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A SIMPLE SPECTROFLUORIMETRIC METHOD FOR THE DETERMINATION OF LOSARTAN IN SOME TABLET DOSAGE FORMS

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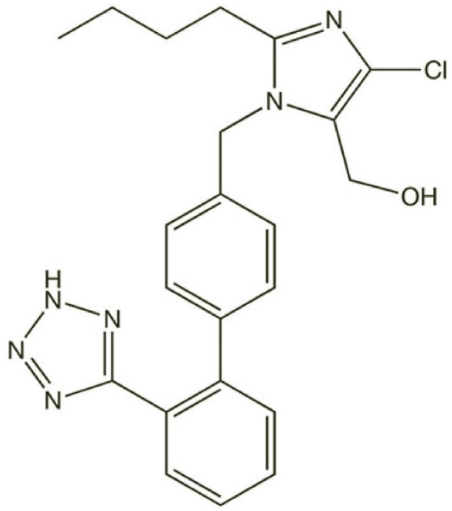
A very simple and sensitive spectrofluorimetric method was developed for the direct determination of losartan in some commercial tablets. The suggested method is based on the linear relationship between 0.1–5.0 μg/ml of losartan and its fluorescence intensity at 400 nm in acidic medium. The detection limit and relative standard deviation (for ten repetitive measurements of 2.0 μg/ml) were obtained as 12.0 ng/ml and 1.35%, respectively. The recommended method was successfully applied for the determination of losartan in three types of commercial tablets from different brands.

Keywords: *losartan, spectrofluorimetry, tablet.*

Introduction. Hypertension or high blood pressure, sometimes called arterial hypertension, is an illness that affects millions of people all over the world. It is a chronic medical condition in which the blood pressure in the arteries is elevated. High blood pressure can cause serious consequences such as cardiovascular problems and kidney diseases. The best way to prevent this disease is a change in lifestyle such as a healthy diet, engaging in sports, etc. Physicians and scientists try to make more powerful and effective drugs for the treatment of hypertension [1]. Among the common drugs, losartan potassium is a selective and powerful antihypertensive recommended for oral use [2]. Losartan, chemically described as 2-butyl-4-chloro-1-{[2′-(1H-tetrazol-5-yl)(1,1′-biphenyl)-4-yl]methyl}-1H-imidazol-5-methanol



is an angiotensin II receptor (type AT1) antagonist. Losartan has superior efficacy compared with previous peptide receptor antagonists and angiotensin converting enzyme (ACE) inhibitors because of its high specificity, selectivity, and tolerability [3]. Several methods have been reported for the analysis of losartan potassium and its degradation products such as conductometry [4], voltammetry [5], high-performance liquid chromatography (HPLC) [6], high-performance thin-layer chromatography

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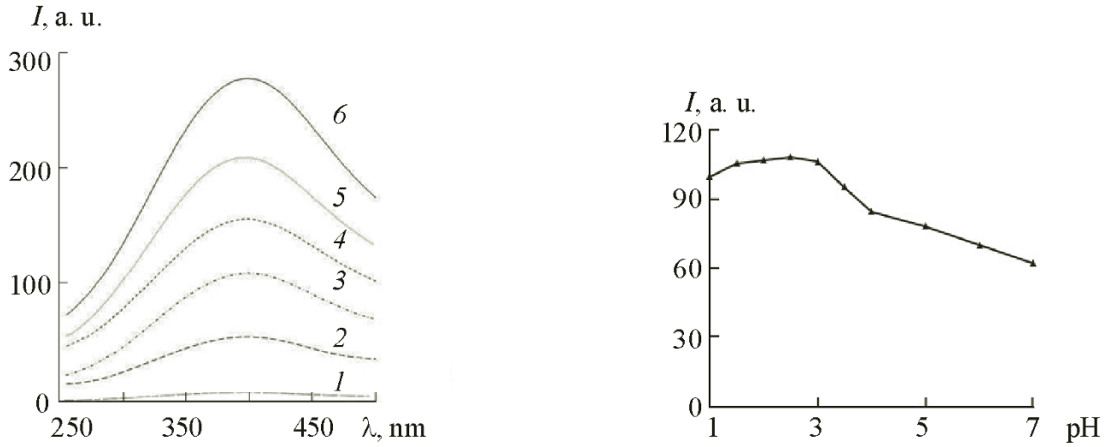

Fig. 1. The fluorescence spectrum of losartan; amount of losartan 0.1 (1), 1 (2), 2 (3), 3 (4), 4 (5), and 5 μg/ml (6); pH 2.0; temperature 10°C.

Fig. 2. The effect of pH on the fluorescence intensity; amount of losartan 2.0 μg/ml, temperature 10°C.

(HPTLC) [7], and spectrophotometry [8]. All of the mentioned methods use a reagent or ligand and sophisticated apparatus, but our suggested method is direct (without the use of any reagent) using a simple spectrofluorimeter. In this paper, a direct method based on the relationship between the fluorescence intensity of losartan at 400 nm and its concentration was applied for the determination of losartan content. This method is a simple, convenient, and low-cost spectrofluorimetric method for the determination of losartan in some tablet samples from different companies.

Experimental. A stock solution of losartan potassium (100 μg/ml) was prepared by dissolving 0.01 g of its pure form (Merck, Darmstadt, Germany) in a 100.0 ml volumetric flask and diluting to the mark with deionized water. KH_2PO_4/H_3PO_4 (Merck, Darmstadt, Germany) buffer solution was used for pH adjustment (about 2.0). HCl (37%), HNO_3 (65%), and NaOH (97%) were purchased from Merck (Darmstadt, Germany).

All fluorescence measurements were recorded on a Shimadzu (Tokyo, Japan) RF 5301 spectrofluorimeter equipped with a xenon lamp and a quartz cell (1.0 cm). Optimum operating parameters for the spectrofluorimeter are as follows: spectrum type: emission; excitation wavelength 247 nm; maximum emission wavelength 400 nm; spectral resolution 0.2 nm; response time 2 s. The pH measurements were carried out with a Metrohm 827 pH-meter (Switzerland) equipped with a combined glass–calomel electrode. The samples were weighed using a Mettler (Switzerland) AE-160 electronic balance. Also, a Sonorex Digitec DT 255 H ultrasonic water bath (frequency 35 kHz, Germany) with temperature control was applied.

Into a 50.0-ml measuring flask, a volume of the sample solution containing losartan (100.0 μg) and 20.0 ml KH_2PO_4/H_3PO_4 (pH 2) was added. This solution was diluted to the mark with deionized water, and the fluorescence intensity was measured at 400 nm (excitation at 247 nm).

Three commercially available losartan tablets from different companies (Pursina, Darou Pakhsh, and Tehran Darou) were powdered. Then the proper amount of each sample was weighed exactly, dissolved in 50 ml of deionized water, and sonicated for 30 min. Each solution was filtered and diluted with deionized water in a 1000.0 ml measuring flask. Then 5.0 ml of each solution was taken, and the suggested procedure was performed according to the given procedure.

Results and Discussion. According to the mentioned method, the fluorescence spectra of different concentrations of losartan were scanned (Fig. 1). The various factors affecting the fluorescence intensity were investigated (λ_{em} = 400 nm and λ_{ex} = 247 nm).

In order to find the optimum pH, the effect of pH on the fluorescence intensity of losartan was investigated in the range 1.0–7.0 (using nitric acid and sodium hydroxide). As can be seen from Fig. 2, the maximum fluorescence intensity of losartan is nearly constant in the pH range of 1.5–3.0. So, pH 2.0 was selected as the optimum value for the subsequent measurements. Temperature has a pronounced effect on the fluorescence intensity. Increase in temperature reduces the fluorescence intensity. The temperature effect on the fluorescence intensity of losartan was investigated between 10 and 50°C, and the results show that the maximum intensity was obtained at 10°C. So, 10°C was chosen for further experiments.

TABLE 1. Determination of Losartan in Different Tablet Samples

Company name	Label claim, g/g	Found [a], g/g	Recovery, %
Pursina Pharmacy, Tehran, Iran	0.235	0.228 ± 0.012	97.0
Darou Pakhsh Pharmaceutical Company, Tehran, Iran	0.320	0.314 ± 0.011	98.1
Tehran Darou Pharmaceutical Company, Tehran, Iran	0.325	0.320 ± 0.009	98.5

[a]Mean±standard deviation (n = 3).

Under the optimum conditions, the calibration curve was linear from 0.1 to 5.0 μg/ml. The regression equation can be expressed as $\Delta I_f = 53.744c + 1.3643$, with the suitable correlation coefficient ($R^2 = 0.9992$). The detection limit and relative standard deviation, obtained from 10 repetitive measurements with 2.0 μg/ml of losartan, were 12.0 ng/ml and 1.35%, respectively.

The suggested method was applied for the determination of losartan in three tablet samples from different companies (Pursina, Darou Pakhsh, and Tehran Darou). As can be seen from Table 1, the obtained results are in good agreement with the declared values of their companies and there is no significant difference between the obtained results and the accepted values. Thus, the procedure is reliable for the analysis of losartan in tablet form.

The analytical characteristics of the proposed method were compared with some previously reported methods for the determination of losartan [9–14]. Various techniques such as spectrophotometry [9–12] and HPLC [13, 14] were applied for the determination of losartan. The recommended method shows better analytical characteristics such as the lowest detection limit and the widest linear range except for only one case [14]. Also, the suggested method has the best relative standard deviation except for the reported RSDs in [9, 10, 13].

Conclusions. We have developed a simple and sensitive spectrofluorimetric method for the determination of losartan. The fluorescence intensity of losartan is proportional to its concentration in the range 0.1–5.0 μg/ml. Beside the considerable simplicity, some other benefits of the recommended method are high fluorescence intensity, high sensitivity and selectivity, good reproducibility, and capability for direct measurement of losartan without using any reagent or sophisticated and expensive apparatus. Also, this method demonstrates good sensitivity for the determination of losartan in tablet forms from different companies.

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