Spectrophotometric Determination and Validation of Telmisartan and Hydrochlorthiazide in Pure Andtablet Dosage Form.

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Abstract

Two simple, precise, accurate and economical UV spectrophotometric methods have been developed and validated for the routine estimation of Telmisartan (TELMI) and Hydrochlorthiazide (HCTZ) in bulk drug and pharmaceutical preparations. The drugs shows maximum absorption at 295.5nm and 273nm obeyed Beer-Lambert's law in the concentration range of 5-25μg/ml.. The same spectrum was derivatised into first order derivative the amplitude of trough at 313nm and 230nm for D_1 were measured. In D_1 method the drug showed linearity in the concentration range of 5-25μg/ml. Recovery studies were carried out by addition of known amount of standard drug (80,100 and 120% of labeled claim of a tablet) to the preanalysed tablet solution. The % recovery was found to be 98.25-99.79, which indicates accuracy and reliability of the validated method as well as noninterference from excipients to the developed method. The intraday and inter day assay was within 2%. The methods were then validated statistically as per the ICH guidelines which yielded good results concerning range, precision, accuracy, specificity and repeatability.

Key Words

Telmisartan, Hydrochlorthiazide**,** λmax, Absorbance ratio method and Derivative spectroscopy.

Introduction

Telmisertan (TEL) & Hydrochlothiazide (HCTZ) combination is used to treat the mild to moderate hypertension[1]. Several methods have been reported for estimation of drug from Pharmaceutical dosage form. Extensive literature survey reveals that no spectrophotometric method is available for simultaneous determination of Telmisartan & Hydrochlothiazide in combined tablet dosage form. Aim of present work was to develop simple, precise, accurate and economical spectrophotometric methods for simultaneous determination of binary drug formulation. The proposed method was optimized and validated in accordance with International Conference on Harmonization (ICH) guidelines[4].
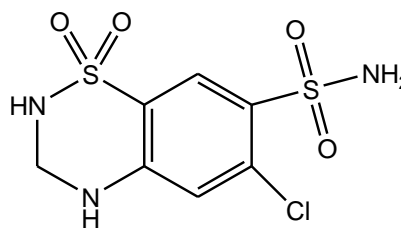
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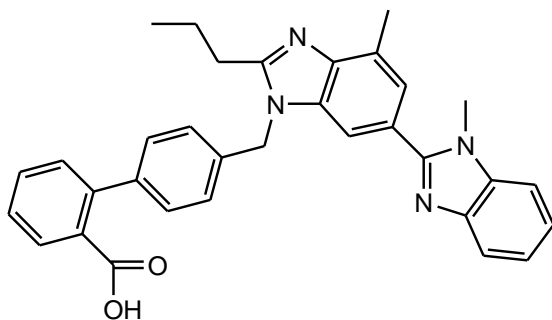
Telmisartan   **Hydrochlorthiazide**

Materials and Methods

UV-visible double beam spectrophotometer, JASCO-V630 with spectral bandwidth of 1 nm, wavelength accuracy of ± 0.3 nm and a pair of 10 mm matched quartz cells were used. The commercially available tablet, (Label claim: Telmisartan 40 mg and Hydrochlorethizide 12.5 mg) was procured from local market.

Selection of solvent[2]

After assessing the solubility of drugs in different solvents 0.1N NaOH has been selected as solvent for developing spectral characteristics.

Preparation of standard stock and calibration curve[3]

The standard stock solutions of drugs was prepared by dissolving 10 mg of drug in 10mL distilled water in 10mL volumetric flask, final volume was adjusted with 0.1N NaOH and sonicated for about 10 min to get 100 μg/mL. Working standard solutions of 10 μg/mL were scanned in the entire UV range of 400-200 nm to obtain the absorbance spectra. The absorbance of resulting solutions were measured at respective λ max at 273nm 280.5nm plotted a calibration curve against concentration to get the linearity and regression equation. The same spectrum was derivatised into first order derivative, the amplitude of trough at 313nm, and at 230nm was measured.

Experimental

Method A: Absorbance ratio method[6]

Two wavelengths selected for the method are 295.5m and 273 nm that are absorption maxima. The stock solutions of both the drugs were further diluted separately with 0.1N NaOH to get a series of standard solutions of 5-25μg/mL concentrations of Telmisartan and 5-25μg/mL concentrations of Hydrochlorthiazide.The absorbance were measured at the selected wavelengths and absorptivities (A 1%, 1 cm) for both the drugs at both wavelengths were determined as mean of six independent determinations. Concentrations in the sample were obtained by using following equations,

$$C_x = (Q_m - Q_y). A_1 / (Q_x - Q_y). a_{x1}$$
$$C_y = (Q_m - Q_x). A_1 / (Q_y - Q_x). a_{y1}$$

Where,

$Qm = A2/ A1$

$Qx = ax2/ ax1$

$Qy = ay2/ ay1$

Where, A1 and A2 are absorbance's of mixture at 295.5 nm and 273 nm respectively ax1 and ax2 are absorptivities of telmisartan at λ1 and λ2 respectively and ay1 and ay2 are absorptivities of hydrichlorthiazide.

Method B: Derivative spectroscopy $(D^1)^6$

The Zero order spectra of both the drugs were derivatised. The same spectrum was derivatised into first order derivative the amplitude of trough at 313nm and 230nm for D_1 were measured. In D_1 method the drug showed linearity in the concentration range of 5-25μg/ml.

Analysis of tablet

Twenty tablets were weighed accurately and reduced to fine powder, drug equivalent to 10mg of powder was weighed and dissolved in 10 ml of 0.1NaOH in a 100ml volumetric flask, final volume was made with 0.1NaOH and sonicated for about 10min. The above solution was filtered by using Whattmann filter paper No.:41. Analysis procedure was repeated five times with tablet formulation. Aliquot was scanned in the UV range (200-400nm). The same spectrum was derivatised into first order, amplitude of the trough at 313nm, and at 230nm for D_1. The amount of drug present in the tablet was calculated from the standard graphs.

Method Validation[4]
Linearity

Appropriate concentration of stock solution was assayed as per developed methods. Beer-Lambert's concentration range was found to be 5- 25μg/ml. The linearity data for both methods are presented in Table.

Accuracy

The accuracy of the methods was determined by performing recovery studies on tablet formulation and for prepared solutions containing known amount of drug by standard addition method in which preanalyzed samples were taken and standard drug was added at three different levels 80%.100% and 120% as per ICH guidelines.

Precision

To check the degree of repeatability of methods, suitable statistical evaluation was carried out. Repeatability was performed for five times with tablets formulation.The standard deviation, coefficient of variance and standard error was calculated.

Intermediate Precision (Interday and Intraday precision)

The experiments were repeated three times in a day to determine intraday precision and on three different days to determine interday precision.

Limit of Detection (LOD) and Limit of Quantization (LOQ)

The LOD and LOQ of Telmisertan & Hydrochlorothiazide by proposed methods were determined using calibration standards.LOD and LOQ were calculated as 3.3σ/S and 10σ/S respectively, where S is the slope of the calibration curve and σ is the

standard deviation of response. The results of the same are shown in Table 3.

Results and Discussion

The proposed methods are simple, rapid and precise and do not suffer from any interference due to excipients of tablet. The proposed spectrophotometric methods were found to be linear in the range of 5-25μg/ml at 273nm and 280.5 absorbance ratio method with correlation coefficients (R^2) 0.994 and 0.996 while in D_1 5-25 μg/ml at 313nm and 230nm with correlation coefficients (R^2) for D_1 were found to be 0.992 and 0.993 respectively. The methods were validated in terms of accuracy, precision, repetabiltiy and the results are recorded in Table.The accuracy of the method was determined by performing recovery studies by standard addition of method in which preanalyzed samples were taken and standard drug was added at three different levels. Values of recovery greater than 98.0% indicate that proposed method is accurate for the analysis of the drug. The precision of the proposed method was estimated in terms of interday precision and intraday precision wherein the method was repeated on three different days and repeated for three different time periods in the same day respectively. The selectivity of the method was checked by monitoring a standard solution of Drugs in presence of excipients at the same concentration level as used in tablet using the method described in the procedure for calibration curve in pharmaceutical tablets. The excipients did not show any effect on the estimation of Telmisartan and Hydrochlorthiazide. Rigorous analysis of the results indicates that the presence of excipients in tablet formulation did not interference with the final determination of the active component. This reveals that the potential utility of this method for the routine analysis of Telmisartan and Hydrochlorthiazide in pharmaceutical preparations.

Conclusion

Two new, simple precise, accurate and selective spectrophotometric methods were developed for the analysis of Telmisartan and Hydrochlorthiazide in bulk and in pharmaceutical formulation. The Absorbance ratio method is useful for tablet formulations where there is no interference of excipients in the absorbance of Telmisartan and Hydrochlorthiazide, method D_1 can be utilized for formulations containing any interfering excipients. The developed methods were also validated and from the statistical data, it was found that methods were accurate, precise, reproducible and can be successfully applied to the pharmaceutical formulations without interference of excipients.

References
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Table 1: Analysis of Tablet formulation.

| Drug	Label claim (mg/ tab.)	Amount found (mg)	%Drug found ±SD
TELMI	40	39.5	98.75 ± 0.31
HCTZ	12.5	12.1	96.8 ± 0.20

Table 2: Recovery study of TELMI AND HCTZ.

| Drug	Level of addition (%)	Amount added (µg/ml)	Amount recovered (µg/ml)	%Recovery ± SD
TELMI	80	4	3.93	98.25 ± 0.052
	100	5	4.96	99.2 ± 0.056
	120	6	5.92	98.66 ± 0.071
HCTZ	80	4	3.93	98.25 ± 0.042
	100	5	4.95	99.00 ± 0.049
	120	6	5.96	99.33 ± 0.055

Values expressed mean± SD (n=3)

**Table 3:** Optical characteristics data and validation parameters.

| Parameters	Values for TELMI	Values for CLOXA
Absorption maxima (λ max)	296.5nm	273nm
Beer's law limit (µg/ml)	5-25	5-25
Regression equation	y = 0.049x + 0.032	y = 0.045x - 0.029
Correlation coefficient (R2)	0.996	0.994
Molar absorptivity	1.6×10^3	4.1×10^4
Accuracy (%Recovery ± SD)	98.37±1.41	98.86±0.45
Precision		
Intraday*(Analyst 1)	98.97±0.43	99.01±0.4
Interday*(Analyst 2)	99.79±0.98	98.97±0.81
LOD (µg/ml)	0.346	0.35
LOQ (µg/ml)	1.061	1.04
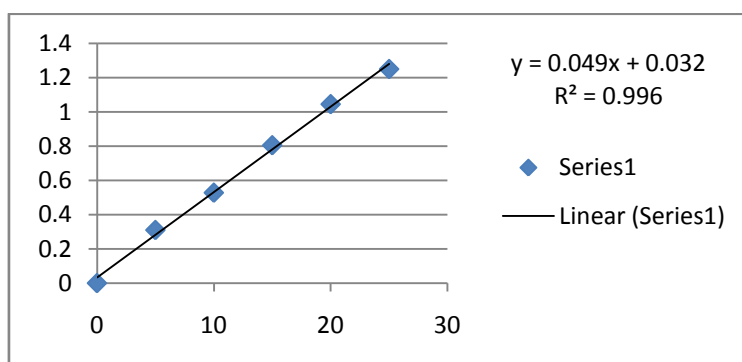
Fig 1: Linearity of Telmisartan.
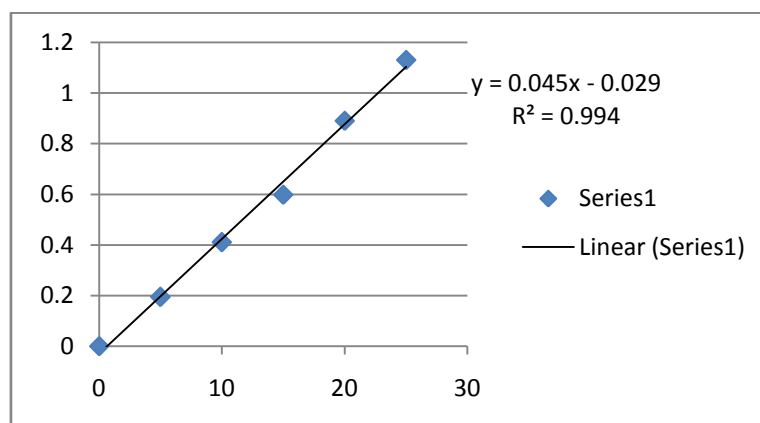
Fig2: linearity of HCTZ.
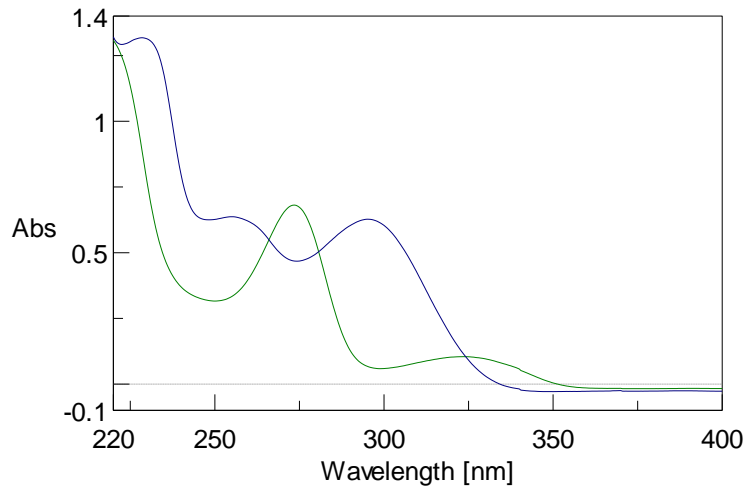
Fig 3: Overlain spectra of TELM and HCTZ.
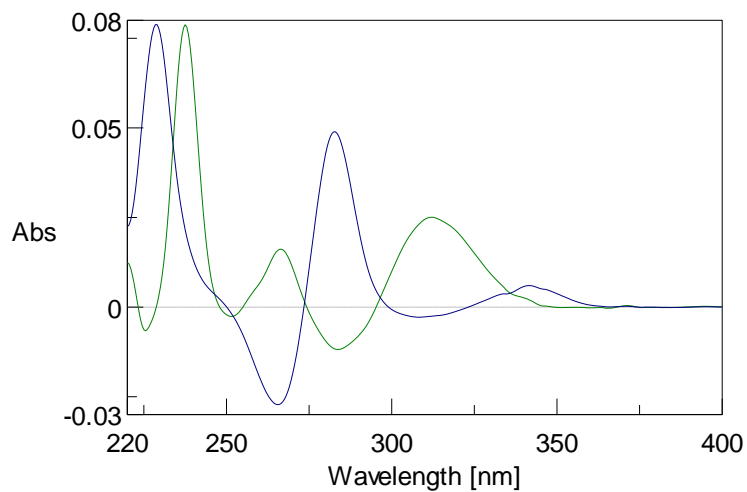
Fig 4: 1[st]Derivative spectra of TELM and HCTZ.

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