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SIMULTANEOUS ESTIMATION OF TELMISARTAN AND INDAPAMIDE IN PHARMACEUTICAL DOSAGE FORM BY UV SPECTROPHOTOMETRIC METHOD

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ABSTRACT

Keywords:

Telmisartan, Indapamide,
UV Spectrophotometric,
Simultaneous equation

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A simple, precise, accurate, rapid and economical spectrophotometric method have been developed for simultaneous estimation of Telmisartan and Indapamide in pure and in combined capsule dosage form. Simultaneous equations method by using 295 nm and 239 nm as absorbance maxima (λ_{max}) for Telmisartan and Indapamide respectively. Methanol and distilled water combinedly used as Solvent. Linearity was observed in the concentration range of 2-10 $\mu\text{g/ml}$ for Telmisartan and 2-14 $\mu\text{g/ml}$ for Indapamide respectively. The method was validated statistically and recovery study was performed to confirm the accuracy of the method.

INTRODUCTION

Telmisartan (TEL) is an angiotensin receptor blocker that shows high affinity for the angiotensin II type 1 receptors, has a long duration of action, and has the longest half-life of an ARB. In addition to blocking the Renin-Angiotensin System (RAS), telmisartan acts as a selective modulator of Peroxisome proliferators - activated receptor gamma (PPAR- γ), a central regulator of insulin and glucose metabolism¹. Telmisartan molecular formula is C₃₃H₃₀N₄O₂. Mol. mass is 514.617 g/mol and IUPAC Name is 2-(4-{{4-methyl-6-(1-methyl-1H-1, 3-benzodiazol-2-yl)-2-propyl-1H-1, 3-benzodiazol-1-yl} methyl} phenyl) benzoic acid.

Indapamide (IND), chemically is a 4-chloro-N-(2-methyl-2, 3-dihydroindol-1-yl)-3-sulfamoyl-benzamide used as an antihypertensive agents and as a diuretics, which inhibits the reabsorption of sodium and calcium at the beginning of distal convoluted tubules. Nebivolol hydrochloride, chemically is a α , α' -(Iminobis (methylene)) bis (6-fluoro-3, 4-dihydro-2H-1-benzopyran-2-methanol) is an antihypertensive agent and α -adrenergic receptor blocker. It produces sympatholytic effect on heart.

Telmisartan and Indapamide both drug are official in British Pharmacopeia. A survey of literature revealed that few chromatographic and Spectrophotometric methods are reported for determination Telmisartan and Indapamide individually and with other drug combination. The present work describes simple, precise, accurate and economical spectrophotometric method have been developed for simultaneous estimation of Telmisartan and Indapamide from combined dosage form.

MATERIAL AND METHOD

Instrument

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.

Reagents and Chemicals

Reference Standards of TELMISARTAN and INDAPAMIDE were obtained as gift samples from the Cadila Pharmaceutical Ltd. The drug sample (capsules) INDITEL D manufactured by Cadila were procured from market. All other reagents were of analytical grade for Spectrophotometric method.

Procedures

Preparation of Standard Stock Solution and Calibration curve:

Standard stock solution of pure drug containing 1000 µg/ml of TELMISARTAN and 1000µg/ml of INDAPAMIDE were prepared separately in methanol and final volume was adjusted with same solvent to get 1000 µg/ml of each drug. From the above solution prepare 100µg/ml solution for both drugs using distilled water. Working standard solution of 10 µg/ml were scanned in the entire UV range 400-200nm to determine the λ max of both drug. The λ max of Telmisartan and Indapamide is 295 nm and 239 nm respectively. Five working standard solution with concentration 2,4,6,8, 10 µg/ml of Telmisartan and 2,5,8,11,14 µg/ml of Indapamide. The absorbance of resulting solution were measured at their respective λ max and plotted a calibration curve to get linearity and regression equation.

Simultaneous Equation Method

The Simultaneous Equation Method of analysis based on the absorption of the drugs Telmisartan and Indapamide at their λ max. Two wavelength selected for the development of Simultaneous Equation are 295nm (λ_1) and 239nm (λ_2). Absorptivities of both the drugs at both the wavelengths were determined. 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 A_1 and A_2 are absorbance of Sample solution at 295 and 239 nm respectively.

a_{X1} = Absorptivity of Telmisartan at 295 nm

a_{X2} = Absorptivity of Telmisartan at 239 nm

A_{Y1} = Absorptivity of Indapamide at 295 nm

A_{Y2} = Absorptivity of Indapamide at 239 nm

C_X and C_Y are concentration of Atorvastatin and Indapamide in sample solution.

Procedure for capsule formulation

Twenty capsules were accurately weighed, and contents were removed. Average weight of the content per capsule was calculated. The contents of a capsule were reduced to fine powder. A quantity of capsule powder equivalent to 40 mg of Telmisartan and 1.5 mg of Indapamide

was transferred to 100ml volumetric flask and dissolved in methanol with sonicated for 40 min, For standard addition of pure Indapamide (10 ml from 1000 μ g/ml) was taken, then filtered through Whatman filter. The Aliquot portion of filtrate was further diluted to get a final concentration of about 8 μ g/ml Telmisartan and 2.3 μ g/ml of Indapamide. For Simultaneous equation method The absorbance of sample solution was measured at 295nm and 239nm in 1cm cell against the blank. The content of Telmisartan and Indapamide in a capsule was calculated by the simultaneous equation method.

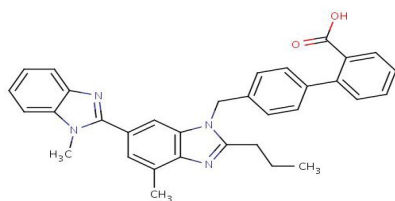


Figure-1 Telmisartan

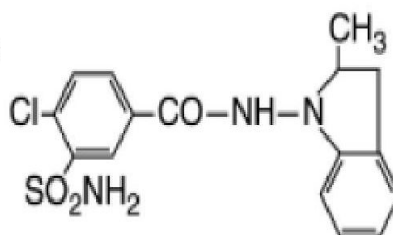


Figure-2 Indapamide

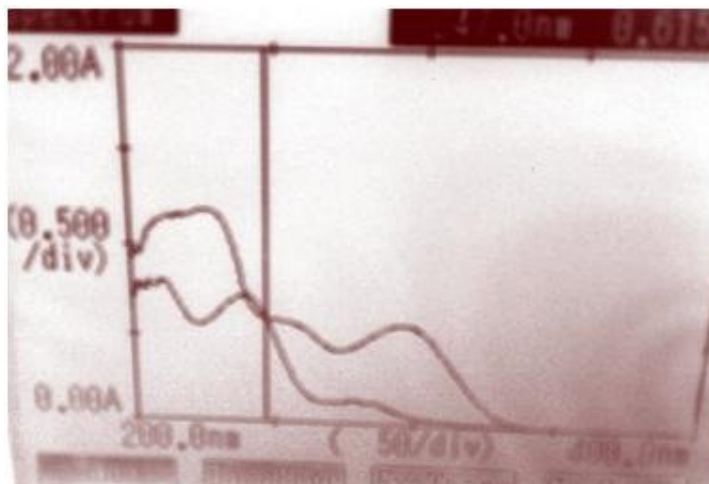
Figure-3 Overlain spectra of Telmisartan (10 μ g/ml) and Indapamide (10 μ g/ml)

Table-1 Optical Characteristic:

Simultaneous equation method				
Parameters	Telmisartan		Indapamide	
Wavelength (nm)	295	239	295	239
Beer's law limit ($\mu\text{g/ml}$)	2-10	2-10	2-14	2-14
Regression equation ($y = mx + c$)	$y = 0.0478x - 0.0113$	$y = 0.0714x - 0.020$	$y = 0.0044x + 0.0139$	$y = 0.0561x - 0.006$
Slope (b)	0.0478	0.0714	0.0044	0.0561
Intercept (a)	0.0113	0.020	0.0139	0.006
Correlation coefficient (r^2)	0.9995	0.9991	0.9998	0.9982
LOD ($\mu\text{g/ml}$)	0.076	0.090	0.323	0.117
LOQ ($\mu\text{g/ml}$)	0.233	0.274	0.976	0.355

Table-2 Results of the recovery studies

Level of recovery %	Amount of pure drug added ($\mu\text{g/ml}$)		Simultaneous equation method % recovery	
	TEL	IND	TEL	IND
80	6.4	1.8	99.44	100.0
100	8	2.3	99.25	100.04
120	9.6	2.7	100.4	100.04
% recovery			99.69	100.02
%RSD			0.6164	0.023

* RSD=Relative Standard deviation

Table-3 Results of analysis of capsule formulation

Drugs	Simultaneous Equation Method
Telmisartan(40mg)	$99.83\% \pm 1.285$
Indapamide(1.5mg)	$100.83\% \pm 0.481$

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. TEL was linear with the concentration range of 2-10 µg/ml at 295 nm. IND showed the linearity in the range of 2 – 14 µg/ml at 239 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 TEL and IND.

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.

RESULTS AND DISCUSSION

In this method, two wavelengths were used for the analysis of the drugs. 295 nm (λ_{max} of TEL) and 239 nm (λ_{max} of IND) are the wavelengths at which calibration curves were prepared for both the drugs. Linear correlation was obtained between absorbances and concentrations of TEL and IND in the concentration ranges of 2-10 µg/ml and 2-14 µg/ml for both drugs respectively. The linearity of the calibration curve was validated by the high values of correlation coefficient of regression. LOD and LOQ values for TEL were found to

be 0.076 and 0.233 $\mu\text{g/ml}$ and 0.0906 and 0.274 $\mu\text{g/ml}$ at 295 and 239 nm respectively. LOD and LOQ values for IND were found to be 0.322 and 0.9765 $\mu\text{g/ml}$ and 0.1172 and 0.3553 $\mu\text{g/ml}$ at 295 and 239 nm respectively. These data show that the method is sensitive for the determination of TEL and IND. Both drugs showed good regression values at their respective wavelengths, and the results of a recovery study revealed that any small change in the drug concentration in the solution could be accurately determined by the proposed method. The proposed validated method was successfully applied to determine TEL and IND in their combined dosage form. Results obtained for TEL and IND were comparable with corresponding labeled amounts (Table-3).

CONCLUSION

The proposed methods are simple, rapid and validated in terms of linearity, precision, accuracy, reproducibility, and can be used successfully for routine simultaneous estimation of Telmisartan and Indapamide in pure and capsule dosage forms.

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