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Spectrophotometric Simultaneous Determination of Hydrochlorothiazide and Telmisartan in Combined Dosage Form

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ABSTRACT

Simple, sensitive, specific and economic spectrophotometric method was developed and validated for simultaneous quantitation of Hydrochlorothiazide and Telmisartan in tablet dosage form. New method based on the simultaneous estimation of drugs in a binary mixture without previous separation was developed. In simultaneous equation method, Hydrochlorothiazide and Telmisartan were quantified using their absorptivity values of at selected wavelengths, viz., 273 nm and 295 nm respectively. The accuracy and reproducibility of the proposed method was statistically validated by recovery studies. The simultaneous equation method permits simple, rapid and direct determination of Hydrochlorothiazide and Telmisartan in commercially available tablet dosage form without previous separations and can therefore be used for routine analysis of both drugs in quality control laboratories.

Keywords: Telmisartan, Hydrochlorothiazide, Vierodt's method.

1. INTRODUCTION

Telmisartan is chemically designated as 4'-[(1,4'-dimethyl-2'-propyl [2,6'-bi-1H-benzimidazol]-1'-yl) methyl] [1,1'-biphenyl]-2-carboxylic acid (O'Neil et al, 1969). It is an angiotensin II type I blocker and is used as an antihypertensive (Wienen et al, 2000) along with Hydrochlorothiazide. It is a thiazide diuretic which reduces the reabsorption of electrolytes from the renal tubules, thereby increasing the excretion of sodium and chloride ions and consequently of water (Jain et al, 1991). Chemically Hydrochlorothiazide is 6-chloro-3,4-dihydro-2H-1,2,4-benzothiazine-7-sulfonamide 1, 1-dioxide. The combination of Hydrochlorothiazide and Telmisartan is useful in treatment of mild to moderate hypertension, and is well tolerated with a lower incidence of cough than ACE inhibitors. The marketed tablets contain Telmisartan and Hydrochlorothiazide in ratio of 40:12.5 [Wankhede et al 2007]. The widespread use of these drugs in combination, necessitates development of analytical methods for their simultaneous estimation. Several analytical procedures have been proposed for the quantitative estimation of Telmisartan and Hydrochlorothiazide separately and in combination with other drugs. Linear sweep polarography (Maotian et al, 2004), HPLC (Palled et al 2006), and UV (Palled et al 2005) methods for estimation of Telmisartan alone in pharmaceutical preparation have been reported. Hydrochlorothiazide in combination with other drugs is estimated by HPLC (Erk et al, 1999), LC and HPTLC-densitometry (Gindy et al, 2001), capillary electrophoresis, capillary electrochromatography [10] and spectrophotometric methods (Saglik et al, 2001). Simultaneous estimation of Telmisartan and Hydrochlorothiazide has been reported by RP-HPLC (Bhat et al, 2007) which is an expensive method.

To our knowledge simple and economical analytical method for simultaneous determination of Telmisartan and Hydrochlorothiazide has not been reported so far. The present communication describes two simple, sensitive, accurate, rapid and economic methods for simultaneous estimation of Telmisartan and Hydrochlorothiazide in tablet formulation. The developed methods were validated and found to be accurate, precise and reproducible.

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2. MATERIAL AND METHODS

2.1. Apparatus

A double beam UV/Vis spectrophotometer, Shimadzu UV- 1700 Pharmaspec, was employed with a pair of 1 cm quartz cells for all analytical work.

2.2. Reagents and chemicals

Telmisartan and Hydrochlorothiazide were obtained from Troikaa Pharmaceuticals Ltd. Dehradun, Uttaranchal, India as a gift sample and were used as working standards. Sodium hydroxide of analytical grade and double distilled water were used throughout the analysis.

2.3. Commercial formulation

A commercial pharmaceutical preparation, Telmikaa H tablet (40 mg Telmisartan and 12.5 mg hydrochlorothiazide) was procured from the local market.

2.4. Preparation of standard solution

Standard stock solution of Telmisartan and Hydrochlorothiazide was prepared by dissolving 10 mg of each drug separately in 10mL volumetric flask using 0.1N sodium hydroxide as solvent. Stock solutions of 1000 µg/mL were obtained in this manner. From these stock solutions, working standard solutions of concentration 100 µg/mL each were prepared by appropriate dilutions. Working standard solutions were scanned in the entire UV range to determine the λ_{max} . The λ_{max} of Hydrochlorothiazide and Telmisartan were found to be 273 nm and 295 nm respectively.

2.5. Calibration curves

Seven standard dilutions of each drug were prepared separately having concentrations of 2-20 µg/mL. The absorbances of these standard solutions were measured at 273 nm and 295 nm and calibration curve was plotted. The absorptivity coefficients of the two drugs were determined using calibration curve.

2.6. Preparation of sample solution

Sample solution containing both the drugs was prepared by dissolving 10 mg of each drug in 10mL volumetric flask using 0.1N sodium hydroxide to give stock solutions of 1000 µg/mL. From this stock solution, working standard solution of 100 µg/mL concentration was prepared by appropriate dilution. Seven standard dilutions of concentrations of 2, 4, 8, 10, 12, 16 and 20 µg/mL was prepared from working standard solution. The absorbance of this sample solution was measured at 273 nm and 295 nm and their concentrations were determined using proposed analytical methods.

Simultaneous equations method

Method was based on simultaneous equation method of Vierodt. The method is applicable in the case of sample containing two drugs, each of which absorbs at the λ_{max} of the other (Beckett et

al, 1997). Two equations were constructed based upon the fact that the absorbance of the mixture of Hydrochlorothiazide and Telmisartan at 273nm and 295nm is the sum of the absorbances at respective wavelengths. Two equations were developed using absorptivity coefficient values.

$$C_H = A_2 326.597 - A_1 454.964 / 59.761 \times 326.597 - 497.328 \times 454.964 \quad \text{---(1)}$$

$$C_T = A_1 59.761 - A_2 497.328 / 59.761 \times 326.597 - 497.328 \times 454.964 \quad \text{---(2)}$$

Where C_H and C_T are concentrations of Hydrochlorothiazide and Telmisartan in g/100 mL respectively in the sample solution. A_1 and A_2 are absorbances of the mixture at 273 nm and 295 nm, respectively. Solving these two equations, the concentrations C_H and C_T can be readily determined.

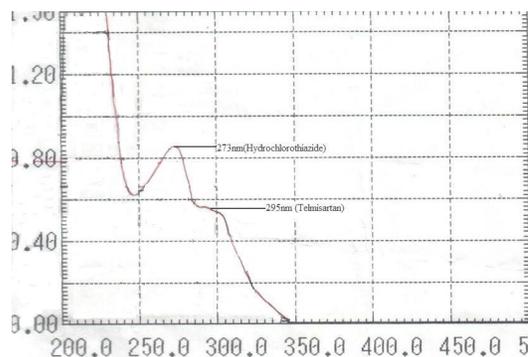


Fig:1 Spectra of Mixture (Hydrochlorothiazide and Telmisartan)

2.9. Estimation in the marked formulation

Twenty tablets were weighed and crushed to a fine powder. An accurately weighed powder sample equivalent to 10 mg of Telmisartan was transferred to a 10 ml volumetric flask, dissolved in 5 ml 0.1N sodium hydroxide, shaken for 10 min and the volume was made up to the mark with 0.1N sodium hydroxide. The solution was then filtered through Whatman filter paper no. 41. The solution was further diluted to get different concentrations in the range of 2-20 µg/mL of both the drugs. For this method the absorbances of the sample solution, i.e., A_1 and A_2 , were recorded at 273 nm and 295 nm respectively, and concentration of two drugs in the sample were determined using the equations(1) and (2). The analysis procedure was repeated three times with the formulation. The result of analysis of the formulation is shown in Table 1.

2.10. Method validation

The method validation parameters like linearity, precision, accuracy, repeatability, limit of detection and limit of quantitation were checked as per ICH guidelines.

2.11. Linearity and range

The linearity for Telmisartan and Hydrochlorothiazide were determined at seven concentration levels, ranging from 2-20µ/mL using working standards.

2.12. Precision and accuracy

The precision of the method was evaluated by inter day and intra day variation studies. In intra day studies, working solutions of standard and sample were analysed thrice in a day and percentage relative standard deviation (% RSD) was calculated. In the inter day variation studies, working solution of standard and sample were analysed on three consecutive days and percentage relative standard deviation (% RSD) was calculated. The data is shown in table 2. The accuracy of the method was determined by recovery studies. The recovery studies were performed by the standard addition method at 80%, 100% and 120% level and the percentage recoveries were calculated and are shown in Table 1.

2.13. Limit of detection and limit of quantitation

The Limit of Detection (LOD) is the smallest concentration of the analyte that gives the measurable response. LOD was calculated using the following formula and shown in Table 2.

$$\text{LOD} = 3.3 (\sigma / S)$$

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

The Limit of Quantification (LOQ) is the smallest concentration of the analyte, which gives a response that can be accurately quantified. LOQ was calculated using the following formula and shown in Table 2.

$$\text{LOQ} = 10 (\sigma / S)$$

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

3. RESULTS AND DISCUSSION

In the present work, new method, namely, simultaneous equation method (Vierordt's method) was used for the simultaneous spectroscopic estimation of Hydrochlorothiazide and Telmisartan in commercially available tablet dosage form.

The concentrations in the range of 2-20 $\mu\text{g/mL}$ of mixed working standard and two sampling wavelengths of 273 nm (λ_{max} of Hydrochlorothiazide), and 295 nm (λ_{max} of Telmisartan) gave optimum accuracy, precision, time, economy, and sensitivity for this method. The proposed procedure was successfully applied to the determination of Hydrochlorothiazide and Telmisartan in the commercially available tablets dosage form, and the results are shown in Table 1.

The recovery studies were carried out at different concentrations by spiking a known concentration of standard drug to the pre-analysed sample and contents were reanalysed by proposed methods. The results of marketed formulation analysis and recovery studies are depicted in Table 1. The method was validated statistically for range, linearity, precision, accuracy, repeatability, LOD, and LOQ Table 2. Accuracy was ascertained on the basis of recovery studies. Precision was calculated as inter and intra day variation for both the drugs. The percentage recoveries for Hydrochlorothiazide and Telmisartan were found to be 97.69 ± 0.98 - 99.44 ± 0.95 and 98.93 ± 0.32 - 99.93 ± 0.14 for this

method respectively. The contents estimated using the proposed method was found in agreement with the labelled amount Table 1. The relative standard deviations was found to be within the limit, indicating good accuracy, precision, and repeatability of the proposed method

Table 1: Result of tablet analysis

Drug	Label claim	Vierordt's method	
		mg/tab	% found \pm RSD*
HCT	12.5	95.84 \pm 0.93-98.76 \pm 0.95	97.69 \pm 0.09-99.44 \pm 0.95
TMS	40	98.99 \pm 0.27-101.01 \pm 0.32	98.93 \pm 0.32-99.93 \pm 0.14

*Mean \pm RSD of three observations, n=no of determinations

Table 2: Summary of validation parameters for Vierordt's method

Parameter	HCT	TMS
Linearity range($\mu\text{g/mL}$)	2-20($\mu\text{g/mL}$)	2-20($\mu\text{g/mL}$)
Correlation coefficient(r^2)	0.999	0.999
Precision(RSD)^a		
Inter day(n=3)	0.0-0.961	0.164-0.565
Intra day(n=3)	0.102-0.618	0.194-0.459
Accuracy (%)	97.69 \pm 0.09-99.44 \pm 0.95	98.93 \pm 0.32-99.93 \pm 0.14
Repeatability(RSD, n^b=3)	0.062-0.176	0.069-0.483
LOD^c	0.041($\mu\text{g/mL}$)	0.074($\mu\text{g/mL}$)
LOQ^d	0.125($\mu\text{g/mL}$)	0.226($\mu\text{g/mL}$)

^aRSD=Relative standard deviation

^bn=Number of determination

^cLOD=Limit of detection

^dLOQ= Limit of quantitation

4. CONCLUSION

The Vierordt's method permits simple, rapid and direct determination of Hydrochlorothiazide and Telmisartan in commercially available tablet dosage form without previous separation. The results of analysis of two drugs from tablet formulation using method was found close to 100%, Standard deviation was satisfactorily low indicating accuracy and reproducibility of the method. Recovery studies was satisfactory which showed that there is no interference of excipients.

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