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Short communication

Determination of lisinopril from pharmaceutical preparations by derivative UV spectrophotometry☆

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1. Introduction

Lisinopril, a lysine analog of the nonsulphydryl angiotensin-converting enzyme (ACE) inhibitor enalapril [1]. It is used for the treatment of hypertension and congestive heart failure [2,3].

Lisinopril can be determined by high performance liquid chromatograph (HPLC) [4,5], miceller electrokinetic chromatography [6], gas chromatography–flame ionization detector [7], spectrometry [8], fluoroimmunoassay [9] and radioimmunoassay [10]. No derivative spectroscopic studies on lisinopril have been found in the literature.

In this study, accurate and precise derivative UV spectrometric method was developed for the determination of lisinopril.

The solvent, the degree of the derivatives, the range of the wavelength and the value of smoothing were determined. As a result of these studies it has been observed that lisinopril was determined by using 1 N NaOH solution with the values obtained from second derivative spectrum which are in the linearity range of 30–2000 ppm between 220 and 340 nm at $\Delta\lambda = 4$.

Developed derivative UV spectrophotometric method was applied the five different pharmaceutical preparations which contain lisinopril. The values obtained from this method were compared with the ones that of obtained from the HPLC method given in the literature. No difference was found.

It has been concluded that developed derivative method is sensitive, accurate, precise and reproducible. This method can be applied pharmaceutical preparations easily [11].

2. Experimental

2.1. Instruments

A Shimadzu UV-2101 with data processing system was used. The second order curves of standard lisinopril were generated between 220 and 340 nm in 1 N NaOH. Shimadzu LC-6A Model

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HPLC with UV detector (SPD-6A) was used for the chromatographic analysis of lisinopril.

2.2. Reagent and solutions

Lisinopril stock solution was prepared by using methanol: H_2O (1:4) for HPLC analysis. The lisinopril standard was obtained from Eczacıaşı Drug Marketing Company. Purity of lisinopril was tested by controlling its melting point, UV and IR spectra. No impurities were found. All analytical and HPLC grade chemicals were supplied by Merck.

2.3. Chromatographic conditions

The 4.6 mm × 20 cm C8 column was used. The flow rate 1.5 ml min^{-1} isocratic elution was employed with the following eluent: 1 g sodium hegzan sulphonate + 800 ml phosphate buffer (pH 2.0) + 200 ml acetonitrile. Detection was effected at 215 nm and the column temperature was 40°C.

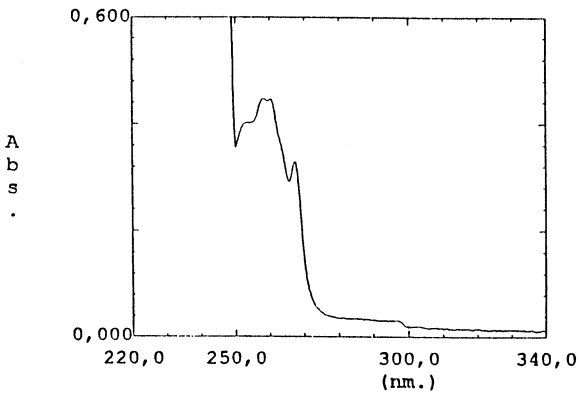


Fig. 1. Zero order spectrum of lisinopril (1000 ppm) in 1 N NaOH.

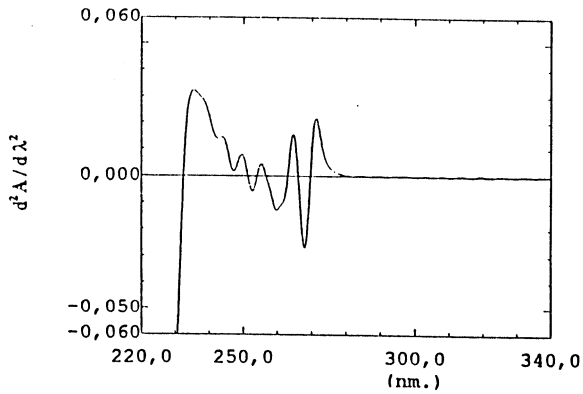
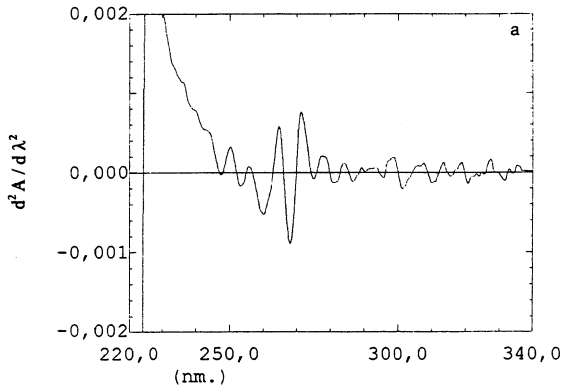


Fig. 2. Second order spectrum of lisinopril (1000 ppm) in 1 N NaOH.



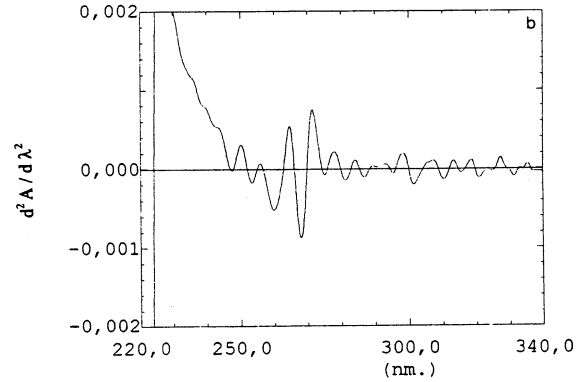


Fig. 3. Second order spectrum of lisinopril (30 ppm) in 1 N NaOH. (a) Without smoothing; (b) smoothing value $\Delta\lambda = 2$.

3. Procedure

Ten tablets of lisinopril was accurately weighted and powdered. An amount corresponding to one tablet was weighted in to a 20 ml volumetric flask, 10 ml 1 N NaOH was added and sonicated. The flask was filled to volume. The second order derivative UV spectra were recorded against 1 N NaOH as reference solution.

HPLC studies were performed by preparing the

Table 1
The results of calibration curves with three methods measured[a]

Method	Calibration curve	R	r^2	S.D. of slope	CV of slope %
Peak to peak	$C = 21632.45A - 8.89$	0.9999	0.9997	338.50	1.70
Peak to zero	$C = 36797.74A - 8.18$	0.9998	09996	774.55	2.16
Tangent	$C = 20242.77A - 9.49$	0.9999	0.9997	310.76	146

[a] S.D., standard deviation, CV, coefficient of variation.

tablets in methanol: H_2O (1:4, v:v) solution. The last concentration of injected solution were 8 ppm.

4. Results and discussion

Derivative spectroscopy is a simple powerful technique for enhancing the resolution. It is also suitable for analyzing of turbid solutions [12].

Lisinopril shows better-defined spectroscopic peaks in the basic solutions than asidic solutions. The stability of lisinopril were tested in acidic and basic solutions. Lisinopril can be decomposed in acidic media as given in literature [13]. For this reason lisinopril solutions were prepared in 1 N NaOH. The original UV spectrum (zero order derivative) of lisinopril has broad absorption bands and maximum at different wavelengths (Fig. 1). But second order derivative UV spectrum has sharper and better defined peaks than the original (Fig. 2). As shown in Fig. 2, the second derivative spectrum offers a new method for determination of lisinopril. Owing to the extent of the noise levels observed in the second derivative spectrum a smoothing function was used. The degree of smoothing depends on wavelengths range. Smoothing is more effective when wavelength range ($\Delta\lambda$) increases. However, an excessive value of $\Delta\lambda$ spoils the spectral resolution. Therefore the optimum value of $\Delta\lambda$ should be determined. The optimum value was found to be $\Delta\lambda = 2$ for smoothing function (Fig. 3).

Quantitations were carried out by preparing calibration curve from seven standard solutions of lisinopril in 1 N NaOH. Second order derivative spectrums were measured by using peak to peak, peak to zero and tangent methods. The values of the slope of the calibration curves of three different measured methods were investigated (Table 1). These results show that three derivative spectrum measuring methods can be used.

The linearity range was found 30–2000 ppm by spectrophotometric method. Developed second derivative UV spectroscopic method was applied to five different commercial tablet preparations. Second derivative spectroscopy present and an

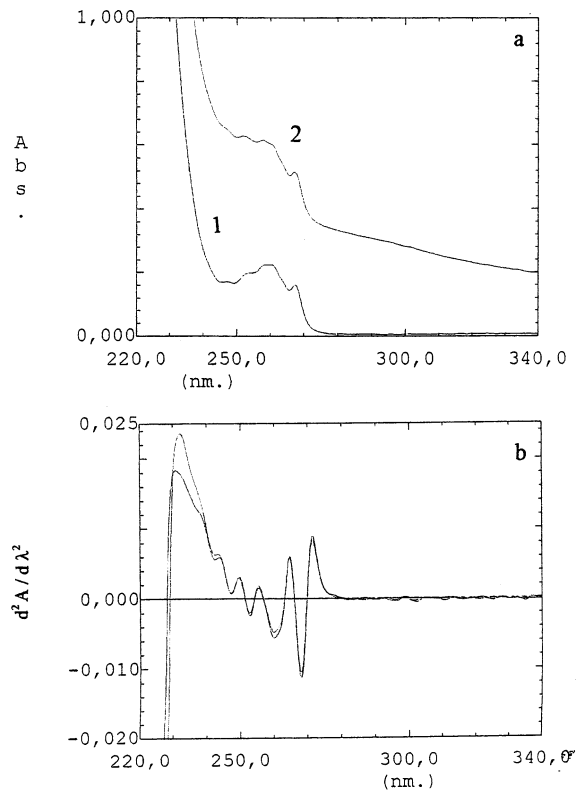


Fig. 4. The spectrum of standard (1) and turbid pharmaceutical preparat solutions (2) of lisinopril (400 ppm) in 1 N NaOH. (a) UV spectrums (zero order); (b) second order spectrums

Table 2
The results of analysis of tablets containing lisinopril by second derivative UV spectroscopic methods[a]

Sample number	Lisinopril found (mg tablet^{-1})				
	Brand A (10 mg)	Brand B (20 mg)	Brand C (20 mg)	Brand D (10 mg)	Brand E (5 mg)
1	9.88	18.19	20.09	10.05	15.20
2	19.98	18.40	20.30	10.10	15.20
3	9.09	18.82	20.09	10.22	15.20
4	9.94	18.19	19.98	10.05	5.20
5	9.52	17.77	19.87	10.05	5.16
6	9.20	18.82	19.98	10.10	5.22
7	10.04	18.19	19.98	10.10	15.20
8	9.99	18.82	19.98	10.10	5.26
9	9.67	18.40	20.09	10.10	5.32
10	10.04	17.87	19.92	10.10	5.20
Found	$x = 9.74 \pm 0.11$ S.D.: 0.5 CV: % 3.63	$x = 18.35 \pm 0.12$ S.D.: 0.38 CV: % 2.08	$x = 20.03 \pm 0.12$ S.D.: 0.12 CV: % 0.60	$x = 10.10 \pm 0.02$ S.D.: 0.05 CV: % 0.49	$x = 5.22 \pm 0.01$ S.D.: 0.04 CV: % 0.84

[a] Results are means of seven separate measurements, x, mean.

Table 3
Results of lisinopril in tablets by derivative UV spectroscopy and HPLC[a]

Sample number	Derivative UV spectroscopic method	HPLC method
A (10 mg)	9.74	10.04
B (20 mg)	18.35	18.82
C (20 mg)	20.03	20.09
D (10 mg)	10.10	10.10
E (5 mg)	15.20	5.16

[a] $P > 0.05$ no significance found between two analysis procedure. Results are means of 10 separate measurements.

advantage over spectrophotometry in the determination of lisinopril in formulations, because pharmaceutical preparations yielded turbid solutions. In the proposed method there was no need clean-up procedure (Fig. 4). Tangent method was used to determine the amount of pharmaceutical preparations. The results were shown in Table 2 and compared with these obtained by the chromatographic method. There was no difference was found statistically between two methods (Table 3).

Recover studies were performed on reference lisinopril standard solutions. Mean recovery and relative standard deviation were found to be 103.1 and 3.79%.

Chromatographic analysis of lisinopril in pharmaceuticals has time consuming analysis. The proposed method may be preferred to chromatography to analyze of lisinopril from pharmaceuticals.

It has been concluded that developed second derivative UV spectroscopic method is simple, rapid, sensitive, accurate and reproducible for the rutin determination of lisinopril in tablets.

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