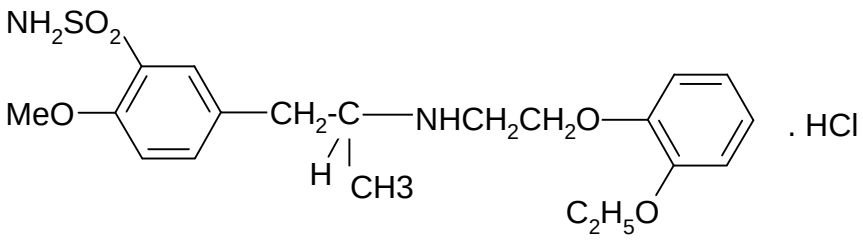


Fig.1: Chemical structure of TAM

Some analytical methods which include HPLC [3-11], LC-MS-MS [12-18], HPTLC [19-21] Radioreceptor assay [22-23], Non aqueous potentiometric[24], voltametry[25], Capillary electrophoresis[26], spectroflorimetric[27] , UV[28-29] and visible spectrophotometric [30-31] have been reported in the literature for the determination of TAM in biological fluids (more) and pharmaceutical preparations(less). The main purpose of the present study was to establish relatively simple, sensitive, validated and inexpensive extraction free visible spectrophotometric method for the determination of TAM in pure form and in pharmaceutical preparations, since most of the previous methods involve critical reaction conditions or tedious sample preparations and less specificity. So the authors have made some attempts in this direction and succeeded in developing the methods based on the reaction between the drug and BCN-IO_4^- reagent [32]. The

proposed method for TAM determination has many advantages over other analytical methods due to its rapidity, normal cost and environmental safety. Unlike HPLC, HPTLC procedures, the instrument is simple and is not costly. Economically, all the analytical reagents are inexpensive and available in any analytical laboratory. The method can be extended for the routine quality control analysis of pharmaceutical products containing TAM.

MATERIALS & METHODS (EXPERIMENTAL)

Apparatus and chemicals: A Shimadzu UV-Visible spectrophotometer 1601 with10mm matched quartz cells was used for all spectral measurements. All the chemicals used were of analytical grade. Pure TAM drug was obtained as a gift sample from M/s Tychy Industries, Hyderabad (AP) .Tablets was purchased from local market.

Aqueous solution of brucine (Loba, 0.2%, $506.7x10^{-3}$M prepared by dissolving 200mg of brucine initially in minimum amount of 0.16M sulphuric acid and then made up to 100ml with distilled water), sodium metaperiodate (BDH, 0.2%, $9.35x10^{-3}$M prepared by dissolving 200mg of sodium metaperiodate in 100ml distilled water and standardized iodometrically) and sulphuric acid (Qualigens,1.2M prepared by diluting 126ml of conc. H_2SO_4 to 100ml of distilled water initially, followed by diluting to 1000ml with distilled water) were prepared.

Preparation of Standard stock solution: The standard stock solution (1mg/ml) of TAM was prepared by dissolving 100mg of TAM in 100 ml distilled water. The working standard solutions of TAM were obtained by appropriately diluting the standard stock solution with the same solvent.

Preparation of Sample solution: About 20 tablets or capsules were weighed to get the average tablet or capsule weight and pulverized. The powder equivalent to 100mg of TAM was weighed, dispersed in 25ml of Isopropyl alcohol, sonicated for 15 minutes and filtered through Whatman filter paper No 41.The filtrate was evaporated to dryness and the residue was dissolved as under standard solution preparation.

Determination of wavelength maximum (λ_{max}):

The 3.0 ml of working standard solution of TAM (200µg/ml) was taken in 25ml calibrated tube. To this, 3.0ml brucine, 1.5ml of $NaIO_4$ solution and 2.0ml of sulphuric acid were added successively and the volume was brought up to 10ml with distilled water and kept in boiling

water bath for 15min. for complete color development .The solution was cooled to room temperature and the volume was made up to the mark with distilled water. In order to investigate the wavelength maximum, the above colored solution was scanned in the range of 400-760 nm UV-Visible spectrophotometers against a reagent blank. From the absorption spectra (Fig.2) it was concluded that 520 nm is the most appropriate wavelength for analyzing TAM with suitable sensitivity.

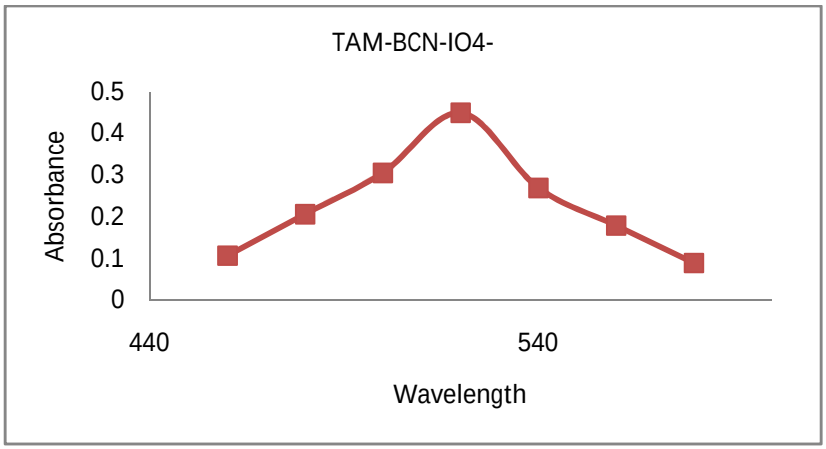


Fig.2: Absorption spectra of TAM-BCN-IO_4^-

Preparation of calibration curve: Aliquots of the standard TAM solution [1.0-3.0ml, 200µg/ml] were placed in a series of 25ml standard flask. Then 3.0ml brucine, 1.5ml of $NaIO_4$ solution and 2.0ml of sulphuric acid were added successively and the volume was brought up to 10ml with distilled water and kept in boiling water bath for 15min. for complete color development. The solution was cooled to room temperature and the volume was made up to the mark with distilled water. The absorbance was measured at 520nm against a reagent blank within the stability period (5minutes to 30min). The calibration graph was constructed by plotting the drug concentration versus absorbance. The amount of drug was computed from its calibration graph (Fig.3).

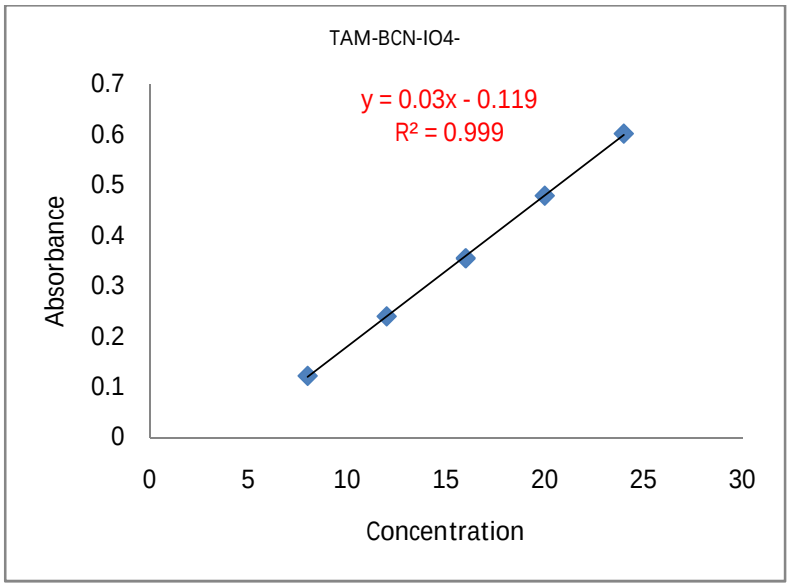


Fig.3: Calibration graph

6. RESULTS AND DISCUSSION

In the present investigation, the presence of aliphatic secondary amino group of TAM permits the development of visible spectrophotometric method for its determination through the oxidative coupling reaction with BCN-IO_4^- reagent.

Optimum operating conditions used in the procedure were established by adopting variation of one variable at a time (OVAT) method. The effect of various parameters such as time, volume and strength of reagents, the order of addition of reagents and solvent for final dilution of the colored species were studied. The other oxidants such as Fe (III), Cr (IV), IO_3^-, and $S_2O_8^{-2}$ were tried in place of $NaIO_4$ and found to be inferior. Distilled water was found to be best solvent for final dilution. Other water miscible solvents like methanol, ethanol, propan-2-ol and acetonitrile have no additional advantage in increasing the intensity of the color in proposed method. The optical characteristics such as Beer's law limit, Sandell's sensitivity, molar absorptivity, percent relative standard deviation, (calculated from the six measurements containing $3/4^{th}$ of the amount of the upper Beer's law limits), Regression characteristics like standard deviation of slope (S_b), standard deviation of intercept (S_a), standard error of estimation (S_e) and % range of error (0.05 and 0.01 confidence limits) were calculated and the results are summarized in Table-1.

Commercial formulations containing TAM were successfully analyzed by the proposed method. The values obtained by the proposed and reference methods for formulations were compared statistically by the t-and F-test and found not to differ significantly. As an additional demonstration of accuracy, recovery experiments were performed by adding a fixed amount of the drug to the pre analyzed formulations at three different concentration levels. These results are summarized in Table-2.

TABLE-1: OPTICAL CHARACTERISTICS, PRECISION AND ACCURACY OF PROPOSED METHOD

Parameter	**Values**
λ_{max}	520
Sandell's sensitivity ($\mu g/cm^2$/0.001 abs. unit	0.001797753
Molar absorptivity (Litre/mole/cm)	247520.125
Correlation coefficient	0.999
Regression equation (Y)*	
Intercept (a)	-0.119
Slope(b)	0.03
%RSD	1.163
% Range of errors(95% Confidence limits)	
0.05 significance level	1.22
0.01 significance level	1.915

*Y = a + b x, where Y is the absorbance and x is the concentration of TAM in µg/ml

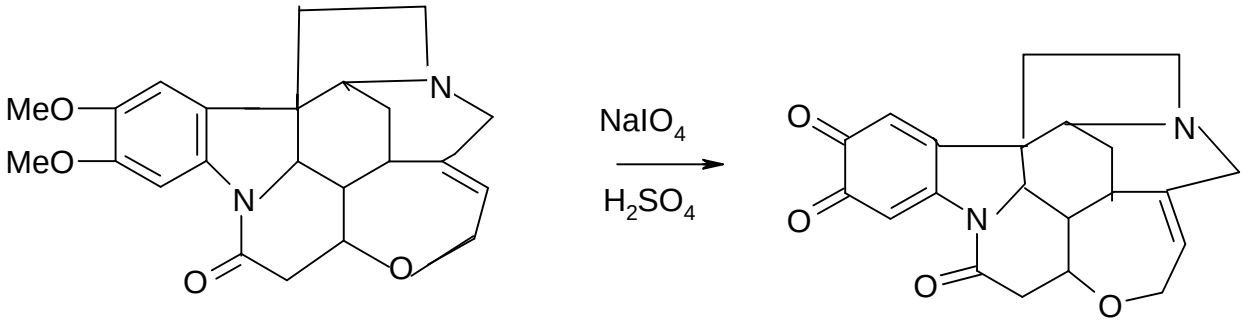
TABLE-2: ANALYSIS OF TAMSULOSIN HYDROCHLORIDE IN PHARMACEUTICAL FORMULATIONS BY PROPOSED AND REFERENCE METHODS.

Method	*Formulations	Labeled Amount (mg)	Found by Proposed Methods			Found by Reference Method ± SD	#% Recovery by Proposed Method ± SD
			**Amount found ± SD	t	F		
BCN-$IO4^-$	Batch-1	0.2	0.198 ± 0.0005	0.245	1.98	0.199 ± 0.0007	99.43 ± 0.24
	Batch-2	0.4	0.397 ± 0.003	0.289	2.07	0.397± 0.0044	99.22 ± 0.75

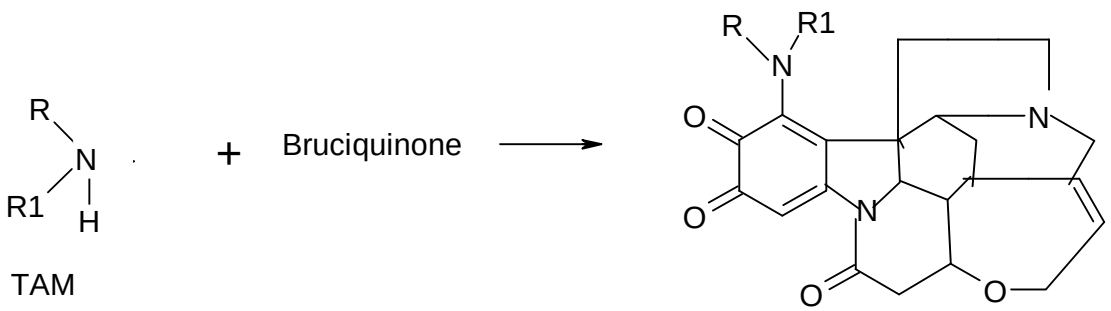
* Different batches from two different companies **Average ± Standard deviation of six determinations, the t- and F-values refer to comparison of the proposed method with reference method (UV). Theoretical values at 95% confidence limits t =2.57 and F = 5.05.

Recovery of 10mg added to the pre-analyzed sample (average of three determinations). Reference method (reported UV method) using distilled water (λ_{max}=279nm).

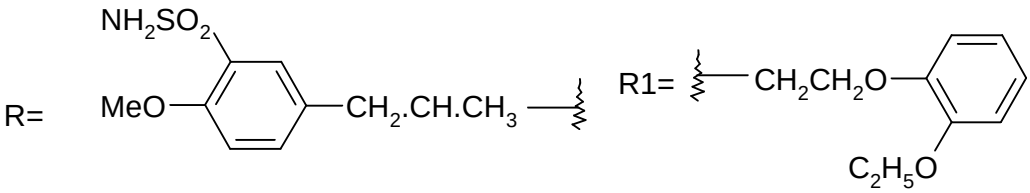
Chemistry of colored species: The dimethoxy benzene nucleus of brucine is attacked by IO_4^- with the formation of o-quinone (bruciquinone) which in turn undergo nucleophillic attack on the most electron-rich position of the coupler (aliphatic secondary amino group of TAM) to give 1-monosubstituted bruciquinone derivative(purple red colored species).



Brucine Bruciquinone



1-Mono substituted bruciquinone derv.
(Colored species)



CONCLUSION

The reagents utilized in the proposed method are cheap, readily available and the procedure does not involve any critical reaction conditions or tedious sample preparation. The proposed colorimetric methods possesses reasonable precision, accuracy, and are simple, sensitive and can be used as alternative methods to the reported ones for the routine determination of TAM depending on the need and situation.

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