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Spectrophotometric Determination of Telmisartan Sulphate in Pharmaceutical Dosage Forms

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ABSTRACT

Two simple, sensitive and economical spectrophotometric methods have been developed for the estimation of telmisartan in pharmaceutical dosage forms. The method was based on the formation of chloroform extractable complex of telmisartan with wool fast blue. The absorbance of the extractable ion pair complex is measured at the wavelength of maximum absorbance 585 nm against the reagent blank. Method B was based on the charge transfer reactions of telmisartan as *n*-electron donor with acceptor, 2,5-dichloro-3,6-dihydroxy-1,4-benzoquinone. The absorbance of the highly intensive coloured solution was measured at 460 nm against reagent blank treated similarly. Statistical analysis proves that the proposed methods are reproducible and selective for the estimation of telmisartan in bulk drug and in its tablet dosage form

INTRODUCTION

Telmisartan is described chemically as 4[(1,4-dimethyl-2-propyl(2,6-bi-1H-benzimidazol]-1-yl)methyl],1-biphenyl]-2-carboxylic acid. Telmisartan is a recently introduced angiotensin II receptor antagonist, for the treatment of essential hypertension. It is useful in the treatment of mild to moderate hypertension, well tolerated, with a lower incidence of cough than ACE inhibitors. The present study describes simple, sensitive, accurate, rapid and economical spectrophotometric methods for the estimation of telmisartan in bulk & its tablet dosage forms. Literature survey reveals that, spectrophotometric[1,2] methods, Liquid Chromatography-Tandem Mass Spectrometry[3] and RP-HPLC[4] method, have been reported for the estimation of telmisartan in pharmaceutical formulations. Various analytical methods were reported in literature for the determination of telmisartan and in combinations with other drugs, which includes spectrophotometric method [5-7]densitometric method [8], HPTLC[9], TLC-densitometry method[10] and LC method[11].

Spectrophotometry is the technique of choice even today in the laboratories of research, hospitals and pharmaceutical industries due to its low cost and inherent simplicity. This paper describes two rapid, simple, sensitive and economical spectrophotometeric methods for the determination of telmisartan in commercial dosage forms. Method A is based on the formation of chloroform extractable complex of telmisartan with wool fast blue. Method B utilizes the charge transfer reactions of telmisartan as *n*-electron donor with acceptor, 2,5-dichloro-3,6-dihydroxy-1,4-benzoquinone. The molecular interactions between electron donors and electron acceptors are generally associated with the formation of intensely colored charge-transfer complexes, which absorb radiation in the visible region. Hence the author has made an attempt to develop two simple and sensitive spectrophotometric methods for the estimation of telmisartan in bulk drugs and in pharmaceutical formulations.

MATERIALS AND METHODS

All absorbance measurements were made on a Spectronic 1001 plus spectrophotometer (Milton Roy Company, USA) with 1 cm matched quartz cells. All the solutions were freshly prepared. All solvents and other chemicals used through this study were of analytical grade. Wool fat blue solution (0.2%) was prepared in distilled water, freshly prepared. 2,3-dichloro 5,6-dicyano-p-benzoquinone(DDQ; Merck, Schuchardt, Munich, Germany) solution(0.1%) was prepared in methanol and it was prepared afresh daily. Buffer solutions of required pH were prepared by mixing appropriate volumes of glycine, sodium chloride and 0.1M Hydrochloric acid.

Preparation of standard solution

A standard stock solution containing 1 mg/ml was prepared by dissolving 50 mg of telmisartan in 50 ml of distilled water for method A and B. From this, a working standard solution containing 100 µg/ml was prepared for both method A and B.

Assay procedures

Method A

Aliquots of standard drug solution of telmisartan 0.5–2.5 ml were taken and transferred into a series of 125 ml of separating funnels. To each funnel 0.5 ml of 0.2% wool fast blue and 1.0 ml buffer solution was added. Reaction mixture was shaken gently for 5 min. Then 5 ml of chloroform was added to each of them. The contents were shaken thoroughly for 5 min and allowed to stand, so as to separate the aqueous and chloroform layer. Colored chloroform layer was separated out and absorbance was measured at 585 nm against reagent blank. Calibration curve was prepared from absorbance values so obtained.

Method B

Various aliquots of standard solution of telmisartan ranging from 0.5-2.5 ml were transferred into10 ml calibrated flasks. To each flask 1.0 ml of the acceptor solution (DDQ) was added, and the reaction was allowed to proceed at room temperature (25±5°C). The reaction was achieved instantaneously. The solutions were diluted to volume with distilled water. The absorbance of the resulting solutions was measured at the wavelengths of maximum absorption 460 nm against reagent blanks treated similarly. The amount of drug present in sample is read from the calibration graph.

Pharmaceutical preparations

Twenty tablets containing telmisartan were weighed and finely powdered. An accurately weighed portion of the powder equivalent to 50 mg of telmisartan was dissolved in a 25ml of methanol and mixed for about 5 minutes and then filtered. Then the volume was diluted to 50 ml with methanol and analyzed as given under the assay procedures for bulk samples. The results are represented in Table No.2.

Recovery Studies

To ensure the accuracy and reproducibility of the results obtained, known amounts of pure drug was added to the previously analyzed formulated samples and these samples were reanalyzed by the proposed methods and also performed recovery experiments. The percentage recoveries thus obtained were given in Table No.2.

RESULTS AND DISCUSSION

Telmisartan forms ion-pair complexes in acidic buffer with wool fast blue, in method A and the complex was quantitatively extracted into chloroform. The absorption spectra of the ion-pair complex extracted into chloroform are shown in Fig.1. The ion-pair complex with wool fast blue absorbed maximum at 585 nm. In method B telmisartan forms charge transfer complex with acceptor, 2,5-dichloro-3,6-dihydroxy-1,4-benzoquinone. The absorption spectra of the charge transfer complex are shown in Fig. 2. The colorless reagent blanks under similar conditions showed no absorption. The optimum conditions were established by varying one parameter at a time and keeping the others fixed and observing the effect on absorbance of chromogen for method A and method B**.** Statistical analysis was carried out and the results were found to be satisfactory. Recovery studies were close to 100 % that indicates good accuracy of the methods. The optical characteristics such as absorption maxima, Beer´s law limits, molar absorptivity and Sandell´s sensitivity are presented in Table No.1. The regression analysis using method of least squares was made for the slope (b), intercept (a) and correlation (r) obtained from different concentrations and results are summarized. The high molar absorptivities of the resulting colored complexes indicate the high sensitivity of the methods. The percent relative standard deviation, standard deviation and student's 't' test values calculated from the five measurements of telmisartan are presented in Table No.3. Relative standard deviation values and

Table No 1: Optical characteristics of proposed method.

Statistical parameters	Method A	Method B
λ_{max} nm	585	460
Beer's limits, mcg/ml	50-250	50-250
Sandell's , sensitivity, ($\mu g\ cm^{-2}$)	0.167	0.273
Molar absorptivity, ($L\ mol^{-1}\ cm^{-1}$)	$1.6x10^3$	$2.7x10^3$
Regression equation, Y*		
Correlation coefficient, ®	0.999	0.999
Intercept (a)	0.005	0.003
Slope (b)	0.023	0.007

*Y = a+bX, where Y is the absorbance and X concentration in µg / ml
a= Intercept
b= Slope

Table No. 2: Assay and recovery of telmisartan in tablet formulations

Tablet formulation	Labeled amount (mg/tab)	*Amount found by proposed method		% Recovery by proposed method	
		Method A	Method B	Method A	Method B
Tablet 1	40	40.16	39.99	99.97	100.03
Tablet 2	40	39.96	40.02	100.2	100.5
Tablet 3	40	40.034	40.15	100.8	99.98

*Average of five determination based on label claim

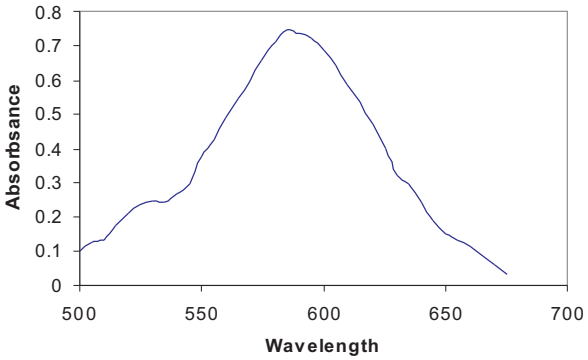

Fig. 1: Absorption spectrum of telmisartan with wool fast blue at 585 nm (Method A)

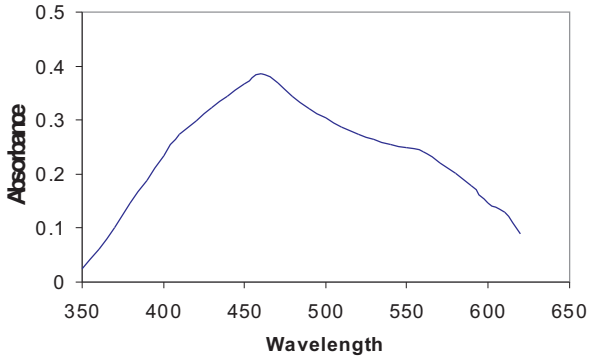

Fig. 2: Absorption spectrum of telmisartan with DDQ at 460 nm (Method B)

Table No. 3: Results of statistical analysis of the proposed methods

Tablet formulation	*Standard deviation		% Relative standard deviation*		*t value	
	Method A	Method B	Method A	Method B	Method A	Method B
Tablet 1	0.2833	0.1879	0.7079	0.4698	0.1263	0.0952
Tablet 2	0.1086	0.2698	0.2717	0.6741	0.8237	0.1657
Tablet 3	0.1310	0.5662	0.3272	1.410	0.5811	0.5924

*Average of five determination based on label claim

standard deviation were low that indicates the reproducibility of the proposed methods. In the student's 't' tests, no significant differences were found between the calculated and theoretical values of both the proposed methods at 95% confidence level. This indicated similar precision and accuracy in the analysis of telmisartan in its tablets.

CONCLUSION

The proposed methods make use of simple reagents, which an ordinary analytical laboratory can afford. The proposed methods canbe used for the routine quality control analysis of telmisartan in industry, research laboratories and hospitals. The commonly used additives such as starch, lactose, titanium dioxide, and magnesium stearate do not interfere with the assay procedures.

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