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Short communication

Determination of Lansoprazole in pharmaceutical dosage forms by two different spectroscopic methods

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Abstract

Two different ultraviolet (UV) spectroscopic methods were developed for determination of Lansoprazole in pharmaceutical dosage forms. The solutions of the standard and the sample were prepared in 0.1 M NaOH and phosphate buffer pH 6.6. Both UV spectrophotometric and derivative spectroscopic techniques were applied. Second-order derivative spectra were generated between 200 and 400 nm at $N = 9$, $\Delta\lambda = 31.5$. The linear range for the UV spectrophotometric method was 3.0–25.0 μg ml^{-1} and that for the derivative spectroscopic method was 0.5–25.0 μg ml^{-1}. The developed methods were applied to three different pharmaceutical preparations. The percentage recovery was 100.2%. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Lansoprazole; Ultraviolet spectrophotometry; Derivative spectroscopy; Pharmaceutical preparations

1. Introduction

Lansoprazole (**L**), (±)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]-sulphinyl]benzimidazole, is a new (H^+, K^+)-ATPase inhibitor (Fig. 1). It has been demonstrated to be effective in the treatment of duodenal and gastric ulcers, reflux oesophagitis and Zollinger–Ellison Syndrome [1–3]. Current evidence indicates that **L** should be considered as an alternative to omeprazole and H_2-receptor antagonists in the short-term treatment of duodenal and gastric ulcer, and reflux oesophagitis, particularly in light of the potential of **L** for faster healing and more rapid symptom resolution [4]. **L** is acid labile and thus administrated in the form of enteric coated granules in capsules [4].

In the literature, one spectrophotometric [5] and few high performance liquid chromatographic (HPLC) methods are proposed for the analysis of **L** in pharmaceuticals [6] and biological materials [7–11].

In this study, ultraviolet (UV) spectroscopic methods were developed for the analysis of **L**. Both original UV and second-order derivative UV spectroscopic methods were investigated. All stud-

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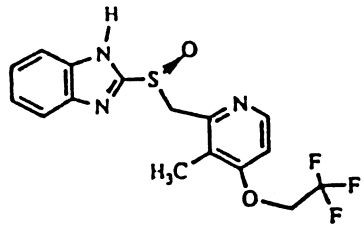

Fig. 1. Chemical structure of Lansoprazole.

ies were done by these two methods. Proposed methods are simple, easy to use and cheaper than chromatographic methods. Also, the sensitivity of the methods were found better than spectrophotometric [5] and HPLC [6] methods. The two developed methods were applied to three different commercial preparations of capsules containing enteric coated granules, and the data of the two methods were compared. Since the excipients did not interfere with quantitation of **L**, the methods do not include any extraction steps. In addition, there was no spectral interaction in the analysis of pharmaceutical preparations by these methods. That is why quantifications were made by using a

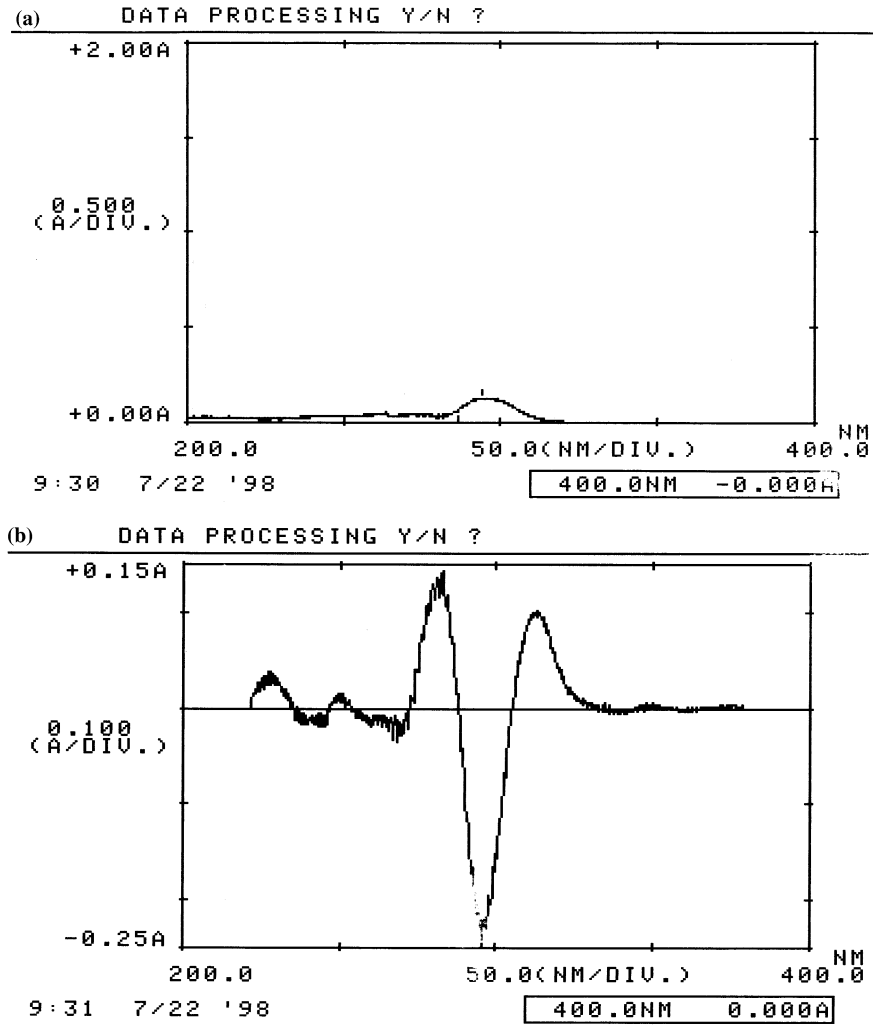

Fig. 2. (a) Zero-order derivative spectrum of 3.0 μg ml^{-1} Lansoprazole solution; (b) second-order derivative spectrum of 3.0 μg ml^{-1} Lansoprazole solution.

Table 1
Features of the calibration curves of two spectroscopic methods

Features	Zero-order spectroscopy	Second-order spectroscopy
Regression equation	$A = 3.47 \times 10^{-2}C + 4.35 \times 10^{-2}$	$A = 7.1 \times 10^{-2}C + 2.43 \times 10^{-2}$
Standard error of slope	2.94×10^{-4}	2.10×10^{-3}
Standard error of intersept	3.70×10^{-3}	6.47×10^{-4}
Correlation coefficient	0.9988	0.9999
Determination coefficient	0.9976	0.9998
Linear range (μg ml^{-1})	3.0–25.0	0.5–25.0
Signal-to-noise ratio	>3	3.65

calibration curve, which is easier and quicker than the standard addition technique. These features saved time for routine analysis.

2. Experimental

2.1. Apparatus

A Shimadzu UV-160 recording double-beam UV–visible spectrophotometer with data processing capacity was used. UV spectra of reference and test solutions were recorded in 1 cm quartz cells at a scan speed of 50 nm min^{-1} and a fixed slit width of 3 nm, as in a previous study for omeprazole [12]. The second-order derivative curves were generated over the 200–400 nm range ($N = 9$, $\Delta\lambda = 31.5$ nm)

2.2. Reagents and solutions

The Lansoprazole standard was supplied by the Central Institute of Hygiene of Turkey. It was tested for purity by controlling its melting point, UV and infrared spectra and no impurities were found. All other chemicals used in the experiments were the products of E. Merck and of analytical grade. All solutions were prepared with distilled water. Lansoprazole stock solution (1000 μg ml^{-1}) was prepared by dissolving 100.0 mg **L** in 60 ml 0.1 N NaOH and adjusting to 100 ml with phosphate buffer pH 6.6. Dilutions were made with 0.01 N NaOH solution. The mixture of 0.1 N NaOH and phosphate buffer pH 6.6 (3:2) was used as reference solution.

2.3. Procedure

The contents of 10 hard gelatine capsules were weighed and powdered. The average of one capsule content was calculated. A sample equivalent to one capsule was weighed and transferred to a 100 ml volumetric flask. Sixty millilitres of 0.1 N NaOH was added and the flask was sonicated for 20 min, then filled to volume with phosphate buffer pH 6.6. Appropriate dilutions were made in a linear range with 0.01 N NaOH. The spectra were recorded against the reference solution.

3. Results and discussion

Lansoprazole is acid labile, so solutions were prepared in 0.1 N NaOH and phosphate buffer pH 6.6. Dilutions were made both by water and by 0.01 N NaOH. Solutions, diluted by 0.01 N NaOH, have shown higher absorbance than that of water. Thus, 0.01 N NaOH was used for dilutions.

Fig. 2 shows the original (zero-order) and second-order derivative UV spectra of **L** solution. Both spectra could be used for the determination of this drug. In the original spectrum, **L** shows a single well-defined peak at 296 nm. The second-order derivative spectrum has three peaks and the opposite peak at 296 nm could be useful for determination of **L**. In the derivative method, odd-numbered derivatives are of most use in determining the exact points of absorbance maxima of the original spectrum and, hence, the qualitative properties of the substance under investigation; even-numbered derivatives are helpful in quantitative determinations [13]. Owing to extent

of noise levels observed in the second-order derivative spectrum, a smoothing function was used. The derivative wavelength difference ($\Delta\lambda$) depends on the measuring wavelength range and the key entry N (a kind of smoothing factor). Practical derivative techniques include some degree of low-pass filtering or smoothing to control the increase in noise. The process of smoothing involves a convolution of the data series with a smoothing function consisting of a set of weighting coefficients. The various smoothing methods differ only in the way that the coefficients are calculated. The simplest type of smooth is the equally weighted sliding average, in which the weighting coefficients are equal. Each point in the smoothed series is the simple average of N adjacent points in the original series, where N is the smooth width. The value of the smoothing coefficients is therefore simply $1/N$ [14]. Various N values were tested (Fig. 3). Optimum results were obtained in the measuring wavelength range 200–400 nm and $N = 9$ ($\Delta\lambda = 31.5$ nm).

In quantitative analysis, the calibration curves were plotted for both zero- and second-order derivative spectra. The slope of the calibration curve of the second-order derivative spectrum is bigger than that of the original spectrum. Thus, it is clearly said that the sensitivity is better in derivative spectroscopy.

The regression equation of the calibration curve of the zero-order spectrum was $y = 3.47 \times 10^{-2}X + 4.35 \times 10^{-2}$, where y is the absorbance and X is the concentration of **L**. Standard errors of the slope and intercept were 2.94×10^{-4} and 3.7×10^{-3}, respectively. The correlation coefficient of this curve was 0.9988 and $r^2 = 0.9976$.The linear range was 3.0–25.0 μg ml^{-1}. The regression equation of the calibration curve of the second-order derivative spectrum was $y = 7.1 \times 10^{-2}X + 2.43 \times 10^{-2}$, where y is the

Table 2
The results of pharmaceutical preparations containing Lansoprazole, analyzed by two spectroscopic methods[a]

Method	Number	Brand A	Brand B	Brand C
Zero order	1	30.19	31.46	30.80
	2	30.52	30.57	30.86
	3	31.64	30.35	30.25
	4	31.92	30.85	31.09
	5	30.95	31.26	30.78
	6	31.18	31.31	30.59
	7	31.04	31.07	31.15
		$X = 31.06 \pm 0.226$	$X = 30.98 \pm 0.155$	$X = 30.79 \pm 0.115$
		SD = 0.60	SD = 0.44	SD = 0.31
		$V = 1.93\%$	$V = 1.33\%$	$V = 0.99\%$
Second order	1	30.25	31.51	30.89
	2	30.50	31.28	30.98
	3	31.71	30.60	30.41
	4	31.84	30.65	30.81
	5	31.01	30.81	30.60
	6	30.99	31.42	30.68
	7	31.02	31.11	30.71
		$X = 31.05 \pm 0.219$	$X = 31.05 \pm 0.140$	$X = 30.73 \pm 0.072$
		SD = 0.58	SD = 0.37	SD = 0.19
		$V = 1.86\%$	$V = 1.19\%$	$V = 0.62\%$
		$t_c = 0.032$, $t_T = 2.45$	$t_c = 0.330$, $t_T = 2.45$	$t_c = 0.441$, $t_T = 2.45$
		$p > 0.05$	$p > 0.05$	$p > 0.05$

[a] Results are means of 10 separate measurements and each capsule contains theoretically 30 mg of Lansoprazole. X, Mean; SD, standard deviation; V, relative standard deviation $(SD/X) \times 100$; t_c, $t_{calculated}$; t_T, $t_{tabulated}$.

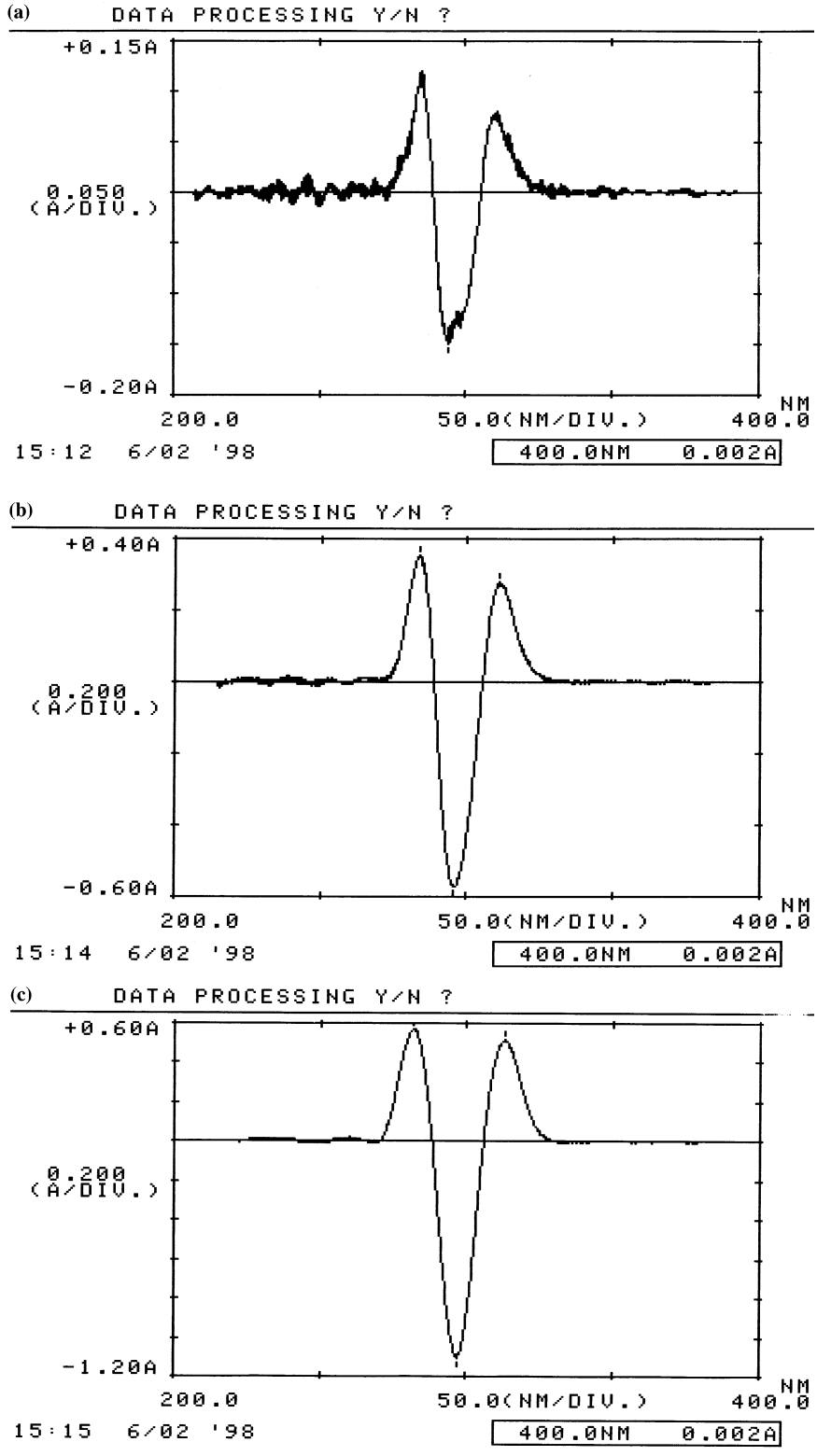

Fig. 3. Second-order derivative spectra of 15.0 μg ml^{-1} Lansoprazole solution. (a) $N = 3$ ($\Delta\lambda = 10.5$ nm), (b) $N = 6$ ($\Delta\lambda = 21.0$ nm), (c) $N = 9$ ($\Delta\lambda = 31.5$ nm).

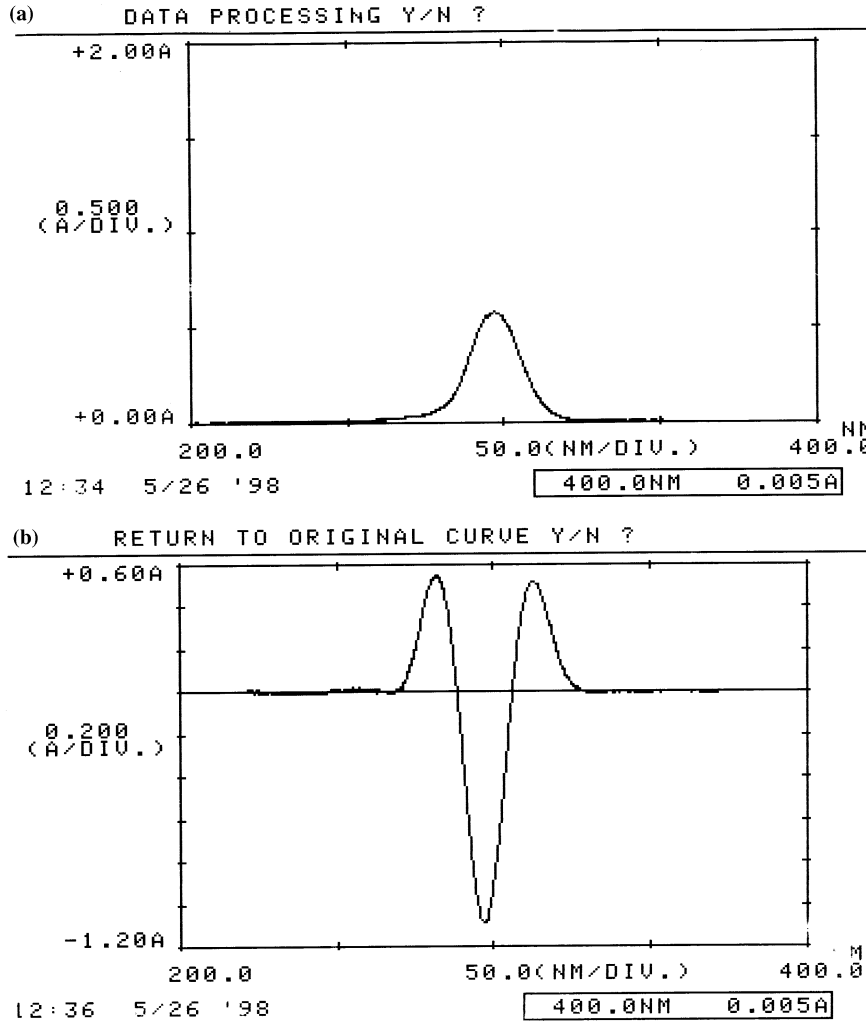

Fig. 4. (a) Zero-order, and (b) second-order derivative spectrums of Lansoprazole in pharmaceutical preparation.

amplitude of the second derivative spectrum and X is the concentration of **L**. Standard errors of slope and intercept were 2.1×10^{-3} and 6.47×10^{-4}, respectively. The correlation coefficient of this curve was 0.9999 and $r^2 = 0.9998$. The linear range was 0.5–25.0 μg ml^{-1}. The signal-to-noise ratio was found to be 3.65 in 0.5 μg ml^{-1} **L** solution. These values were summarized in Table 1. The limit of quantification (LOQ) for **L**, was established by analysing nine different standard solutions containing the lowest concentration on the standard curves (3.0 μg ml^{-1} **L** for zero-order and 0.5 μg ml^{-1} **L** for second-order spectroscopic methods). The relative standard deviations were 1.45 and 1.08%, respectively. The limit of detection (LOD) was considered as the concentration of **L** giving a signal-to-noise ratio greater than 3:1 [15].

Developed methods were applied to three different commercial hard gelatine capsule preparations, containing enteric coated granules. A summary of the results is shown in Table 2. The results of two spectroscopic methods for the same preparations were compared by Student's t-test.

The calculated (experimental) t-values did not exceed the tabulated (theoretical) values in the test, indicating that there was no significant difference between the methods compared (Table 2).

In order to detect interactions of the excipients in this method, the standard addition technique was applied to one brand of preparations analyzed by the calibration curve. The regression equations of standard addition curves were found to be $y = 3.47 \times 10^{-2}X + 0.252$ for original UV spectrophotometry and $y = 7.1 \times 10^{-2}X + 0.512$ for second-order derivative spectroscopy. Since the slopes of the standard calibration and standard addition curves of the two methods were identical, it has been concluded that there was no spectral interaction in the analysis of pharmaceutical preparations. Therefore, the calibration curve, which is easier and quicker than for the standard addition technique, was used in quantitative analysis.

Comparision of the zero- and second-order derivative spectra of **L** in standard (Fig. 2) and drug formulation (Fig. 4) solutions showed that the wavelength of maximum absorbance did not change. It has been decided that excipients did not interfere with quantitation of **L** in those methods.

Recovery studies were conducted, adding a known quantity of the standard to the placebo solution and calculating the percentage recovery in each case. Mean recovery and relative standard deviation were found to be 100.2 and 1.23%, respectively (Table 3). The percentage recovery of **L** was calculated by comparing the found and added concentrations [(mg found/mg added) × 100].

Table 3
Recovery data of Lansoprazole obtained by derivative spectroscopic method ($n = 6$)

Added (mg)	Found (mg)	Recovery (%)
30	30.24	100.8
30	30.45	101.5
30	29.61	98.7
30	30.21	100.7
30	29.79	99.3
30	30.48	101.6
30	29.64	98.8
		$X = 100.2$
		SD = 1.24
		$V = 1.23\%$

The spectrophotometric method in the literature [5], involved the reaction of **L** with p-dimethylamino benzaldehyde, which caused the contamination problems and loss of sample according to the yield of reaction.

The liquid chromatographic (HPLC) method for analysis of **L** in pharmaceuticals [6] needs expensive equipment and material such as columns and HPLC grade solvents, and also includes time-consuming extraction steps to eliminate the excipients. The linear range of the method is 10.0–50.0 mg ml^{-1}. Consequently, the proposed methods seemed to be more sensitive than the HPLC method. In addition, the described methods are direct methods for analysis of **L**, and do not include any extraction process to eliminate the excipients. They also do not need any expensive equipment. The methods can be easily applied in routine practices made in any laboratory possessing a spectrophotometer with a derivative accessory. Spectrophotometry is a considerable time saver when compared with HPLC and the global cost of analysis is less than a chromatographic method.

Therefore, the methods proposed are sensitive, saved time, cheap, easy to use and might be preferred to HPLC and the spectrophotometric methods in the literature.

It has been concluded that the two spectroscopic methods developed, are simple, easy to apply, rapid, sensitive, accurate, precise and reproducible for the determination of **L** in capsules containing enteric coated granules.

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