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NEW SPECTROPHOTOMETRIC METHOD FOR ESTIMATION OF LOSARTAN POTASSIUM USING ALIZARIN RED REAGENT

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A simple, rapid, precise, and sensitive analytical method has been developed to identify losartan potassium in its pure and pharmaceutical dosage forms. This method involves a proton transfer between the losartan reagent and the Alizarin Red reagent in an acidic medium while standing to complete the reaction to obtain a colored product bound to the amount of losartan potassium, this product having a maximum absorption at 493 nm. A linear calibration curve was obtained over a concentration range of 1.5–12.5 μg·ml^{-1} with a correlation coefficient of 0.9991. The molar absorptivity was $4.522 \cdot 10^4$ l·mol^{-1}·cm^{-1}, and Sandell's sensitivity index was equal to 0.010 μg·cm^{-2}. The limit of detection (LOD) and quantification (LOQ) values were 0.359 and 1.121 μg·ml^{-1}, the available pharmaceutical preparations (tablets). The results confirmed that the technique is successful by studying the recovery using the standard addition method.

Keywords: losartan potassium, proton transfer, determination, spectrophotometry, Red Alizarin.

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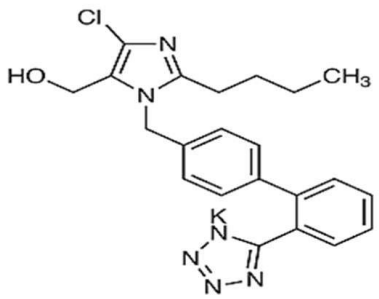
Introduction

Losartan potassium (LON-P) is a monopotassium salt 2-butyl-4-chloro-1-[[2'-(1H-tetrazol-5-yl) [1,1'-biphenyl]-4-yl]methyl]-1H-imidazole-5-methanol, with the structure is shown in Scheme 1. It is described as a white to off-white powder [1].



Scheme 1. Chemical composition of losartan potassium $C_{22}H_{22}ClN_6OK$ (M.Wt.=461.01 g·mol^{-1})

LON-P is a water-soluble compound, slightly soluble in acetonitrile and soluble in isopropyl alcohol [2]. LON-P is a new prototype of potent and orally active non-peptide angiotensin II receptor antagonists [3]. It is an angiotensin II receptor antagonist medication used to treat hypertension, heart failure, and diabetic neuropathy; the hypotensive effect is caused by blocking the angiotensin receptors, which causes the narrowing of the blood vessels [4].

Several methods for analytical determination of LON-P have previously been developed in pharmaceutical doses and biological fluids, including spectrophotometric methods [5–8], chromatographic methods [9,10], RP-HPLC [11], and electro-analytical methods [12,13].

This study aims to create a simple, fast, selective, and sensitive spectrophotometric method for determining losartan potassium in its pure form and pharmaceutical preparations based on the proton transfer between losartan potassium and alizarin red reagent in an acidic medium. This method can be used for routine determination of this drug.

Materials and methods

Apparatus

A double-beam UV-visible spectrophotometer (JASCOV-630) was used for all absorbance measurements using 1.0 cm quartz cells.

Chemical reagents and solution preparation

Because all the chemical compounds used in the tests were analytical grade, they did not need to be purified further.

Preparation of LON-P stock solution (100 μg·ml^{-1}) was conducted as follows: 0.01 g of pure LON-P was dissolved in 10 ml of distilled water with shaking and slight heating, then diluted to 100 ml with distilled water using a volumetric flask. Working standard solution (25 μg·ml^{-1}) ($5.423 \cdot 10^{-5}$ mol·l^{-1}) was formed by appropriately diluting the stock solution.

Preparation of Alizarin Red (AR) solution (100 mg·ml^{-1}): it was created by dissolving 0.01 g of dye powder in distilled water and diluting it to 100 ml in the same solvent with a calibration vial.

Preparation of sulfuric acid solution (1 mol l^{-1}) was performed as follows: 5.55 ml of concentrated hydrochloric acid was diluted to 100 ml with distilled water to make it.

Dosage forms procedure

LON-P tablets (Losartan) stock solution 100 μg·ml^{-1}:

This solution was prepared from the weight of six tablets (50 mg LON-P/tablet) and crushed well so that their combined weight reached 0.976 g. Then the weighed sample of 0.0325 g of this powder, which is equivalent to 0.01 g of pure LOP-P, was dissolved in 10 ml of distilled water, stirring well and lightly. Heating until the substance is completely dissolved, filtering with filter paper, transferring the filtrate to a 100 ml volumetric flask, and completing the volume to mark with distilled water.

Initial procedure

The following ingredients were added to a 10 ml volumetric flask: 1.0 ml of 25 μg ml^{-1} LON-P, 1.0 ml of 100 g ml^{-1} AR solution, and 1.0 ml of 1 mol l^{-1} HCl. Over a brief period, we noticed that an orange hue gradually developed, peaking at a maximum absorption wavelength of 493 nm and remaining stable at room temperature.

Results and discussion

Principle of procedure and suggested chemical reaction

Following the previous literature, we note that the proton transfer is from the red alizarin reagent to losartan potassium, as shown in Scheme 2.

The proton transfers result in a colored solution whose absorbance is measured at 493 nm and proportional to the LON-P concentration.

Conditions for optimal reaction

The following experiments were carried out in 10 ml volumetric flasks with 25 μg of LON-P, measuring absorption for the colored product at 493 nm.

Effect of Alizarin Red reagent amount

The effects of the AR quantity were studied by changing the added volume and keeping other factors constant. It was found that 1.0 ml of 100 μg·ml^{-1} of the AR reagent gave the highest absorption; consequently, it was used in subsequent experiments based on the findings (Fig. 1).

Effect of acidic medium

The effects of various acids at 1 molar concentration on the absorption of the colored product were investigated. It was discovered that H_2SO_4 was the best acid with the highest absorption value, as shown in Table 1. Furthermore, the optimal amount of acid was investigated, and 1.2 ml of 1 M H_2SO_4 was determined to be the best (Fig. 2).

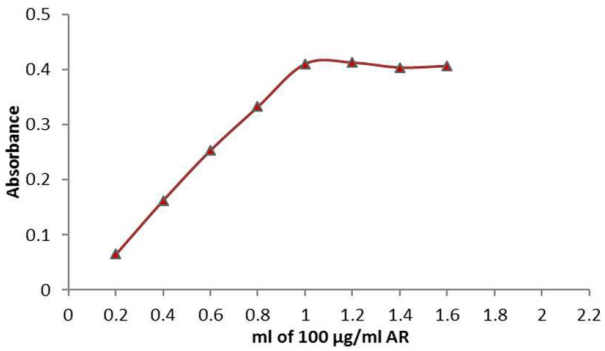
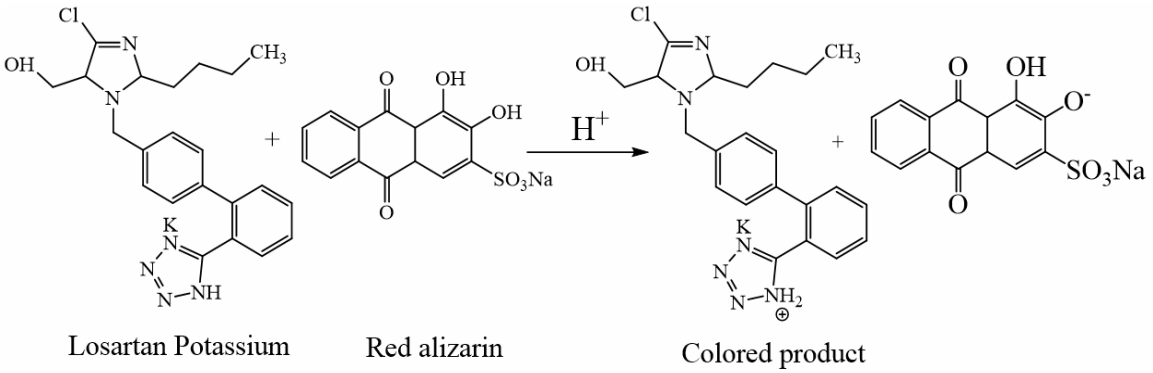


Fig. 1. Effect of AR concentration on absorbance



Scheme 2

Table 1

Effect of acid type on absorbance

Acid solution (1.0 ml of 1 M solution)	Absorbance
HCl	0.412
H_2SO_4	0.435
HNO_3	0.277
CH_3COOH	0.153

Surfactant effect

Using different types of surfactants and different amounts of each type at 1% concentration, it was discovered that these substances do not positively affect the absorption of the colored product. Still, there is a negative effect in some cases, as shown in Table 2.

Temperature and stability effects

The procedure was carried out at various temperatures to determine the effect of temperature on absorption as well as to study the stability of the colored product, and it was discovered that the absorption was stable for at least an hour at room temperature (25±2°C), as shown in Fig. 3.

Influence of addition sequence

The order of addition of the reaction components was investigated to see if it affected the color intensity of the product, and the results are shown in Table 3.

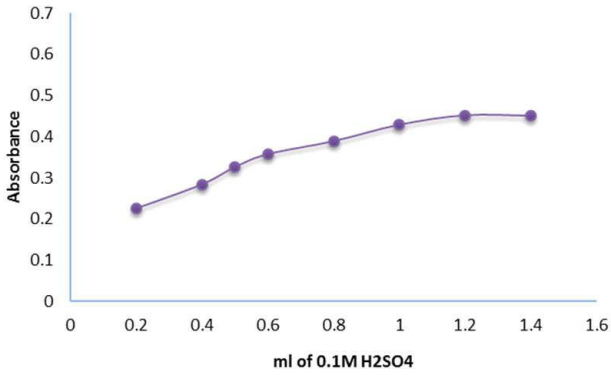


Fig. 2. Effect of H_2SO_4 amount on absorbance

According to the results given in Table 3, the addition sequence number 2 was adopted, which is reagent+acid+drug and under the same conditions. The other orders of the sequences yielded lower absorbance.

Final absorption spectra

In a 10 ml volumetric flask at the experimentally proven optimum reaction conditions, 1 ml of 100 μg·ml^{-1} of the AR reagent solution was added, and then 1 ml of the 25 mg·ml^{-1} LON-P solution was added, followed by adding 1.2 ml of 0.1 M H_2SO_4

Table 2

Effect of surfactants on absorbance

Surfactant	Absorbance				
	volume of added surfactant 1% solution				
	0.0	0.5	1.0	2.0	3.0
Triton X 100	0.430	0.437	0.435	0.432	0.452
SDS	0.309	0.321	0.339	0.308	0.453
CTAB	0.446	0.442	0.447	0.401	0.451
CPC	0.430	0.439	0.441	0.440	0.452

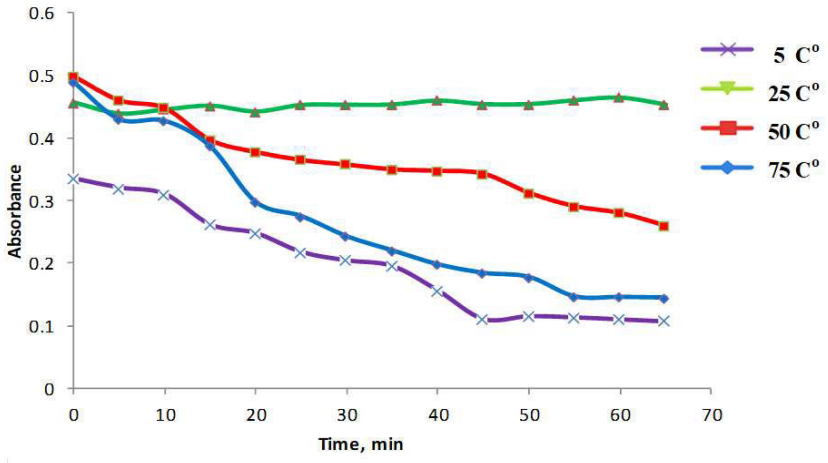


Fig. 3. Effect of time at different temperatures on absorbance

Table 3

Effect of sequence of additions on absorbance

No.	Sequence of additions	Absorbance
1	LON-P+H^++R	0.415
2	R+LON-P+H^+	0.478
3	LON-P+R+H^+	0.454

acid. After completing the volume to the mark with distilled water, the solution was kept for 5 minutes, and then the absorbance of this solution was measured against the blank reagent at 493 nm. Figure 4 shows the final absorption spectrum.

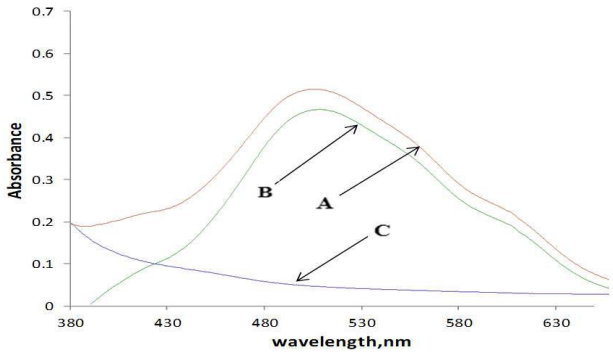


Fig. 4. Absorption spectra of 25 μg LON-P vs. (A) distilled water, and (B) blank; (C) blank vs. distilled water

Calibration curve

In several volumetric jugs of 10 ml and at ideal experimental conditions, 1.0 ml of 100 μg·ml^{-1} AR reagent in each one, followed by increasing volumes of 25 μg·ml^{-1} LON-P solution was added to cover the range of 1.0–20 μg·ml^{-1}, then 1.2 ml of 0.1 M H_2SO_4, completed the volume of all flasks to the mark with distilled water. It was waited at room temperature for 5 min before taking the absorbance against the blank at 493 nm. Figure 5 shows the standard curve obtained from applying the absorbance values, indicating that the range of concentrations following Beer's law was 1.5–12.5 μg·ml^{-1} with a molar absorption of $4.522 \cdot 10^4$ l·mol^{-1}·cm^{-1} and a perception of Sandell of 0.010 μg·cm^{-2}.

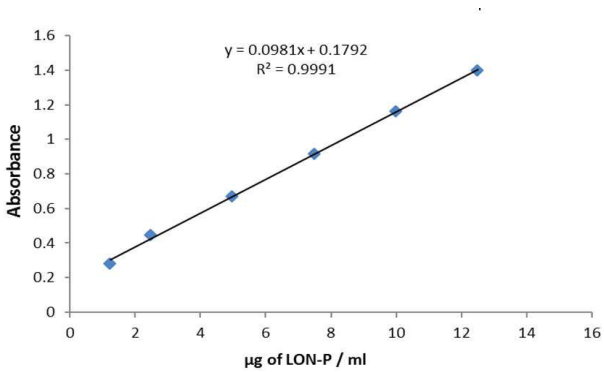


Fig. 5. Calibration curve for LON-P determination

Accuracy and precision

LON-P is determined with two concentrations and repeated several times for each concentration to determine the accuracy and compatibility of the calibration curve. As shown in Table 4, the proposed method is reliable.

Application of the method

The available medicinal preparation (as tablets) has been successfully determined using the proposed method. The results obtained (Table 5) confirmed that the method is applicable and accurate.

Table 4

Accuracy and precision

Amount of LON-P, μg/10 ml present	Amount of LON-P, μg/10 ml found	Recovery, %	Relative error*, %	Relative standard deviation*, %
20	19.24	96.2	–3.8	±1.26
50	48.98	97.96	–2.04	±0.97
90	91.06	101.17	1.17	±1.23

* – Note: average of five determinations.

Table 5

Method implementation

Pharmaceutical drug	The present amount of LON-P, μg/10 ml	Found the amount of LON-P, μg/10 ml	Recovery, %	Relative error*, %	Relative standard deviation*, %
Losartan, 50 mg/tablet, U.K	40	39.44	98.6	–1.4	±0.687
	90	90.95	101.05	1.05	±1.43

* – Note: the mean of three determinations.

Table 6

Results of the standard addition method

Pharmaceutical preparation	Amount of LON-P, presence μg/10 ml	Amount of LON-P, measured μg/10 ml	Recovery, %
Losartan, 100 mg/tablet, U.K	40	41.17	102.94
	70	69.71	99.51

Fig. 6. Standard addition curves for determination of LON-P in pharmaceutical drug

Evaluation of the suggested method

The standard addition method [14] was used to ensure the selectivity of the proposed method by using two different quantities of the drug solution and then calculating the recovery for each of them. As shown in Fig. 6 and Table 6, it appears to us that the proposed method has good selectivity.

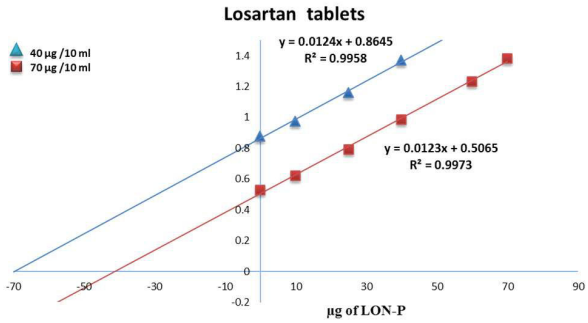


Fig. 6. Standard addition curves for determination of LON-P in pharmaceutical drug

Conclusions

For the determination of losartan potassium, a simple and quick spectrophotometric method was proposed based on the transfer of a proton between the losartan molecule and the Alizarin Red reagent molecule to produce a colored solution that gives the highest absorption at the wavelength 493 nm. The applicability of the proposed method to pharmaceutical preparations was confirmed, and the method was accurate, selective, and acceptable sensitivity.

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НОВИЙ СПЕКТРОФОТОМЕТРИЧНИЙ МЕТОД ВИЗНАЧЕННЯ ЛОЗАРТАНУ КАЛІЮ З ВИКОРИСТАННЯМ РЕАКТИВУ АЛІЗАРИНОВИЙ ЧЕРВОНИЙ

Асма Х. Аль-Машадані, Давуд Х. Мохаммед

Було розроблено простий, швидкий, точний і чутливий аналітичний метод для ідентифікації лозартану калію у його чистих і фармацевтичних лікарських формах. Цей метод передбачає перенесення протона між реагентом лозартану та реагентом алізаринового червоного у кислому середовищі під час витримування для завершення реакції з одержанням забарвленого продукту, зв'язаного з лозартаном калію, де цей продукт має максимальне поглинання при 493 нм. Лінійну калібрувальну криву було отримано в діапазоні концентрацій 1,5—12,5 мкг/мл з коефіцієнтом кореляції 0,9991. Молярний коефіцієнт поглинання становив $4{,}522 \cdot 10^4$ л/моль·см, а індекс чутливості Санделла дорівнював 0,010 мкг/см^2. Значення межі виявлення (LOD) і кількісного визначення (LOQ) становлять 0,359 і 1,121 мкг/мл, відповідно. Запропонований підхід застосовано для визначення лозартану калію у доступних фармацевтичних препаратах (таблетках). Результати, отримані за допомогою стандартного методу додавання, підтвердили, що метод є успішним для визначення даного реагенту.

Ключові слова: лозартан калію, перенесення протона, визначення, спектрофотометрія, червоний алізарин.

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