



Available online on 15.01.2021 at <http://ujpr.org>  
**Universal Journal of Pharmaceutical Research**  
 An International Peer Reviewed Journal

Open access to Pharmaceutical research  
 This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial Share Alike 4.0 License which permits unrestricted non commercial use, provided the original work is properly cited



Volume 5, Issue 6, 2020

Open Access

## RESEARCH ARTICLE

# UV SPECTROSCOPY DETERMINATION OF CILAZAPRIL AND HYDROCHLOROTHIAZIDE ACTIVE AGENTS USED IN THE TREATMENT OF HYPERTENSION

A. Hakan AKTAŞ

Süleyman Demirel University, Faculty of Science and Art, Department of Chemistry, Isparta-Turkey.

### ABSTRACT

**Background:** Antihypertensive and diuretic drugs are widely used in patients to regulate high blood pressure. Objective of current study was to prepare various cilazapril and hydrochlorothiazide mixtures, to create a matrix effect in the drug and to determine the determination of these active substances in drug samples after optimum conditions.

**Method:** In the spectrophotometric method, 100 mgL<sup>-1</sup> solutions were prepared in cilazapril, hydrochlorothiazide in methanol + 0.1 m HCl solvent and then mixtures of these solutions were prepared between specific ppm. The absorbance's of the solvent against the blind were read at 0.1 nm intervals. After the mixture, tablet (drug) sample was prepared and chemometrics methods were applied to the values obtained by saving the absorbance values.

**Results:** It was observed that the main component analysis applied as a result of spectrophotometric determination of various mixtures of cilazapril and hydrochlorothiazide used in the study gave correct results. These results were validated using various chemometric parameters.

**Conclusion:** The proposed chemometric method can be used in routine analysis in industrial laboratories.

**Keywords:** Cilazapril, Hydrochlorothiazide, Principal component analysis.

**Article Info:** Received 7 November 2020; Revised 8 December; Accepted 4 January, Available online 15 January 2021



### Cite this article-

AKTAŞ AH. UV spectroscopy determination of cilazapril and hydrochlorothiazide active agents used in the treatment of hypertension. Universal Journal of Pharmaceutical Research 2020; 5(6):49-51.

DOI: <https://doi.org/10.22270/ujpr.v5i6.512>

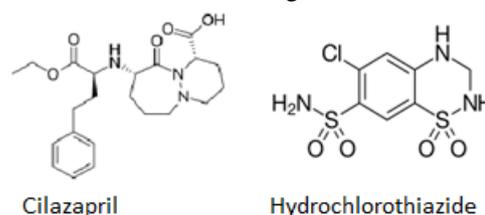
### Address for Correspondence:

Prof. Dr. A. Hakan AKTAŞ, Süleyman Demirel University, Faculty of Science and Art, Department of Chemistry, Isparta-Turkey. Tel- +902462114080; E-mail: [hakanaktas@sdu.edu.tr](mailto:hakanaktas@sdu.edu.tr)

## INTRODUCTION

The systematic name of the cilazapril (CIL) closed formula is C<sub>22</sub>H<sub>31</sub>N<sub>3</sub>O<sub>5</sub> (1S, 9S) -9 - {[ (2S) -1-ethoxy-1-oxo-4-phenylbutan-2-yl] amino} -10-oxo-octahydro 1 H-pyridazino [1,2-a] [1,2] diazepine-1-carboxylic acid is given in Figure 1 as the open formula, and is an angiotensin converting enzyme (ACE) inhibitor class (Thiol and sulfhydryl group) drug free. Cilazapril is a drug used in the treatment of hypertension and heart failure<sup>1</sup>. Hydrochlorothiazide (HCT) is a white powder with a closed formula C<sub>7</sub>H<sub>8</sub>ClN<sub>3</sub>O<sub>4</sub>S<sub>2</sub> and its systematic name is 6-chloro-3, 4-dihydro-2H-1, 2, 4-benzothiazine-7-sulfonamide 1,1 dioxide, which leads to fluid retention in the body. It is a diuretic that helps to prevent the absorption of excess salt by the body. Hydrochlorothiazide is among the thiazide group diuretics<sup>2</sup>. Figure 1 shows the open formula. Drug active substances tend to accumulate in human vital organs, which are generally toxic, non-spontaneous in

nature, and which can move gradually throughout the food chain for a long period of time. Studies on the determination of active substances in drug samples are of increasing interest. In recent years, the scope of monitoring and determination of these active substances has been increasing.

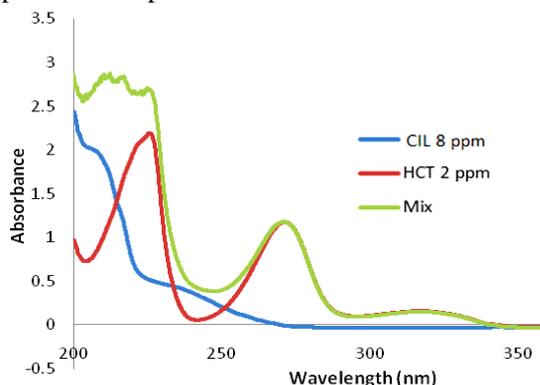


**Figure 1: Structures of the studied compounds.**

In this study, various mixtures of cilazapril and hydrochlorothiazide were prepared and matrix effect was formed in the drug and optimum conditions were determined. These optimum conditions were then used

in the determination of the drug samples of these active substances. As it is known, the combination of cilazapril and hydrochlorothiazide in pharmaceutical formulations is usually given as an antihypertensive and diuretic agent to patients with high blood pressure. On the other hand, quality control of these drugs in commercial pharmaceutical tablets is important<sup>2</sup>. For this, especially in recent years, various chemometric calibration techniques have been applied<sup>3-6</sup>. Several researchers have used these techniques simultaneously for binary analysis and a triple mix. Several analytical procedures have been described for concurrent determination of hydrochlorothiazide, benazepril hydrochloride, Triamterene and cilazapril in mixtures with other drugs, including spectrophotometry<sup>7-9</sup>.

The multivariate calibration methods, which are widely used today, use all the advantages of the selected calibration model, such as using the entire spectrum, simplifying the automation process, and minimizing the noise that may occur in the environment. In addition, these methods do not require any separation process, they are very popular today due to their easy application and precision.



**Figure 2: CIL, HCT and their mixtures in methanol.**

In the study, principal component analysis method, which is a powerful chemometric method, was applied for the combined analysis of SIL - HCT as an active substance, which is used as a hypertension drug. The application of the chemometric method is very important in interpreting multivariate data and determining the simultaneous determination of drugs.

## MATERIALS AND METHODS

At this stage of the study, 100 ppm SIL (Aldrich, Steinheim, Germany) and HCT (Aldrich, Steinheim, Germany) stock solutions were prepared in methanol (Merck, Darmstadt, Germany) solvent to form the calibration set and a symmetrical concentration set was prepared from this. The most important reason for preparing a symmetrical calibration set is to prevent vital errors that may occur during analysis. An independent validation set was used to test the application of the applied principal component regression chemometric method. "Minitab 16" software was used to perform the PCR method.

## RESULTS AND DISCUSSIONS

### Principal Component Regression

PCR is a multivariate method that includes factor analysis. Its biggest advantage is that it is applied to the entire spectrum. When performing PCR, it involves a calibration step and spectral separation for all models in the spectrum and where the unknown component content is estimated from the sample spectrum. PCR separation is based on spectral changes as a whole, regardless of the content of the component. Of course, the optimal calibration method varies depending on the particular experimental conditions as with other methods.

### Method development

The overlapping spectra of CIL and HCT are shown in Figure 1. As can easily be seen from the spectrum, it is not possible to determine both compounds together by classical spectroscopic methods. In such cases, chemometry helps us and we try to overcome such problems with various chemometric methods. Therefore, principal component regression has been successfully applied in this study, preferring the chemometric method.

### Chemometric parameters

The application capability of a calibration model can be explained in several different ways and the results obtained can be examined numerically. One of the most used of these models is to examine the estimated residual error squares (PRESS). To calculate PRESS, the general formula given below is applied.

$$\text{PRESS} = \sum_{i=1}^n (C_i^{\text{added}} - C_i^{\text{found}})^2$$

It should be kept in mind that there is no correct way to normalize the PRESS values, since not all of these studied data sets contain an equal number of samples. In such case, the conversion should be made to the standard prediction error (SEP) formula given below.

$$\text{SEP} = \sqrt{\frac{\sum_{i=1}^n (C_i^{\text{added}} - C_i^{\text{found}})^2}{n-1}}$$

The resulting SEP value is an important indicator of the performance of the calibration model. A small drawback of this value, the performance of the calibration model is variable depending on the analyte concentration. Calibration parameters for this study were calculated and shown in Table 1. As can be seen from the same table, the parameter between actual and estimated concentration of the mixture in CIL and HCT in values are given.

**Table 1: Statistical parameters for PCR**

PCR			
Step	Parameter	CIL	HCT
Calibration	SEC	-	-
	PRESS	0.0658	0.0458
	Slope	1.0000	0.9999
	Intercept	0.0118	0.0220
	r	0.9999	0.9999
Prediction	Slope	0.9952	0.9692
	Intercept	0.0124	0.0382
	r	0.9999	0.9999

### Method validation

The accuracy of the principal component regression method applied by preparing a mixture containing 15 different concentrations of CIL and HCT was determined by the performance of the reliable results obtained from the analyzes. Table 2 shows the recoveries and standard deviations obtained in the study. As can be seen here, the applied basic components of the numerical values obtained from regression method it is already appropriate. Both compounds gave very high accuracy and precise results and analysis process, it was determined that any intervention or systematic errors.

**Table 2: Recovery values for the applied chemometric method.**

Mixtures added (µg/ml)		Recovery (%)	
CIL	HCT	CIL	HCT
2.0	0.2	99.98	99.86
4.0	0.4	99.86	100.04
6.0	0.6	100.02	100.00
8.0	0.8	100.08	100.14
10.0	1.0	100.00	100.08
5.0	0.2	100.04	100.04
5.0	0.4	99.68	99.96
5.0	0.6	100.12	100.02
5.0	0.8	100.10	99.88
5.0	1.0	99.98	100.06
2.0	0.5	100.02	100.04
4.0	0.5	100.00	100.02
6.0	0.5	100.04	100.00
8.0	0.5	99.98	99.98
10.0	0.5	100.02	100.00
Mean		99.99	100.01
RSD <sup>a</sup>		0.1062	0.0708

RSD<sup>a</sup> : Relative Standard Deviation

### CONCLUSION

In this study, PCR, a powerful chemometric technique, was proposed for the simultaneous determination of CIL and HCT in binary mixtures. This technique has been successfully applied to pharmaceutical products. Solubility of the overlapping drug mixtures was

achieved using PCR techniques. Consider the choice of wavelength having a high correlation value with the concentration of additional matrix due to interference from outside the operating range of sample or analyte. Recommended chemometric methods, without any preliminary chemical separation and was found to be applicable for routine analysis without the time the pharmaceutical formulation.

### CONFLICT OF INTEREST

No conflict of interest associated with this work.

### REFERENCES

- Hutchison TA, Shahan DR. DRUGDEXW System", Edition Electronic Version. MICROMEDEX, Greenwood Village, CO.2003.
- Dinc E, Baleanu D. Spectrophotometric quantitative determination of cilazapril and hydrochlorothiazide in tablets by chemometric methods. J Pharm Biomedical Analysis 2002; 30: 715–723.  
[https://doi.org/10.1016/S0731-7085\(02\)00359-X](https://doi.org/10.1016/S0731-7085(02)00359-X)
- Aktaş AH. Chemometric assisted for the simultaneous spectrophotometric determination of calcium and magnesium in natural water. Chem Xpress 2016; 9(2), 099-10. PMID: 18967586
- Kramer R. Chemometric Techniques in Quantitative Analysis, Marcel Dekker, New York, 51-97, 1998
- Adams MJ. Chemometrics in Analytical Spectroscopy, The Royal Society of Chemistry, Thomas, Graham House, Science Park, Cambridge, 187, 1995.  
<https://doi.org/10.1039/9781847559661-FP001>
- Martens H, Naes T. Multivariate Calibration. J Wiley and Sons Chichester, UK, 1991.  
<https://doi.org/10.1002/bimj.4710330407>
- Erk N. Comparative study of the UV spectra derivative spectrophotometry derivative spectrophotometry and Vierordt's method applied to the analysis of lisonopril and hydrochlorothiazide in tablets. Spect Lett 1998; 31(3): 633-645.<https://doi.org/10.1080/00387019808002756>
- Salem H, El-Maamli M, El-Sadek M, Kheir AA. UV and UV Derivative spectrophotometric determination of two-component mixtures. Spect Lett 1991; 24(3), 451-470.  
<https://doi.org/10.1080/00387019108020669>
- Erk N, Onur F. Simultaneous determination of analgine and paracetamol in tablets by spectrophotometric methods. Anal Lett 1997; 30(6): 1201-1210.  
<https://doi.org/10.1080/00032719708004049>