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Title: Spectrophotometric Determination of Losartan Potassium and Hydrochlorothiazide in tablets by Wavelet Transform Approach

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develop new signal processing method based on the combined use of CWT with zero crossing technique simultaneous quantitative determination of losartan potassium (LOS) and hydrochlorothiazide (HCT) in tablets without the use of a separation step. Several analytical methods for the analysis of LOS and HCT have been reported in pharmaceutical and biological studies, including spectrophotometric methods [15-18], spectrofluorometric method [19] and chromatographic methods [20-24].

2. MATERIAL AND METHOD

The absorption spectra of mixtures and tablet solutions in the spectral range 200-305 nm were measured by a Shimadzu UV-1601 dual-beam UV-VIS spectrophotometer with a constant gap width (2 nm).

2.1. Commercial Tablet

A pharmaceutical tablet (HYZAAR[®] Tablet, MSD Ind., Istanbul, Turkey) including 50 mg LOS and 12.5 mg HCT per tablet was gathered from the Turkish market.

2.2. Standard solutions

Standard LOS and HCT stock solutions were arranged respectively by dissolving 25 mg of each drug in 100 mL of methanol. A calibration ranges between 4.0-26.0 $\mu\text{g mL}^{-1}$ for LOS and 2.0-24 $\mu\text{g mL}^{-1}$ HCT in solvent was prepared for spectrum analysis from standard stock solutions for each active ingredient.

2.3. Sample solutions preparation

For testing tablets; twenty tablets of LOS and HCT were weighed and powdered. Transfer an equal amount of powder to a 100 ml volumetric flask and solved with methanol. The contents of the flask were mechanically stirred. After filtration, the supernatant is diluted with methanol to an ultimate concentration. This procedure was repeated ten times.

3. RESULTS AND DISCUSSION

The purpose of this work is to apply the Symlets5-CWT (SYM5-CWT) method to the spectra of LOS and HCT in mixtures and preparations for the simultaneous assay. The LOS and HCT standards and the UV spectra of the tablet solution were measured between 200 and 305 nm as can be seen in Figure 1.

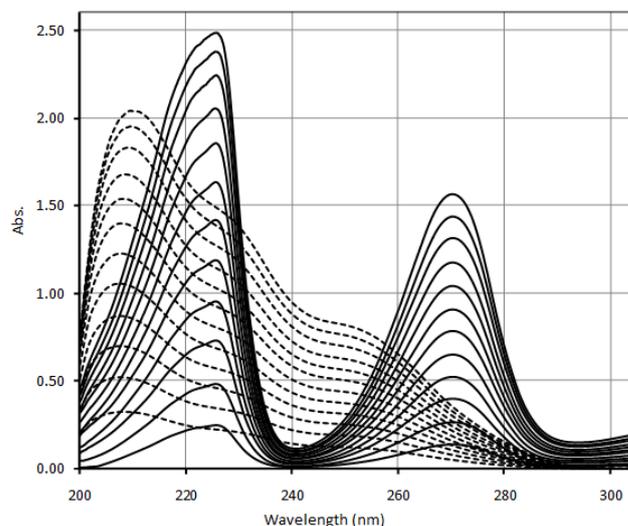


Figure 1 The UV-Absorption spectra of 4.0-26 $\mu\text{g mL}^{-1}$ LOS (---) and 2.0-24 $\mu\text{g mL}^{-1}$ HCT (—) in methanol

3.1. Symlets5 Continuous Wavelet Transform Method (SYM5-CWT)

For the analysis of artificial mixtures and tablets containing LOS and HCT compounds by the SYM5-CWT method, calibration mixtures were prepared as described in the above section, using methanol as a solvent in a linear concentration range of 4.0-26 $\mu\text{g mL}^{-1}$ for LOS and 2.0-24 $\mu\text{g mL}^{-1}$ for HCT. The original UV spectra of these calibration solutions were recorded in the 200-305 nm wavelength range with $\Delta\lambda = 0.1$ nm intervals. The SYM5-CWT method applied to the spectra of LOS and HCT (Figure 2). Regression equation, correlation coefficient and their statistical data were shown in Table 1. The calibration equation of the SYM5-CWT method was validated by using the quantitative assay of artificial mixtures. Recovery results and with relative standard deviation were shown in Table 2.

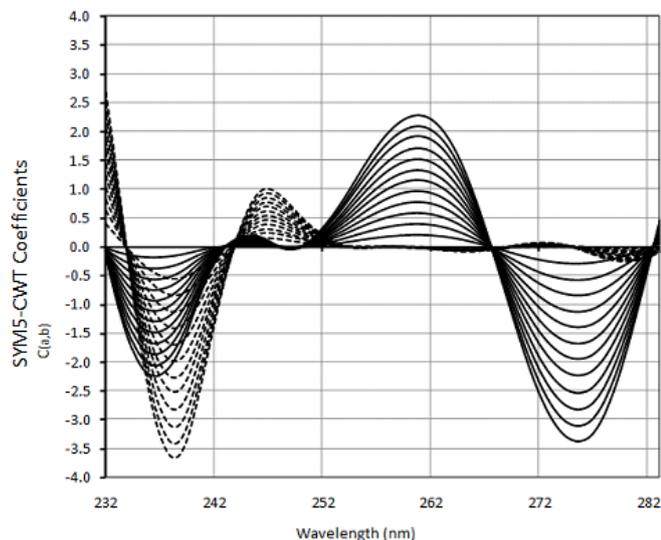


Figure 2 SYM5-CWT spectra obtained by transforming the UV absorption spectra of LOS (---) and HCT (—)

The outcome of the regression analysis obtained are shown in Table 1. The amounts of LOS and HCT in the samples were computed using the calibration equations obtained from the linear regression analysis in Table 1.

Table 1 Statistical outcome for the SYM5-CWT method

Method Parameter	SYM5-CWT	
	LOS	HCT
λ (nm)	247.7	259.1
m	3.63×10^{-2}	8.93×10^{-2}
n	5.06×10^{-4}	1.74×10^{-2}
r	0.9999	0.9998
SE(m)	1.76×10^{-3}	1.90×10^{-4}
SE(n)	1.06×10^{-4}	2.79×10^{-3}
SE(r)	2.54×10^{-3}	4.54×10^{-3}
LOD	0.54	0.35
LOQ	1.81	1.17

3.2. Validation of the Proposed Methods

A validation kit consisting of 16 artificial solutions of dissimilar concentrations in methanol in a working range of 4.0-36.0 $\mu\text{g ml}^{-1}$ for LOS and 2.0-9.0 $\mu\text{g ml}^{-1}$ HCT was produced. This validation set tested the accuracy and precision of the SYM5-CWT method. The results gathered by performing the SYM5-CWT method to artificial

mixtures prepared as a verification set are shown in Table 2.

Table 2 Recovery outcome calculated by using artificial mixtures

Intra-day Results						
	Added ($\mu\text{g mL}^{-1}$)	Found ($\mu\text{g mL}^{-1}$)	SD	RSD	RE	Recovery (%)
LOS	4	3.95	0.09	2.21	-0.90	98.8
	16	15.91	0.14	0.91	-0.37	99.5
	20	21.06	0.15	0.70	0.29	105.3
HCT	4	4.08	0.05	1.27	0.52	101.9
	16	15.71	0.25	1.60	-0.65	98.2
	20	19.75	0.21	1.07	-0.44	98.8
Inter-day Results						
LOS	4	4.02	0.04	0.92	0.38	100.4
	16	15.97	0.29	1.83	-0.75	99.8
	20	20.45	0.52	2.53	1.03	102.2
HCT	4	4.07	0.04	0.89	0.36	101.7
	16	15.90	0.19	1.20	-0.49	99.4
	20	20.28	0.36	1.76	0.72	101.4

Table 3 Intra-day and inter-day outcome by the SYM5-CWT method

SYM5-CWT						
Added ($\mu\text{g mL}^{-1}$)	Found ($\mu\text{g mL}^{-1}$)		Recovery (%)			
	LOS	HCT	LOS	HCT		
4	6	4.02	5.90	100.5	98.4	
6	6	5.93	5.90	98.9	98.3	
8	6	7.97	5.89	99.6	98.2	
10	6	10.01	5.94	100.1	98.9	
12	6	11.91	5.87	99.2	97.8	
14	6	13.90	5.78	99.3	96.4	
16	6	15.89	5.86	99.3	97.7	
18	6	18.17	5.99	100.9	99.9	
20	6	19.92	5.75	99.6	95.8	
22	6	21.92	5.89	99.6	98.1	
24	6	23.83	5.90	99.3	98.4	
26	6	25.74	5.90	99.0	98.4	
24	2	23.94	1.95	99.7	97.7	
24	4	23.95	3.95	99.8	98.6	
24	6	24.02	5.88	100.1	98.1	
24	8	23.89	7.84	99.5	98.0	
24	10	24.07	9.91	100.3	99.1	
24	12	24.00	11.90	100.0	99.2	
24	14	24.18	13.87	100.7	99.1	
24	16	24.20	15.87	100.8	99.2	
24	18	24.30	17.62	101.3	97.9	
24	20	24.43	19.76	101.8	98.8	
24	22	25.18	21.70	104.9	98.6	
24	24	24.85	23.55	103.5	98.1	
				Mean	100.3	98.3
				SD	1.42	0.88
				RSD	1.42	0.87

To appraise the accuracy and precision of the SYM5-CWT method, precision and accuracy survey were applied daily at three dissimilar concentrations and the prepared solutions were used for intra-day and inter-day studies. The results can be seen in Table 3.

Before the SYM5-CWT method was implemented to the commercial tablet preparation, a standard addition technique was used to test the interference effects of tablet excipients on LOS and HCT. The results can be seen in Table 4.

Table 4 Standard addition outcome by the SYM5-CWT method

No.	LOS			HCT		
	2	6	10	2	8	12
	Added ($\mu\text{g mL}^{-1}$)					
	Found ($\mu\text{g/mL}$)					
1	1.99	6.06	9.92	2.07	8.02	11.59
2	2.03	6.42	9.97	2.19	8.03	11.62
3	1.97	6.07	9.95	2.13	8.00	12.04
4	2.02	5.95	10.02	2.07	8.04	11.92
5	2.04	5.87	10.06	2.08	8.03	11.74
	Recovery (%)					
No.	LOS			HC		
1	99.4	101.1	99.2	103.4	100.2	96.6
2	101.6	107.0	99.7	109.5	100.3	96.9
3	98.4	101.1	99.5	106.4	100.0	100.3
4	101.1	99.2	100.2	103.4	100.5	99.3
5	101.9	97.9	100.6	103.8	100.4	97.9
Mean	100.5	101.3	99.8	105.3	100.3	98.2
SD	1.51	3.48	0.53	2.68	0.19	1.62
RSD	1.50	3.44	0.53	2.55	0.19	1.65
RE	0.49	1.25	-0.16	5.28	0.29	-1.81

Recovery and other calculations for LOS and HCT were performed by subtracting the quantity of LOS and HCT from the tablets. These surveys were performed with five replicas at three dissimilar concentration grades.

3.3. Tablet Analysis

The outcomes gathered by applying the proposed technique to the LOS-HCT commercial preparation solutions are shown in Table 5. Accomplished results have been gathered for the quantification of tablets containing LOS and HCT. In the determination of tablets, no interference with the tablet excipients in the determination of the concerned compounds was monitored when the SYM5-CWT method was applied to commercially available tablets.

Table 5 Tablet assay by the SYM5-CWT method (50.0 mg LOS and 12.5 mg HCT per tablet)

Method	SYM5-CWT	
	LOS (mg)	HCT (mg)
Mean	49.70	12.45
SD	0.26	0.10
RSD	0.53	0.79
SE	0.08	0.03
CL	0.16	0.06

4. CONCLUSION

To summarize the study briefly, the SYM5-CWT method we have developed has been successfully applied to the spectral analysis of artificial mixtures and tablet formulations containing LOS and HCT. This method we have developed can be applied without requiring any pre-separation in cases where the spectra overlap each other in the same spectral region as in this study (see Figure 1). It was performed with analytical validation parameters to indicate the validity and applicability of the method. We think that this developed SYM5-CWT method is a promising approach for the quantification of the related compounds.

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The Declaration of Conflict of Interest/ Common Interest

No conflict of interest or common interest has been declared by the authors.

Authors' Contribution

The authors contributed equally to the study.

The Declaration of Ethics Committee Approval

This study does not require ethics committee permission or any special permission.

The Declaration of Research and Publication Ethics

The authors of the paper declare that they comply with the scientific, ethical and quotation rules of SAUJS in all processes of the paper and that they do not make any falsification on the data collected. In addition, they declare that Sakarya University Journal of Science and its editorial board have no responsibility for any ethical violations that may be encountered, and that this

study has not been evaluated in any academic publication environment other than Sakarya University Journal of Science.

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