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Research Article

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SPECTROPHOTOMETRIC SIMULTANEOUS DETERMINATION OF HYDROCHLOROTHIAZIDE AND TELMISARTAN IN COMBINED DOSAGE FORM BY DUAL WAVELENGTH METHOD

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ABSTRACT

Simple, sensitive, specific and economic spectrophotometric method was developed and validated for simultaneous estimation 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 dual wavelength method, Hydrochlorothiazide and Telmisartan were quantified using principle that absorbance difference between two points on mixture spectra is directly proportional to concentration of component of interest and independent of interfering component. The accuracy and reproducibility of the proposed method was statistically validated by recovery studies. The 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, Dual Wavelength method.

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[1]. It is an angiotensin II type I blocker and is used as an antihypertensive[2] 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.[3] Chemically Hydrochlorothiazide is 6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7sulfonamide 1, 1-dioxide[1]. 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.[4] 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[5], HPLC[6], and UV[7] methods for estimation of Telmisartan alone in pharmaceutical preparation have been reported. Hydrochlorothiazide in combination with other drugs is estimated by HPLC[8], LC and HPTLC-densitomerty[9], capillary electrophoresis, capillary electro-chromatography[10] and spectrophotometric methods[11].

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Simultaneous estimation of Telmisartan and Hydrochlorothiazide has been reported by RP-HPLC[4,12] 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.

MATERIALS AND METHODS

Instrument

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

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.

Commercial formulation

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

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 set of two wavelengths λ_1 (258nm) and λ_2 (299nm) for estimation of Hydrochlorothiazide and λ_3 (316nm) and λ_4 (326nm) for estimation of Telmisartan.

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 above λ maxs. Determined absorbance difference (A1-A2) and (A3-A4) values and plotted calibration curves between absorbance difference values and concentration of drug.

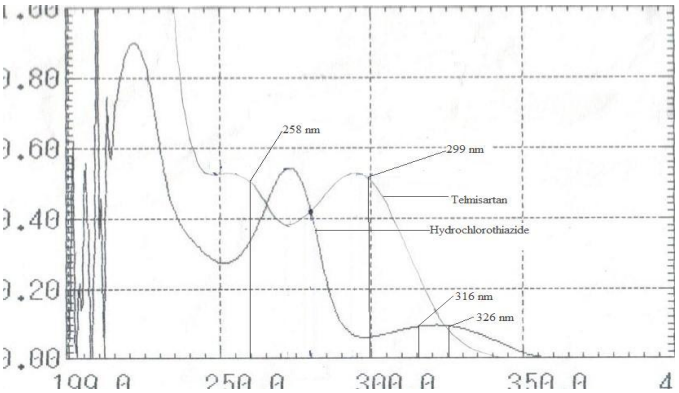
Preparation of sample solution

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 above set of wavelengths their concentrations were determined using proposed analytical method.

Dual wavelength method

This method is based on the principle that absorbance difference between two points on mixture spectra is directly proportional to concentration of component of interest and independent of interfering component.[13, 14] Set of two wavelengths λ_1 (258nm) and λ_2 (299nm) for estimation of Hydrochlorothiazide and λ_3 (316nm) and λ_4 (326nm) for estimation of Telmisartan were selected on above principle and overline spectra. Determined absorbance difference (A1-A2) and (A3-A4) values and plotted calibration curves between absorbance difference values and concentration of drug. (Figure **1**)

Figure 1. Overlain spectra of Hydrochlorothiazide and Telmisartan



Estimation in the marketed 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 absorbance of the sample solution, i.e., A_1, A_2, A_3, and A_4, were recorded at set of two wavelengths λ_1 (258nm) and λ_2 (299nm) for estimation of Hydrochlorothiazide and λ_3 (316nm) and λ_4 (326nm) for estimation of Telmisartan and this method applicable where, out of the two spectra, one should show two wavelengths with equal absorbance. The spectra of Telmisartan and Hydrochlorothiazide when overlaid indicated that the spectra of Telmisartan satisfied this condition while that of Hydrochlorothiazide did not. The result of analysis of the formulation is shown in Table **1**.

Table1. Result of tablet analysis

Drug Label claim		Dual wavelength method	
Drug	mg/tab	%found±RSD*	%recovery±RSD
HCT	12.5	97.33±0.39-102±0.74	96.19±0.81-101.59±1.33
TMS	40	98.96±1.4-103.33±0.75	98.22±0.45-102.66±1.28

*Mean±RSD of three observations, n=no of determinations

Method validation

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

Linearity and range

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

Precision and accuracy

The precision of the method was evaluated by inter day and intraday variation studies. In intraday 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**.

Table2. Summary of validation parameters for Dual wavelength method

Parameter	HCT	TMS
Linearity range (µg/mL)	2-20(µg/mL)	2-20(µg/mL)
Correlation coefficient(r^2)	0.999	0.999
Precision(RSD)[a] Inter day(n=3)	0.01-1.578	0.386-1.968
Intraday(n=3)	0.342-1.602	0.193-1.903
Accuracy (%)	97.69±0.09-101.44±1.95	98.93±0.32-102.93±1.14
Repeatability (RSD, n[b]=3)	0.062-0.176	0.069-0.483
LOD[c]	0.079(µg/mL)	0.127(µg/mL)
LOQ[d]	0.240(µg/mL)	0.384(µg/mL)

[a]RSD=Relative standard deviation; [b]n=Number of determination
[c]LOD=Limit of detection; [d]LOQ= Limit of quantitation

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**.

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**.

LOD = 3.3 (σ / 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**.

LOQ = 10 (σ / S)

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

RESULTS AND DISCUSSION

In the present work, new method, namely, dual wavelength 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 µg/mL of mixed working standard and two set of wavelengths 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-analyzed sample and contents were reanalyzed 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 intraday variation for both the drugs. The percentage recoveries for Hydrochlorothiazide and Telmisartan were found to be 97.69±0.09-101.44±1.95 and 98.93±0.32-102.93±1.14 for this method respectively. The contents estimated using the proposed method was found in agreement with the labeled amount Table **1**. The relative standard deviations were found to be within the limit, indicating good accuracy, precision, and repeatability of the proposed method.

CONCLUSION

The dual wavelength 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 were satisfactory which showed that there is no interference of excipients.

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REFERENCES

1. O'Neil J M, Smith A and Heckelman P F; The Merck index, 14th Edition, NJ: USA, 2001; 827, 1569.
2. Wienen W, Entzeroth M, Meel J C A V, Stangier J, Busch U, Ebner T, Schmid J, Lehmann H, Matzek K, Rowson J K, Gladigau V and Hauel N H A review on Telmisartan: A novel, long-acting angiotensin II-receptor antagonist. Cardiovascular Drug Reviews. 2000; 18(2): 127-154.
3. Jain R and Jain C I; Simultaneous quantification of Captopril and Hydrochlorothiazide using HPLC. Indian Drugs. 1991; 28(18): 380-382.
4. Wankhede S B, Tajne M R, Gupta K R and Wadodkar S G; RP-HPLC method for simultaneous estimation of Telmisartan and Hydrochlorothiazide in tablet dosage form. Indian J. Pharm. Sci. 2007; 69(2):298-300.
5. Maotian X, Junfeng S and Yaodong L; Rapid determination of Telmisartan in pharmaceutical preparations and serum by linear sweep polarography. J. Pharma. Biomed. Anal. 2004; 34(3): 681-687.
6. Palled M S, Rajesh P M N, Chatter and Bhat A R; RP-HPLC determination of Telmisartan in tablet dosage forms. Indian J. Pharm. Sci. 2005; 67(1), 108-110.
7. Palled M S, Chatter M, Rajesh P M N and Bhatt A R Difference spectrophotometric determination of Telmisartan in tablet dosage forms. Indian J. Pharm. Sci. 2006; 68(50): 685-686.
8. Erk N; Determination of active ingredients in the pharmaceutical formulations containing hydrochlorothiazide and its binary mixtures with benazepril hydrochloride, triamterene and cilazapril by ratio spectra derivative spectrophotometry and vierordt's method. J. Pharma. Biomed. Anal. 1999; 20:155–167.
9. Gindy A, Ashour A, Fattah L and Shabana M M; Application of LC and HPTLC densitometry for the simultaneous determination of benazepril hydrochloride and Hydrochlorothiazide. J. Pharma. Biomed. Anal. 25:171–179.
10. Quaglia M G, Donati E, Carlucci G, Mazzeo P and Fanali S Determination of Losartan and Hydrochlorothiazide in tablets by CE and CEC. J. Pharma. Biomed. Anal. 2002; 29(6): 981-987.
11. Saglik S, Sagirli O, Atmaca S and Ersoy L; Simultaneous determination of Fosinopril and Hydrochlorothiazide in tablets by derivative spectrophotometric and high-performance liquid chromatographic methods. Analytica Chimica Acta. 2001; 427(2):253-257.
12. Bhat L R, Godge R K, Vora A T and Mrinalini; Validated RP-HPLC method for simultaneous determination of Telmisartan and Hydrochlorothiazide in pharmaceutical formulation. J. Liq. Chrom. Related. Techno. 2007; 30(20):3059-3067.
13. Beckett A H and Stenlake J B; Practical Pharmaceutical Chemistry, 4th Edition, Volume II, CBS, New Delhi, 1997; 278.
14. Shankar M B, Mehta, F A, Bhatt K K, Mehta R S, Geetha M; Simultaneous spectrophotometric determination of Losartan potassium and Hydrochlorothiazide in tablets. *Indian J. Pharm. Sci*. 2003, 65(2), 167-170.