Available online at *www.ujpronline.com*
Universal Journal of Pharmaceutical Research
An International Peer Reviewed Journal
ISSN: 2831-5235 (Print); 2456-8058 (Electronic)

RESEARCH ARTICLE

SIMULTANEOUS SPECTROPHOTOMETRIC DETERMINATION OF TELMISARTAN AND HYDROCHLOROTHIAZIDE IN PHARMACEUTICAL PREPARATIONS BY RATIO SPECTRA DERIVATIVE METHOD

A. Hakan AKTAŞ*, Hülya SARI
Department of Chemistry, Faculty of Arts and Sciences, Süleyman Demirel University, 62300 Isparta, Turkey.

Article Info:

Article History:
Received: 10 February 2023
Reviewed: 16 March 2023
Accepted: 23 April 2023
Published: 15 May 2023

Cite this article
AKTAŞ AH, SARI H. Prevalence and risk factors of intestinal parasites, malnutrition, and anemia among orphan children in Sana'a city, Yemen. Universal Journal of Pharmaceutical Research 2023; 8(2):40-43.
https://doi.org/10.22270/ujpr.v8i2.924

***Address for Correspondence:**
Dr. A. Hakan AKTAŞ, Department of Chemistry, Faculty of Arts and Sciences, Süleyman Demirel University, 62300 Isparta, Turkey; Tel: +902462114080; E-mail: *hakanaktas@sdu.edu.tr*

Abstract

Background: As it is known, antihypertensive drugs are frequently used for the treatment of individuals with high blood pressure all over the world. This study aims is to precisely determine the active substances of telmisartan and hydrochlorothiazide, which are commercially sold as high blood pressure drugs in the market, and to use the ratio spectrum method for this purpose.
Method: All, solutions of the active ingredients of the drugs studied in the method were prepared in various concentrations. Subsequently, mixtures were prepared in accordance with the commercial drug sample, their spectra were taken by spectrophotometric method, and the spectrum ratio method was successfully applied to these data sets.
Results: The study revealed that the application of the ratio spectra first-order derivative spectrophotometric method yielded highly reliable outcomes in the spectrophotometric analysis of different combinations of telmisartan and hydrochlorothiazide.
Conclusion: The applied method can be used in the field of drug development.
Keywords: Active substances, derivative spectrophotometry, ratio spectra, Telmisartan.

INTRODUCTION

It is aimed to increase the efficiency by obtaining synergistic effects with the use of diuretic mixtures. The incorporation of thiazides and diuretics in drug combinations is a common practice owing to the benefits of low dosage and enhanced efficacy in managing hypertension. Combination of telmisartan (TEL) with hydrochlorothiazide (HCT) is used synergistic anti-hypertensive effects. Various methods including HPLC[1-4], spectrophotometry[5-8], LC-MS[9], spectrofluorimetry[10], and TLC[10,11] for TEL and HCT analysis have been reported. The review of literature indicates that the analysis of these two drugs usually involves methods that are both costly and time-intensive. Also, not every research laboratory may have such expensive instrumental devices. The method we propose is made with a UV spectrophotometer, which is easily available in every laboratory, and analyzes can be done easily and can be expressed as a cheap method. The ratio spectra derivative method was also obtained as a result of the easy processing of the data obtained from the spectrum. For these reasons, it can be stated that the proposed method gives easy, cheap and reproducible results.

The research conducted by Salinas and his team[12] has led to the development of a novel analytical approach for mixtures that generate consecutive spectra. This technique relies on the utilization of ratio spectra, which are frequently employed in contemporary practice. This technique is succinct and enables the straightforward quantification of active constituents by detecting the minimum or maximum points at the designated wavelengths. In recent times, Berzas Nevado *et al.*,[13-14] and Dinç and Onur[15-16] have employed this method to identify active compounds in pharmaceuticals.

The present study employed the ratio spectra derivative method to analyze a drug formulation comprising TEL and HCT, which pose a challenge for conventional UV methods due to their similar absorbance values. Similar to the approach employed by Salinas, analytical signals were gauged at wavelengths that corresponded to the maximum and minimum points in the first derivative values of the ratio spectra. Further, linear regression equations were established for both active components of the drug.

MATERIALS AND METHODS

Apparatus

All measurements were made with the UV 1700 PHARMASPEC SHIMADZU spectrophotometer. Absorbance measurements were performed under room temperature conditions with a pair of matching quartz cuvettes. The data groups taken in a computer environment were converted into graphs with Excel and performed following the operations.

Chemical and reagents

TEL and HCT and dosage forms (Telvis Plus® which contains 80 mg TEL and 12.5 mg HCT) were provided by Neutec Pharma International (Turkey). Methanol (Merck) used as a solvent has a chromatographic purity degree. All the chemicals used in the study were used in analytical purity.

Active ingredient solvents used

At the beginning of the experimental part of our research, stock solutions of the drug active ingredients we used in the study were prepared. For this, 100 ppm solutions of each of our active ingredients, which are weighed precisely in the laboratory, have been prepared. Then, these stock solutions were diluted to the ranges to be studied for spectrophotometric measurements.

Analysis of tablet

The commercial sample containing the active ingredients of the drug was weighed and at least ten tablets were crushed into powder in a mortar. Then, it was transferred to a balloon and the solution, which was sonicated with the solvent for at least 25 minutes to ensure the required dissolution, was completed to the volume to be used with the same solvent. It was observed that there were insoluble parts, these parts were filtered and washed with solvent and the solutions were combined.

RESULTS AND DISCUSSION

Ratio spectra were obtained as a result of dividing each of the spectra of the active ingredient of TEL pharmaceuticals obtained in different concentrations to the HCT spectrum in a certain concentration (Figure 1a). The ratio spectra were subjected to first derivative analysis (^{1}DD) at an interval of $\Delta\lambda$=1 nm, using a scaling factor (SF) of/10 (Figure 1b). The resultant ratio spectra exhibited a maximum at 290 nm and a minimum at 257 nm, both of which were deemed appropriate for TEL quantification in the TEL+HCT mixture, as depicted in Figure 1b. In the experiments of the commercial product, 257 nm was selected from these values for the determination of this active ingredient. The reason for this is the lower RSD value and higher recovery average at the selected wavelength. As can be easily seen, the correlation coefficient at the selected 257 nm is closer to one and the slope is smaller.

This situation is in perfect harmony with the low RSD values mentioned in The HCT standards were subjected to ratio spectra analysis by dividing each spectrum by the TEL spectrum at a specific concentration, as illustrated in Figure 3a.

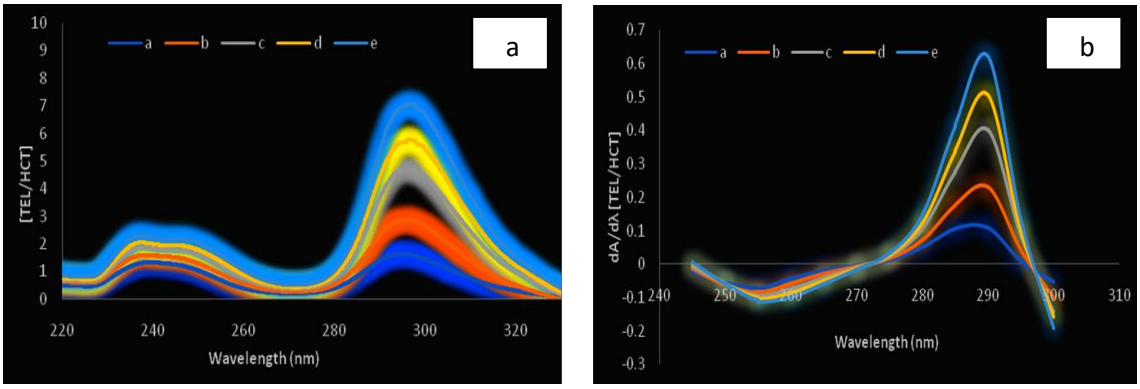

Figure 1:Ratio spectra (a) and first derivative of the ratio spectra (b) of a) 2 ppm b) 4 ppm c) 6 ppm d) 8 ppm and e) 10 ppm solution of TEL in methanol when 8 ppm solutionof HCT in methanol used as divisor.

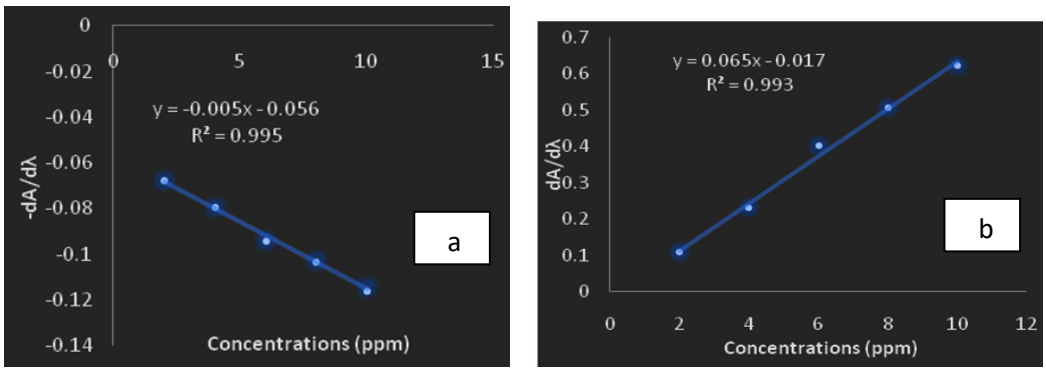

Figure 2: First derivative calibration plot of TEL at 257 nm in methanol solvent (a) and 290 nm in methanol solvent.

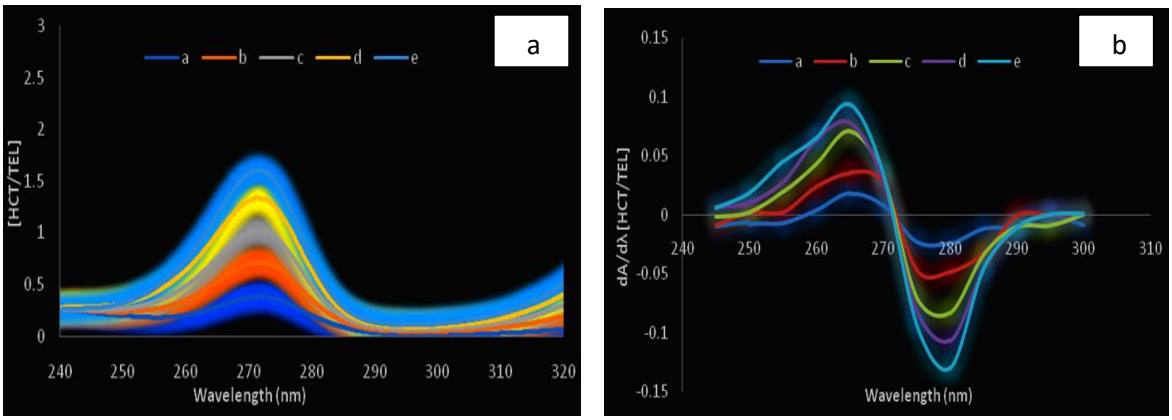

Figure 3: Ratio spectra (a) and first derivative of the ratio spectra (b) of a) 3 ppm (b) 6 ppm (c) 9 ppm (d) 12 ppm and (e) 15 ppm HCT in methanol when 25 ppm solution of TEL in methanol used as a divisor.

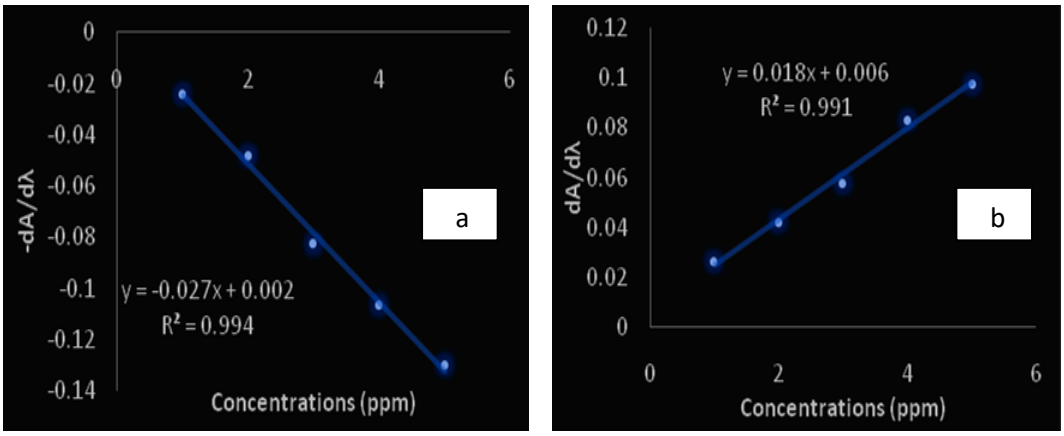

Figure 4: First derivative calibration plot of HCT at 264 nm in methanol solvent (a) and 280 nm in methanol solvent.

The ratio spectra were then subjected to first derivative analysis (^{1}DD) at an interval of $\Delta\lambda$=1 nm, using a scaling factor (SF)=10 (Figure 3b). The resulting ratio spectra exhibited a maximum at 280 nm and a minimum at 264 nm, both of which were deemed appropriate for HCT quantification in the HCT+TEL mixture, as depicted in Figure 3b. Additionally, Figure 4a and Figure 4b present the regression equations and correlation coefficients derived for the two wavelengths assessed in the ratio spectra. For the reasons we mentioned above for Telmisartan, 264 nm was also selected for Hydrochlorothiazide, and successful results were obtained. Table 1 presents the average recoveries and corresponding relative standard deviations obtained for the synthetic mixtures prepared in the laboratory using the applied method, which were deemed highly satisfactory. In such study, the divisor concentration is a crucial factor. In this study, the standard spectra were divided by 25 ppm TEL and 8 ppm HCT concentrations, which were deemed optimal for the quantification of TEL and HCT, respectively.

Table 1: Recovery results for TEL and HCT in synthetic mixtures by ratio spectra first derivative method.

Mixture	Added (ppm)	TEL recovery (%)		Added	HCT recovery (%)	
	257	290	264	280		
1	2	101.0	101.5	7	100.6	100.2
2	4	100.0	100.2	7	101.2	102.5
3	6	100.2	102.6	7	98.8	99.2
4	8	101.4	99.3	7	98.6	100.4
5	10	100.2	96.4	7	101.4	96.8
6	5	100.1	98.8	3	99.6	100.4
7	5	99.8	102.4	6	100.8	98.2
8	5	101.4	102.6	9	99.6	98.8
9	5	100.6	99.2	12	98.8	102.4
10	5	99.9	102.4	15	101.0	101.4
	$\bar{x}$	100.46	100.54	$\bar{x}$	100.04	100.03
	RSD*	0.61	2.11	RSD	1.08	1.82

RSD* Relative standard deviation

Table 2: Application of the ratio spectra first derivative method to tablets containing telmisartan and hydrochlorothiazide together and statistical evaluation of the results.

Number of experiments	The amount of TEL in the tablet (mg/tablet)	Found (mg/tablet)	The amount of HCT in the tablet (mg/tablet)	Found (mg/tablet)
1	80.00	80.12	12.50	12.49
2	80.00	79.94	12.50	12.50
3	80.00	80.02	12.50	12.50
4	80.00	79.98	12.50	12.50
	Average value 80.0.21		Average value 12.50	
	Standard deviation 0.07		Standard deviation 0.03	
	Confidence interval 80.02± 0.08		Confidence interval 12.5± 0.02	

Finally, the application of the method was tested on a commercial sample. The cumulative results are shown in Table 2.

CONCLUSIONS

It has been shown that the ratio spectrum method we proposed for quantitative measurement of TEL and HCT prepared synthetically in the laboratory environment gives repeatable and accurate results without any pretreatment. It has been concluded that the proposed method can be applied routinely in drug development laboratories.

ACKNOWLEDGEMENTS

We would like to thank Süleyman Demirel University Institute of Natural Sciences for enabling such a study to be carried out.

AUTHOR'S CONTRIBUTION

AKTAŞ AH: writing original draft, lab work. **SARI H:** methodology, investigation. **Alrahabi LM:** data analysis, report drafting. All the authors approved the finished version of the manuscript.

DATA AVAILABILITY

Data will be made available on reasonable request.

CONFLICT OF INTEREST

There is no conflict of interest.

REFERENCES

1. Tiris G, Mehmandoust M, Lotfy HM, *et al*. Simultaneous determination of hydrochlorothiazide, amlodipine, and telmisartan with spectrophotometric and HPLC green chemistry applications. Chemosphere 2022; 303: 135074. *https://doi.org/10.1016/ j.chemosphere.2022.135074*
2. Salama I. Simultaneous HPLC–UV analysis of telmisartanand hydrochlorothiazide in human plasma. Bulletin Faculty Pharmacy, Cairo University 2011; 49: 19-24.*https://doi.org/10.1016/j.bfopcu.2011.07.005*
3. Mukhopadhyay S, Kadam K, Sawant L, Nachane D, Pandita N. Simultaneous determination of related substances of telmisartan and hydrochlorothiazide in tablet dosage form by using reversed phase high performance liquid chromatographic method. J Pharm BioalliedSci July-September 2011; 3(3): 375-383. *https://doi.org/10.4103/0975-7406.84441*
4. Bhat LR, Godge RK, Vora AT, Damle MC. Validated RP-HPLC method for simultaneous determination of telmisartan and hydrochlorothiazide in pharmaceutical formulation. J Liquid Chromat Related Tech 2007; 30(20): 3059-3067. *https://doi.org/10.1080/10826070701632774*
5. Patıl KR, Shınde DB. Stability-indicating LC method for the simultaneous determination of telmisartan and hydrochlorothiazide in dosage form. J Chil Chem Soc 2012; 57(1): 1017-1021. *https://doi.org/10.4067/S0717-97072012000100014*
6. Beliz K, Dinç E, Baleanu D. chemometric methods for the simultaneous spectrophotometric determination of telmisartan and hydrochlorothiazide in the commercial pharmaceuticals. Revista Chimie 2009;60(6): 544-550.
7. Lakshmi KS, Lakshmi S. Design and optimization of a chemometric-assisted spectrophotometric determination of telmisartan and hydrochlorothiazide in pharmaceutical dosage form. J Young Pharm 2010; 2(1): 85-89. *https://doi.org/10.4103/0975-1483.62224*
8. Gangola R, Singh N, Gaurav A, Maithani M, Singh R. Spectrophotometric simultaneous determination hydrochlorothiazide and telmisartan in combined dosage form by dual wavelength method. Pharmacie Globale 2011; 2(04): 1-4.
9. Tingting Y, Hao LA, Lili D, *et al*. Liquid chromatographic–tandem mass spectrometric methodfor the simultaneous quantitation of telmisartan and hydrochlorothiazidein human plasma. J Pharm Biomed Anal 2008; 48: 1225–1229. *https://doi.org/10.1016/j.jpba.2008.08.021*
10. Lories IB, Samah SA, Laila AF, Heba HR. Application of first-derivative, ratio derivative spectrophotometry, TLC-densitometry and spectrofluorimetry for the simultaneous determination of telmisartan and hydrochlorothiazide in pharmaceutical dosage forms and plasma. Il Farmaco 2005; 60: 859–867. *https://doi.org/10.1016/j.farmac.2005.06.009*
11. Shah NJ, Suhagıa BN, Shah RR, Shah PB. Development and validation of a HPTLC method for the simultaneous estimation of telmisartan and hydrochlorothiazide in tablet dosage form. Indian J Pharm Sci 2007; 202-205. *https://doi.org/10.4103/0250-474X.33150*
12. F. Salinas F, Berzas NJJ, Espinosa AM.A new spectrophotometric method for quantitative multicomponent analysis resolution of mixtures of salicylic and salicylic acids. Talanta1990; 37: 347-351.
13. Berzas NJJ, Lemus GJM, Castenada PG. Spectra ratio derivative spectrophotometric determination of sulphaquinoxaline pyrimethamine in veterinary formulation. J Pharm Biomed Anal 1993; 11: 601-607.
14. Berzas NJJ, Rodrigeuez FJ, Moreno PML. Determination of sulphamethizole in the presence of nitrofurantoine by derivative spectrophotometry and ratio spectra derivative. Talanta1991; 38: 1261-1264.
15. Dinç E. Onur F. Application of the ratio spectra derivative spectrophotometric and Vierordt's method to quantitative analysis of paracetamol and metamizol in a pharmaceutical formulation. Sci Pharm 1999; 67: 57-68.
16. Dinç E, Onur F. Application of derivative and ratio derivative spectrophotometry for determination of pseudoephedrine and acrivastine. Anal Lett 1997; 30(6): 1179-1191.