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SIMULTANEOUS ESTIMATION OF TELMISARTAN AND METOPROLOL SUCCINATE IN PHARMACEUTICAL DOSAGE FORM BY SIMULTANEOUS EQUATION METHOD

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ABSTRACT

A Versatile, accurate, precise and economic method for simultaneous determination of Telmisartan and Metoprolol succinate in fixed dose combination products was developed. The absorbance values at 295.0 nm and 222.0 nm were used for the estimation of Telmisartan and Metoprolol succinate, respectively without mutual interference. This method obeyed Beer's law in the concentration range of 3–15 µg /ml for Telmisartan and 5-45 µg /ml for Metoprolol succinate. The results of analysis have been validated statistically for linearity, accuracy and precision, LOD and LOQ of the proposed method.

INTRODUCTION

Metoprolol is official in British pharmacopoeia^[1]. It is chemically (\pm)1-(isopropylamino)-3-[p-(2-methoxyethyl) phenoxy]-2-propanol succinate (2:1) (salt). It is used in treatment of Hypertensive diseases, It's Acting on sympathetic system (β blockers). Telmisartan is official in British pharmacopoeia^[2]. It is chemically 4'-[(1,4'-dimethyl-2'-propyl [2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic which is Angiotensin (Specific AT1) receptor blocker. A formulation containing 50mg of METO and 40mg of TELM is available in market. A survey of literature revealed that few chromatographic and Spectrophotometric methods are reported for determination of METO and TELM individually. However there is no method reported so far its simultaneous determination of METO and TELM from combine dosage form by UV Spectrophotometry. The present work describes a validated, simple, precise and accurate spectrophotometric method for simultaneous estimation of METO and TELM from combined capsule dosage form.

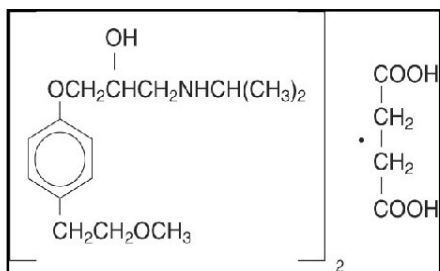


Figure-1 Metoprolol

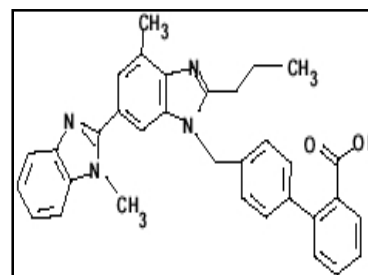


Figure-2 Telmisartan

MATERIALS AND METHODS

Apparatus

A shimadzu model 1700 (Japan) double beam UV-Visible spectrophotometer with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. A Reptech electronic weighing analytical balance based on EMFC technology was used in the study.

Chemicals and Reagents

Reference Standards of Telmisartan and Metoprolol succinate were obtained as gift samples from the Torrent Pharmaceutical. Ltd. The drug sample telsar beta manufactured by unichem labs were procured from market. All other reagents were of analytical grade for Spectrophotometric method.

Preparation of standard stock solutions

An accurately weighed quantity of METO (100 mg) and TELM (100 mg) were transferred to a separate 100 ml volumetric flask and dissolved and diluted to the mark with Metanol to obtain standard solution having concentration of METO (1000 µg/ml) and TELM (1000 µg/ml).

CALIBRATION CURVE

A calibration curve was plotted over a concentration range of 5-45 µg/ml Metoprolol succinate, 3-15µg/ml Telmisartan. Accurately measured standard stock solution of Metoprolol succinate (3, 6,9,12, & 15 mL) and standard stock solution of Telmisartan (5, 15, 25,35 & 45 mL) were transferred to a separate series of 100 mL of volumetric flasks and diluted to the mark with Distilled Water. The absorbance of each solution was measured at the wavelengths 295.0 nm and 222.0nm. Calibration curves were constructed for Metoprolol succinate and Telmisartan by plotting absorbance versus concentrations at both wavelengths. Each reading was average of five determinations.

SELECTION OF ANALYTICAL WAVELENGTH

For selection of analytical wavelength for the simultaneous estimation. The stock solutions of METO and TELM were separately diluted in Distilled Water to get a concentration of 12 µg/ml of TELMI and 15 µg/ml of METO respectively and scanned in the wavelength range of 200 -400 nm. From the overlay spectra of both drugs, wavelengths 295.0 nm (λ max of TELM) and 222.0 nm(λ max of METO) were selected.

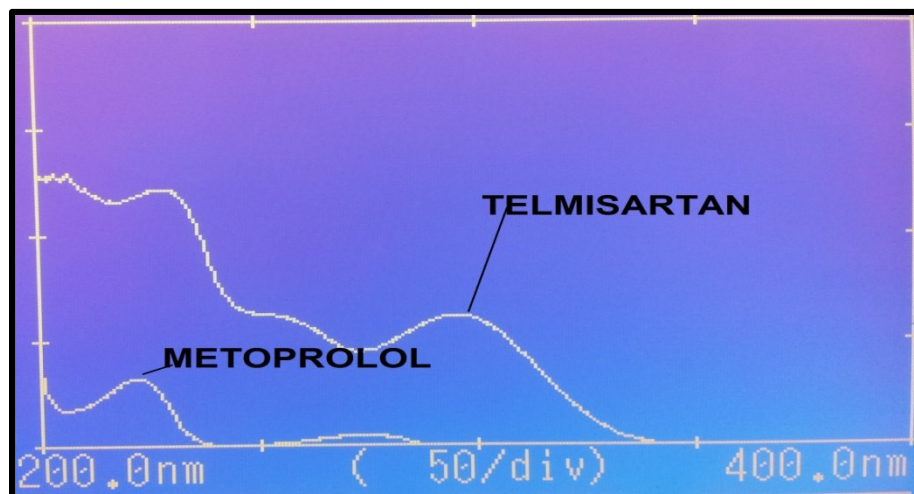


Figure-3 Overlain UV spectra of Metoprolol succinate and Telmisartan

Preparation of sample solution

Twenty Tablet were accurately weighed and average weight per Tablet was calculated. Powder equivalent to 50mg METO and 40mg TELM was accurately weighed and transferred to a 100ml volumetric flask containing methanol. The flask was shaken, and the volume was diluted to the mark with methanol. The above solution was filtered. The aliquot 20ml was transferred to 100ml volumetric flask and volume adjusted to the mark with Distilled Water. Again the aliquot 10ml was transferred to 100 ml volumetric flask and volume adjusted to the mark with Distilled Water. Take the absorbance at wavelength 295.0 nm (λ max of TELM) and 222.0 nm(λ max of METO) of final concentration of Sample solution.

Method (Simultaneous Equation Method)

The Simultaneous Equation Method of analysis based on the absorption of the drugs Telmisartan and Metoprolol succinate at their λ_{max} . Two wavelength selected for the development of Simultaneous Equation are 295nm (λ_1) and 222nm (λ_2). absorptivities of both the drugs at both the wavelengths were determined using distilled water .The equations obtained for the estimation of concentration were,

$$C_x = \frac{A_2 a_{y1} - A_1 a_{y2}}{a_{x2} a_{y1} - a_{x1} a_{y2}}$$

$$C_y = \frac{A_1 a_{x2} - A_2 a_{x1}}{a_{x2} a_{y1} - a_{x1} a_{y2}}$$

Where A1 and A2 are absorbance of Sample solution at 295 and 222 nm respectively.

a_{x1} = Absorptivity of Telmisartan at 295 nm

a_{x2} = Absorptivity of Telmisartan at 222 nm

A_{y1} = Absorptivity of Metoprolol at 295 nm

A_{y2} = Absorptivity of Metoprolol at 222 nm

C_x and C_y are concentration of Telmisartan and Metoprolol in sample solution.

Table-1

Simultaneous equation method				
Parameters	Telmisartan		Metoprolol succinate	
Wavelength	295	222	295	222
Beer's law limit	3-15	3-15	5-45	5-45
Regression equation	$y=0.046x+0.004$	$y = 0.091x + 0.03$	$y = 0.0004x + 0.002$	$y = 0.018x + 0.054$
Correlation coefficient (r^2)	0.9995	0.9997	0.9978	0.9993
LOD ($\mu\text{g /ml}$)	0.22	0.29	0.38	0.34
LOQ ($\mu\text{g /ml}$)	0.75	0.85	0.78	0.72

Table-2 Results of analysis of capsule formulation

Drugs	Simultaneous equation method
	%Assay \pm SD (n=6)
Telmisartan(40mg)	99.84% \pm 0.95
Metoprolol(50mg)	99.51% \pm 0.45

Table-3 Recovery study

Method	Recovery Level	% Recovery	SD	% Recovery	SD
		Telmisartan		Metoprolol	
I	80%	100.55	± 0.27	99.77	± 0.68
	100%	100.33	± 0.67	100.21	± 0.60
	120%	99.81	± 0.32	99.85	± 0.65

Validation of the Method according to ICH Guidelines

Validation of the method was done according to ICH guidelines for Simultaneous Equation method.

Linearity

The linearity of the method is its ability to elicit test results that are directly proportional to the concentration of the analyte in the samples. TELM was linear with the concentration range of 3-15 µg/ml at 295 nm. METO showed the linearity in the range of 5 – 45 µg/ml at 222 nm.

Precision(repeatability)

The repeatability of the method was confirmed by the analysis of formulation was repeated for 6 times with the same concentration.

Intermediate precision(reproducibility):

The intraday and interday precision of the proposed method was determined by analyzing the corresponding responses 3 times on the same day and on 3 different days 3 different concentrations of standard solutions of TELM and METO.

Accuracy (recovery study):

To check the accuracy of the proposed methods, recovery studies carried out at 80%, 100%, and 120% of the test concentration as per ICH Guideline. The recovery study was performed three times at each level.

Limit of detection and Limit of quantification:

The limit of detection (LOD) and the limit of quantification (LOQ) of the drug were derived by calculating the signal-to-noise ratio (S/N) using the following equations designated by International Conference on Harmonization (ICH) guidelines.

$$\text{LOD} = 3.3 \times \sigma/S$$

$$\text{LOQ} = 10 \times \sigma/S$$

Where, σ = the standard deviation of the response and S = slope of the calibration curve.

RESULT AND DISSCUSSION

TELM and METO showed well defined λ_{max} at 295.0 nm and 222.0 nm respectively. The wavelengths 295.0 and 222.0 nm were considered for development of Simultaneous Equation Method. The two drugs individually and in their mixture were found to follow Beer-Lambert's law over the concentration range of 3-15 µg/ml and 5-45 µg/mL for TELM and METO respectively.

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