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Simultaneous Estimation Of Telmisartan And Hydrochlorothiazide In Pharmaceutical Dosage Form

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ABSTRACT

A simple, accurate, fast and precise simultaneous analytical method has been developed for simultaneous determination of Telmisartan and Hydrochlorothiazide in tablet dosage form. The wavelengths selected for these drugs were 296 nm and 270 nm respectively. The linearity at selected wavelength lies between 2 – 10 µg/ml for Telmisartan and 4 – 20 µg/ml for Hydrochlorothiazide. The concentrations of these drugs were evaluated in laboratory mixture of reference standard and different marketed formulation. Recovery studies confirmed the accuracy of proposed method. Precision of method was found out as the values within acceptable limit. Thus the proposed method and results were validated as per ICH guidelines. Statistical analysis proves that the method is reproducible and selective for the simultaneous estimation of Telmisartan and Hydrochlorothiazide.

INTRODUCTION

Telmisartan (TELM) is a non-peptide angiotensin - II receptor antagonist and a derivative of benzimidazole. It selectively and insurmountably inhibits angiotensin - II AT_1 receptor subtype without affecting other systems involved in cardiovascular regulation. TELM is chemically 4'-[(1,4'-Dimethyl-2'-propyl-[2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid. Hydrochlorothiazide (HCT) is one of the widely used thiazide diuretic which reduces reabsorption of electrolytes from the renal tubules and chemically 6-Chloro-3,4-dihydro-2H-1,2,4-benzothiazidine-7-sulfonamide-1,1-dioxide. The combination of TELM and HCT is available as tablet dosage form.

The literature survey [1-21] revealed that TELM is not yet official in any pharmacopoeia. Several analytical methods have been reported for the determination of TELM in biological fluids, and formulation includes HPLC, HPTLC, electrophoretic and fluorimetric methods. Few analytical methods were reported for determination of TELM and HCT in combination which includes HPLC, TLC – densitometric and derivative spectrophotometry. However, no methods are yet reported for simultaneous estimation of TELM and HCT by simple spectroscopic methods in pharmaceutical preparations. Hence, the simultaneous spectroscopic method has been developed to estimate these two drugs from tablet dosage form.

MATERIALS AND METHODS

Instrument used in current research was UV/Visible spectrophotometer with resolution of 1 nm and 0.5 mm slit width (model UV-1700, shimadzu, Japan) connected to a HP computer system loaded with UV probe 2.21software. An electronic balance of (shimadzu) 10 mg sensitivity and ultrasonicator with ultrasonic frequency of 36 ± 3 KHz was used. Standard gift sample of TELM and HCT were supplied by AtoZ Pharmaceutical Ltd, India. TELM and HCT combination tablets (Telma-H, 40 mg TELM and 12.5 mg HCT, manufactured by Glenmark Pharmaceuticals, Nasik, India) were purchased from the local pharmacy. Methanol of analytical grade was used as solvent and purchased from Merck Chemicals, India.

Preparation of standard solution

Standard stock solution 1.0 mg/ml each of TELM and HCT were prepared in 50 ml methanol. A dilution of stock solution was made with methanol to get working standard solution of 100 µg/ml of both drugs. This solution was further diluted with methanol to get final concentration of 10 µg/ml.

Method development

The standard solutions containing 10 µg/ml TELM and HCT were scanned in the wavelength range of 200-400 nm.

The overlain spectra of TELM and HCT showed the ëmax at 296 nm and 270 nm respectively. Hence, these two wavelengths were selected for estimation of TELM and HCT by simultaneous equation method.

Calibration curve and linearity

The standard stock solutions containing 1.0 mg/ml each of TELM and HCT were further diluted to get linearity concentrations of 2 – 10 µg/ml for TELM and 4 – 20 µg/ml for HCT respectively. Each concentration was analyzed in triplicate. Calibration curve was plotted by taking absorbance on Y-axis and concentration on X-axis. The relation between drug and its absorbance is expressed by the equation y = mx + b, where 'm' is slope and 'b' is intercept.

Limit of Detection and Quantification

The limit of Detection (LOD) and limit of Quantification (LOQ) were estimated from the standard calibration curve. The residual standard deviation of regression line or standard deviation of y intercepts of regression lines was used to calculate LOD and LOQ. Here LOD = 3.3×D/S and LOQ = 10×D/S. Where D is the standard deviation of y intercept of regression line S is the slope of calibration curve.

Accuracy and Precision

To establish the reliability of proposed method, three series of mixture of solutions were prepared in the ratio of 3.2:1 6.4: 2 and 12.8: 4 µg/ml of TELM and HCT respectively and analyzed as discussed above. Precision of procedure was as calculated within day and between day variations. The accuracy of the proposed method was checked by performing recovery study by addition of standard drug solution to pre analytical tablet sample solution at three different concentration levels.

Analysis of tablets

A total number of 20 tablets (Telma® H) accurately weighed and powdered by a mortar and pestle. Quantities of the tablet powder equivalent to 40 mg TELM and 12.5 mg of HCT were accurately weighed and transferred to 50 ml volumetric flask. Weighed tablet powder was dissolved in 25 ml methanol and vortexed for 15 minutes. Then the volume made up to 50 ml with methanol and mix well. Solution obtained was filtered through Whatmann filter paper no. 42, diluted with same solvent to get the concentration within linearity and used for the measurement of absorbance. The concentration of TELM and HCT were calculated using simultaneous equation method.

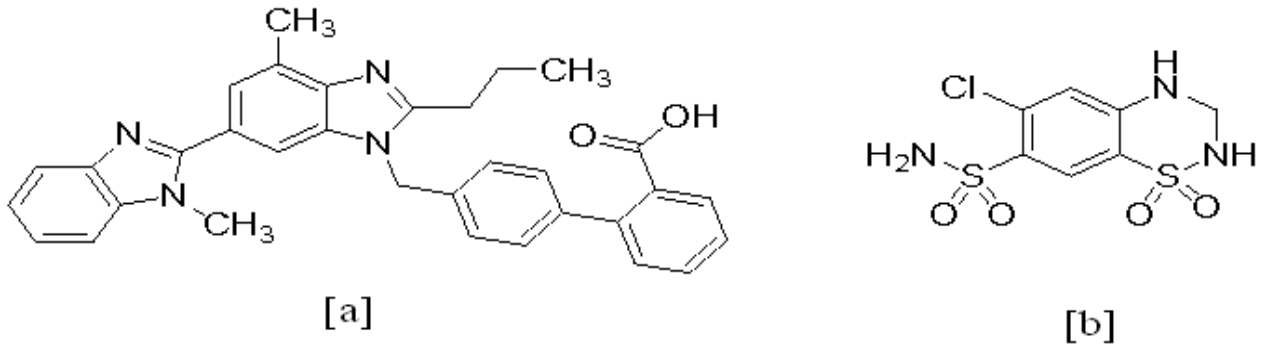

Fig. 1: Chemical structure of Telmisartan and Hydrochlorothiazide

RESULTS AND DISCUSSION

The spectra of TELM and HCT were found to be overlapped in UV range (fig. 2). So, the simultaneous determination of the drugs has been done by simultaneous equation method. Three binary mixture solutions of TELM and HCT were prepared. The quantitative estimation was carried out by solving the simultaneous equations, $Cx = (A_2ay_1 - A_1ay_2) / (ax_2ay_1 - ax_1ay_2)$ and $Cy = (A_1ax_2 - A_2ax_1) / (ax_2ay_1 - ax_1ay_2)$, where, A_1 and A_2 are absorbances of diluted mixture at 296 and 270 nm, respectively. Cx and Cy are the concentration of TELM and HCT, ax_1 (72.6) and ax_2 (55.6) and absorptivities of TELM at 296 and 270 nm, ay_1 (15.5) and ay_2 (55.1) are absorptivities of HCT at 296 and 270 nm.

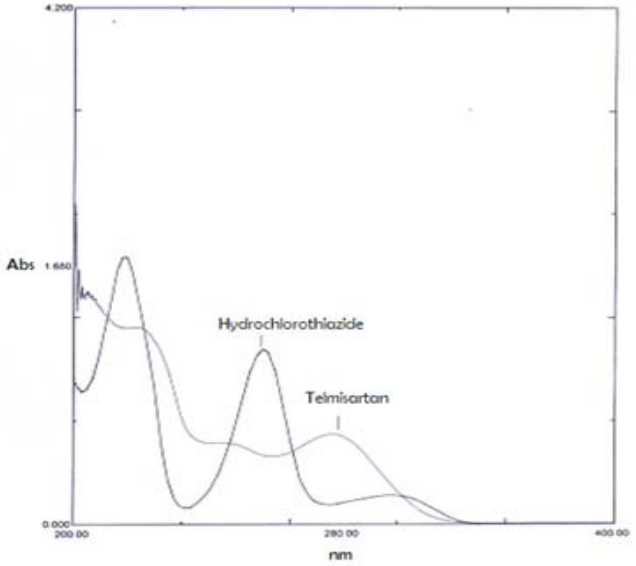

Fig. 2: Overlain spectra of Telmisartan and Hydrochlorothiazide

Linearity, Range, LOD and LOQ

The developed UV-simultaneous equation method has shown the linearity in range of 2 – 10 µg/ml for TELM and 4 – 20 µg/ml for HCT. The calibration curves were plotted for both analytes. The linearity of the calibration curves shows that the proposed method obeys Beer's law in the concentration range discussed above. The LOD and LOQ values are summarized in Table 1.

Table No.1: Regression analysis data for Telmisartan and Hydrochlorothiazide

Statistical parameters	Telmisartan	Hydrochloro thiazide
Regression coefficient (r^2)	0.9998	0.9999
Correlation coefficient (r)	0.9997	0.9998
Standard error in slope	4.21×10^{-4}	4.02×10^{-4}
Standard error on intercept	7.52×10^{-3}	2.21×10^{-4}
Limit of Detection (µg/ml)	0.02	0.04
Limit of Quantification (µg/ml)	0.10	0.58
Concentration range (µg/ml)	2 – 10	4 – 20

Accuracy and Precision

The accuracy of the method was determined from recoveries of TELM and HCT by standard addition method. The mean recoveries and SD are illustrated in Table 2. The results showed a good index of accuracy. The within day and between day variations showed co-efficient of variation values less than 1.4% for both TELM and HCT in all three selected concentrations. The data indicates that the proposed simultaneous equation method is highly precise between different analyses. Also no interference was observed from the presence of excipients. Ruggedness of the method was observed by reproducibility of results under the conditions like different days and different analyst. The method was found to be specific, accurate and precise.

Assay of tablet dosage forms

The proposed method for the simultaneous estimation of TELM and HCT was applied for the assay of commercial tablets, Telma® H (labeled to contain 40 mg TELM and 12.5 mg HCT). The results obtained are in good agreement with the label claim, given in Table 3.

Table No.2: Recovery data for Telmisartan and Hydrochlorothiazide

S. No	Conc. Before spiking (µg/ml)	Reference std. added*(µg/ml)	Conc. After spiking*(µg/ml)	% Recovery
Telmisartan				
1	40	5	45.5	101.11
2	80	10	90.2	100.22
3	160	20	180.2	100.11
Hydrochlorothiazide				
1	12.5	5	17.48	99.88
2	25	10	34.95	99.85
3	50	20	70.01	100.01

* Mean of three determinations

Table No.3: Results of tablet analysis

Drug	Labeled amount (mg/tab)	Amount taken for assay (µg/ml)	Amount obtained* (mg)	% Label claim
Telmisartan	40	10	40.60	101.5
Hydrochlorothiazide	12.5	3.125	12.80	102.4

* Mean of three determinations

CONCLUSION

A simple, accurate, fast and precise UV-simultaneous equation method has been developed for the simultaneous estimation of TELM and HCT. The proposed method is successfully applied for determination of both drugs in tablet dosage forms. The method can be used for the routine quality control analysis of TELM and HCT in combined dosage form.

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