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Determination of omeprazole in pharmaceuticals by derivative spectroscopy[1]

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Abstract

A new derivative UV spectroscopic method was developed for the analysis of omeprazole in borate buffer (pH 10.0; 0.1 M). Second derivative spectra were generated between 200–400 nm at $N = 9$, $\Delta\lambda = 31.5$. The linearity range for values obtained from second derivative spectra was 0.2–40.0 μg ml^{-1}. The developed method was applied to five different commercial preparations of hard gelatin capsules containing enteric coated granules. The relative standard deviations were found to be 2.24% (brand A), 1.87% (brand B), 2.80% (brand C), 4.55% (brand D) and 1.09% (brand E). The data were compared with ones obtained from the polarographic method given in the literature and no difference was found statistically. © 1997 Elsevier Science B.V.

Keywords: Omeprazole; Derivative UV spectroscopy; Pharmaceutical hard gelatin capsules

1. Introduction

Omeprazole, 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1*H*-benzimidazole (Fig. 1), is a substituted benzimidazole that effectively suppresses gastric acid secretion by inhibiting the gastric proton pump (H^+, K^+-ATPase) [1–3]. It has been reported to have improved clinical efficacy in the control of both peptic ulcer [4,5] and reflux oesophagitis [6]. It is also effective in the treatment of Zollinger–Ellison Syndrome [7]. Omeprazole can be determined by high performance liquid chromatography (HPLC) [8,9], high performance thin layer chromatography (HPTLC) [10], polarography [11] and spectrophotometry [12]. No derivative spectroscopic studies on omeprazole have been found in the literature.

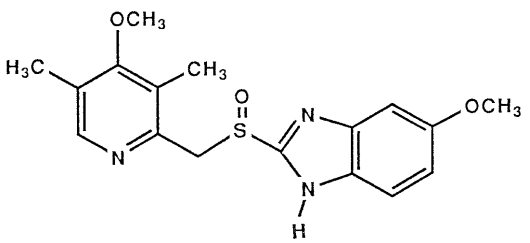

Fig. 1. Chemical structure of omeprazole.

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[1] This work was taken partly from the MSc thesis of A. Koçer.

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This paper describes a method using second derivative UV spectroscopy for the determination of omeprazole. The method was applied to pharmaceutical preparations that were produced by five different companies. The data were compared with those obtained by the polarographic method given in the literature [11].

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 fixed slit width of 3 nm. The second order derivative curves were generated over the 200 to 400 nm range ($N = 9$, $\Delta\lambda = 31.5$).

The polarographic experiments were performed using a PAR Model 174 A polarograph with a PAR Model 303 A static mercury drop electrode in the DPP mode [13]. Modified PAR glass polarographic cells were used.

2.2. Reagents and solutions

The omeprazole standard was obtained from the Central Institute of Hygiene of Turkey. This substance was tested for purity by controlling its melting point, UV and IR spectra and no impurities were found.

In order to prepare omeprazole stock solution (1000 μg ml^{-1}), 1.00 g omeprazole was accurately weighed, dissolved in 100 ml ethanol, and adjusted to 1000 ml with borate buffer (pH 10.0; 0.1 M). Standard solutions over the range of desired concentrations were prepared by appropriate dilutions of the stock solution in borate buffer.

Borate buffer was prepared by dissolving 6.18 g boric acid in 1000 ml 0.1 M KCl solution. pH was adjusted to desired value with 0.1 M NaOH.

All solutions were prepared with distilled water and analytical grade chemicals, supplied by Merck.

2.3. Procedure

The average mass of the contents of ten hard gelatin capsules was determined. The capsule contents were powdered and an amount corresponding to one capsule content was weighed in to a 100 ml volumetric flask, 10 ml ethanol was added and the flask was sonicated for 15 min. The flask was filled to volume with the borate buffer. Appropriate dilutions were made in the range of 0.2–40.0 μg ml^{-1}. The second order derivative UV spectra were recorded against borate buffer as reference solution.

The omeprazole content per hard gelatin capsule, was calculated by referring to a calibration curve obtained by using standard solutions of omeprazole at concentrations of 0.2–40.0 μg ml^{-1} in borate buffer (pH 10).

Polarographic studies were performed as described previously [11].

3. Results and discussion

The results of the stability studies of omeprazole showed that it could be stored at pH 7.5–10.0 for 4 days at room temperature without any degradation [14]. For this reason omeprazole solutions were prepared in borate and phosphate buffers (pH 8.0, 9.0 and 10.0). Among the three buffer systems tested the best-defined spectra were observed in borate buffer (pH 10.0). As shown in Fig. 2a, the original (zero order derivative) UV spectrum of omeprazole has broad absorption bands between 250–350 nm. In contrast second order derivative UV spectrum (Fig. 2b) has sharper and better-defined peaks than the original.

Derivative spectroscopy offers a simple alternative approach for the enhancement of sensitivity and specificity in the analysis of pharmaceuticals. In derivative spectroscopy, fine structural features are sharpened to give improved resolution of overlapping and potentially greater sensitivity [15].

As shown in Fig. 2b, the second derivative spectrum offers a new method for determination of omeprazole. Owing to the extent of the noise

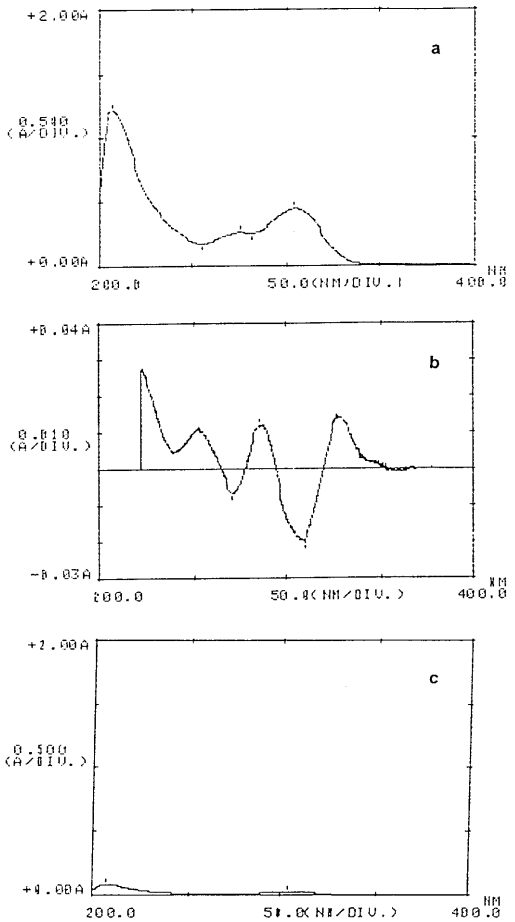

Fig. 2. (a) Zero order spectrum of 10.0 μg ml^{-1} omeprazole; (b) second order derivative spectrum of 1.0 μg ml^{-1} omeprazole; (c) zero order spectrum of 1.0 μg ml^{-1} omeprazole in borate buffer (pH 10.0; 0.1 M).

levels observed in the second 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). Generally the noise decreases with an increase of $\Delta\lambda$, thus decreasing the fluctuation in a derivative spectrum. However an excessive value of $\Delta\lambda$ deteriorates the spectral resolution. Therefore, the optimum value of $\Delta\lambda$ should be determined in consideration of the noise and resolution according to the spectral pattern and the sample concentration. Various N values were tested, optimum results were obtained in the measuring wavelength range of 200–400 nm and $N = 9$ ($\Delta\lambda = 31.5$ nm) (Fig. 3). Quantitations were carried out by preparing calibration curve from standard solutions of omeprazole in borate buffer (pH 10.0).

The regression equation was $y = 5.02 \times 10^{-2}x + 9.90 \times 10^{-3}$ where x is the concentration in μg ml^{-1} and y is absorbance value of peak to peak measurements between wavelengths 303 and 310 nm of the second order derivative spectra of each of ten solutions ($n = 10$). Standard errors of slope and intercept were 6.56×10^{-4} and 4.94 ×

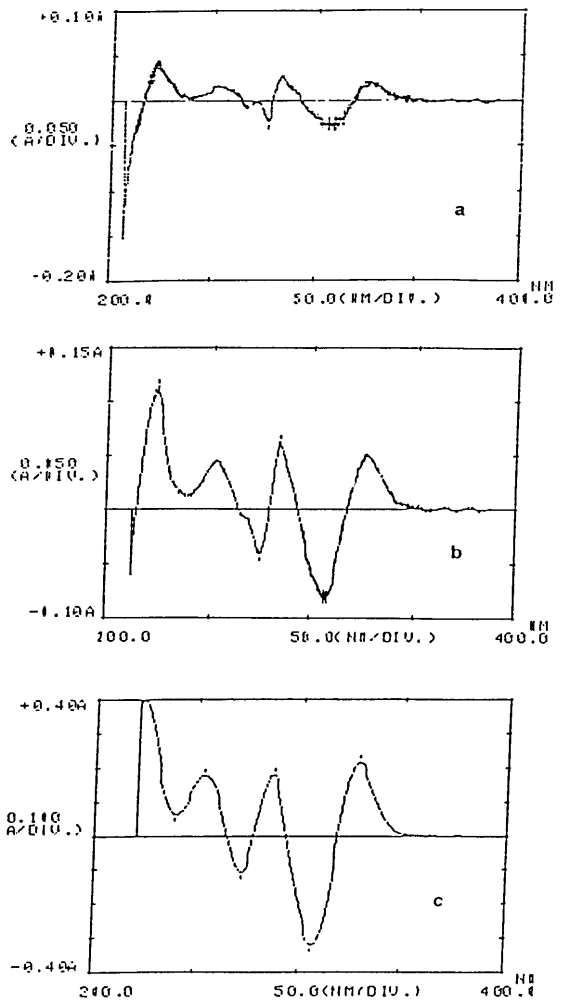

Fig. 3. Second derivative spectrums of 10.0 μg ml^{-1} omeprazole in borate buffer (pH 10.0, 0.1 M); (a) $N = 3$ ($\Delta\lambda = 10.5$ nm), (b) $N = 5$ ($\Delta\lambda = 17.5$ nm), (c) $N = 9$ ($\Delta\lambda = 31.5$ nm).

Table 1
The results of analysis of pharmaceutical preparations containing omeprazole by using second derivative UV spectroscopic method[a]

Sample number	Omeprazole found (mg capsule^{-1})				
	Brand A	Brand B	Brand C	Brand D	Brand E
1	19.11	20.08	20.08	21.06	19.76
2	19.11	19.76	21.06	20.78	19.76
3	19.11	20.41	19.11	20.78	19.76
4	20.08	20.41	21.06	22.81	20.41
5	18.54	21.06	20.74	22.81	20.41
6	18.94	19.76	20.08	22.53	20.08
7	18.94	20.08	20.08	22.53	20.08
8	18.54	20.08	20.41	22.81	20.08
9	18.94	20.08	20.41	20.78	20.08
10	18.94	20.08	20.41	20.78	20.08
	X: 19.03 ± 0.14	X: 20.18 ± 0.12	X: 20.34 ± 0.18	X: 21.77 ± 0.31	X: 19.98 ± 0.06
	S.D.: 0.43	S.D.: 0.38	S.D.: 0.57	S.D.: 0.99	S.D.: 0.22
	V: % 2.24	V: % 1.87	V: % 2.80	V: % 4.55	V: % 1.09

X, mean; S.D., standard deviation; V, relative standard deviation.
[a] Results are means of 10 separate measurements and each capsule contains, theoretically, 20 mg of omeprazole.

10^{-4}, respectively. The correlation coefficient of the calibration curve was 0.9999. The concentration range for compliance with Beer's Law was 0.2 — -40.0 μg l^{-1}. The signal to noise ratio was found as 8.1 in 0.2 μg ml^{-1} omeprazole solution.

Developed second derivative UV spectroscopic method was applied to five different commercial hard gelatin capsule preparations, containing enteric coated granules. Second derivative spectroscopy presents an advantage over spectrophotometry in the determination of omeprazole in formulations, because pharmaceutical preparations yielded turbid solutions. In the proposed method there was no need for centrifugation to make the solution clear. A summary of the results is shown in Table 1. When the results were compared with those obtained by the polarographic method no difference was found statistically (Table 2).

Recovery studies in this method were performed on the synthetic mixture prepared by adding accurately weighed amounts of omeprazole to the excipient mixture. Mean recovery and relative standard deviation were found to be 100.7% and 2.96%.

In order to detect interactions of the excipients in this method, the standard addition technique was applied to the same preparations which analyzed by the calibration curve. In the standard addition method, increasing amounts of omeprazole were added to five different tubes, containing the same amount of sample. The second derivative spectrum of each tube was recorded. Absorbance values of peak to peak measurements were plotted against the omeprazole concentrations added to the samples. The amount of omeprazole in the sample was calculated from the intercept. As shown in Table 3, there is no difference between the relative standard deviations of two techniques. The regression equation of standard addition curve was found as $y = 5.01 \times 10^{-2}x + 5.16 \times 10^{-2}$. Since the slopes of the standard and standard addition curves were identical, it has been concluded that there was no spectral interaction in the analysis of pharmaceutical preparations.

Comparision of the original and second derivative spectra of omeprazole in standard (Fig. 2a, b) and drug formulation (Fig. 4a, b) solutions showed that the wavelength of maximum absorbance did not change. Therefore it has been decided that excipients did not interfere with the quantitation of omeprazole (The original spectra were taken after centrifugation).

Chromatographic analysis of omeprazole in pharmaceuticals includes a time consuming extraction step to eliminate the excipients.

Polarographic analysis takes time to reach equilibrium between supporting electrolyte and electrodes, and deoxygenation of supporting electrolyte. Besides, using standard addition method to calculate omeprazole in pharmaceuticals also extends the analysis time.

Since there is no need to eliminate the excipients and to use time consuming procedures such as standard addition method, the proposed method may be preferred to chromatography and polarography.

The linearity range in the spectrophotometric method reported in the literature [12] (6.0–25.0 μg ml^{-1}), was narrower than that of developed method (0.2–40.0 μg ml^{-1}).

The regression equation of the calibration curve, which was obtained by using original spectrum on the same instrument, was found as $y =$

Table 2
The results of omeprazole-containing commercial capsules analysed by derivative UV spectroscopy and differential pulse polarography (for Brand C)

Sample number	Derivative UV spectrophotometry	
1	20.08	
2	20.78	X: 20.52 ± 0.17
3	20.74	S.D.: 0.46
4	20.81	S^2 :0.2116
5	19.76	V: % 2.25
6	20.41	
7	21.06	
	Differential pulse polarography	
1	20.11	
2	20.80	X: 20.51 ± 0.17
3	20.46	S.D.: 0.43
4	20.84	S^2: 0.1949
5	19.94	V: % 2.10
6	20.28	
7	21.15	
$T_C = 3.0$		$T_T = 1.94$(p = 0.05)

n, number of the sample; X, mean; S.D., standard deviation; S^2, variance; V, relative standard deviation.
T_C, $T_{Calculated}$; T_T, $T_{Tabulated}$.

Table 3
The results of analysis of pharmaceutical capsule preparations, containing omperazole, obtained from standard addition and calibration curve methods

Sample number	Results of standard deviation method (mg $capsule^{-1}$)	
1	21.66	
2	20.78	
3	21.53	X: 21.12 ± 0.19
4	20.78	S.D.: 0.51
5	20.78	V: % 2.43
6	21.78	
7	20.53	
	Results of calibration graph method (mg $capsule^{-1}$)	
1	21.63	
2	20.76	
3	21.60	X: 21.09 ± 0.19
4	20.70	S.D.: 0.51
5	20.66	V: % 2.43
6	21.68	
7	20.60	

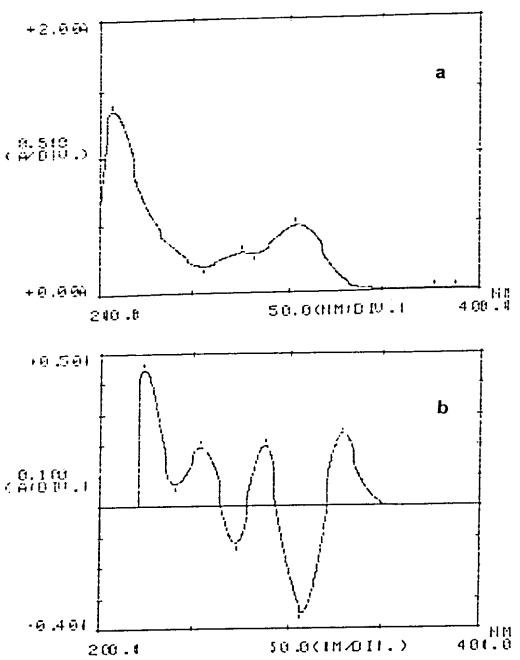

Fig. 4. (a) Zero order spectrum; (b) second order derivative spectrum of omeprazole in pharmaceutical preparation.

$3.24 \times 10^{-2}x + 5.04 \times 10^{-3}$. The correlation coefficient and the linearity range were found as 0.9986 and 0.8–40.0 μg ml^{-1}, respectively.The slope of this curve is lower than that of second derivative spectroscopic method (5.02×10^{-2}). The original and the second derivative spectra of 1.0 μg ml^{-1} omeprazole solutions are shown in Fig. 2c and b. Consequently the proposed method is seemed to be more sensitive than conventional spectrophotometric method.

It has been concluded that, developed second derivative UV spectroscopic method is simple, rapid, sensitive, accurate, precise and reproducible for the determination of omeprazole in capsules, containing enteric-coated granules.

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