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Determination of valsartan in its pharmaceutical preparations using high-performance liquid chromatography technique

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***Abstract*---**High-performance liquid chromatography technique was used to estimate valsartan in its pure form and in some pharmaceutical preparations. It was found through the results obtained that the proposed method is sensitive and accurate, and the estimation was done in a short time. In this work, a No L1, 150mm separation column was used to separate the components as they were type The UV spectrometer was used as a wavelength of 239 nm, the column temperature was 40°C, and the mobile phase consisted of 50:50 (acetonitrile: methanol: drops of triethylamine, pH = 2.4) at a flow rate of 1 ml/min. Through what was reached, we find that the method is sensitive, accurate and compatible, as the percentage recovery reached (100.63-103.35), and the linearity was (40-120 mcg/ml) for valsartan. The method was applied to a number of pharmaceutical preparations available in the local market, and the method was successful in the quantitative estimation of valsartan.

***Keywords*---**high-performance, liquid chromatography, valsartan.

Introduction

Valsartan is a drug belonging to the group of angiotensin II receptor antagonists. Valsartan is selective for the type of angiotensin receptor that is used in the treatment of hypertension, heart failure and diabetic neuropathy [1-2]. Its molecular formula is C24H29N5O3, and Figure (1) shows its chemical structure

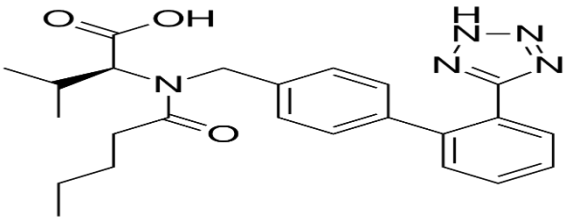


Figure 1: The chemical structure of valsartan.

This drug is in the form of a fine white powder that dissolves well in ethanol. Its molar mass is 435.519 g/mol. Table (1) shows some properties of this drug [3].

Table (1): Some properties of valsartan.	
Additional properties	Valsartan
Chemical Name	s (2S)-3- methyl-2-[pentanoyl-[[4-[2-(2H-tetrazol-5-yl) phenyl] phenyl]methyl]amino]butanoic acid
Color	White to practically white fine powder
Molecular Formula	$C_{24}H_{29}N_5O_3$
M. P.	116-117 °C
Molar mass (g. mole^{-1})	435.519
Solubility	soluble in ethanol, DMSO, and dimethyl formamide at 30 mg/mL

Valsartan selectively and competitively blocks the binding of angiotensin II to the AT1 subtype receptor in vascular smooth muscle and the adrenal gland, preventing AT II-mediated vasoconstriction, aldosterone synthesis and secretion, and renal reabsorption of sodium, resulting in vasodilation, increased sodium and water excretion, decreased plasma volume and hypotension, It is also used in the treatment of hypertension, congestive heart failure and myocardial infarction [4-8].

Experimental part

- Valsartan standard solution (2000 mcg/mL)
  Prepare by dissolving 0.2 g of the standard active ingredient of the drug in an amount of the mobile phase and then complete the volume to the mark in a volumetric bottle of 100 ml of the same solvent.
- Mobile phase solution (50:50 vol/v)
  The mobile phase solution was prepared from mixing equal volumes of acetonitrile, methanol and drops of triethylamine and placed in an ultrasound machine for a period of time to get rid of bubbles.
- Sodium hydroxide solution at a concentration of (2 mo)
  Prepare by dissolving 4 g of sodium hydroxide in an appropriate volume of distilled water and then complete the volume to the mark in a 50 ml volumetric vial with distilled water.
- Hydrochloric acid solution (1 mo)
  Prepare by mixing 4.16 ml of hydrochloric acid in an appropriate volume of distilled water and then complete the volume to the mark in a 50 ml volumetric vial with distilled water.
- Solutions of pharmaceutical preparations

Covert 10mg/320mg

This preparation contains 10 mg amlodipine and 320 mg galsartan, and after handling it as described above, it was diluted to 100 ml in a volumetric vial to obtain 100 µg/ml of amlodipine 3200 µg/ml, and then other dilutions were made to obtain the desired concentration. .

Extor 5mg/80mg

This preparation contains 5 mg amlodipine and 80 mg galsartan, and after handling it as described above, it was diluted to 100 ml in a volumetric vial to obtain 50 µg/ml of amlodipine 80 µg/ml, and then other dilutions were made to obtain the desired concentration.

Preliminary investigations

At the beginning, work was done by choosing initial conditions, such as choosing an initial concentration of the drug 10 µg/ml, and this concentration was worked on in all the optimum conditions, as the temperature at the beginning of the experiments was 25 degrees Celsius, and the separation column that was used first was of type L1, 15 cm, and a flow velocity 0.8 ml/min, the purpose of these experiments is to obtain an initial separation, on the basis of which the best conditions can be selected to obtain a good separation, in addition to the importance of the above conditions, but the role of the mobile phase is the most important among them, so a variety of mobile phases were used, among them The mobile phases were (acetonitrile: methanol: triethylamine) and it was the only one through which the drug under study was separated and other conditions were then controlled.

Results and Discussion

Evaluation results for valsartan

Wavelength selection

To indicate the most appropriate wavelength at which VAL drug is detected, a solution (10 µg/ml) of the compound was prepared in the same selected solvent (mobile phase), the solution was read by a UV spectrophotometer for the range of 200-400 nm and it showed the UV spectrum. The maximum absorption value at 239 nm was used in the preliminary tests. Figure (2) shows the absorption spectrum of the drug against the mobile phase used as a mock solution.

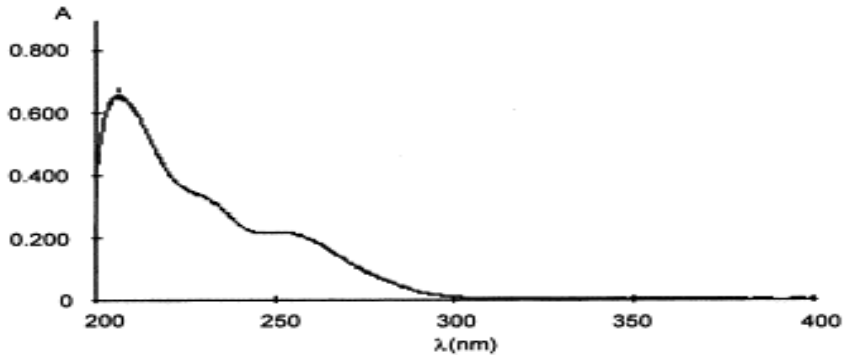


Figure 2: UV absorption spectrum of VAL.

Effect of wavelength

Choosing the optimum wavelength depends on the response chosen, the more the response is good in terms of the equivalent height of the theoretical plate or the efficiency (number of theoretical plates) and within the limits of the linear range of the detector (Detector), it is the optimum wavelength, and it should be noted here that the wavelength must be chosen The greater λmax because it reduces the spectral interference resulting from the measurement of the detector, and the selection of the greatest wavelength leads to an increase in the sensitivity of the method more, three wavelengths were chosen that are close to the largest wavelength (232, 239 and 245 nm), Table (2) and Figure No. (3) shows that the best wavelength was 239 nm in terms of HETP and N of the drug

Table (2): Optimum wavelength

Wavelength nm.	Drugs	Parameter	
		N	HETP
232	VAL	4312	34.78
239		4431	33.851
245		4112	36.47

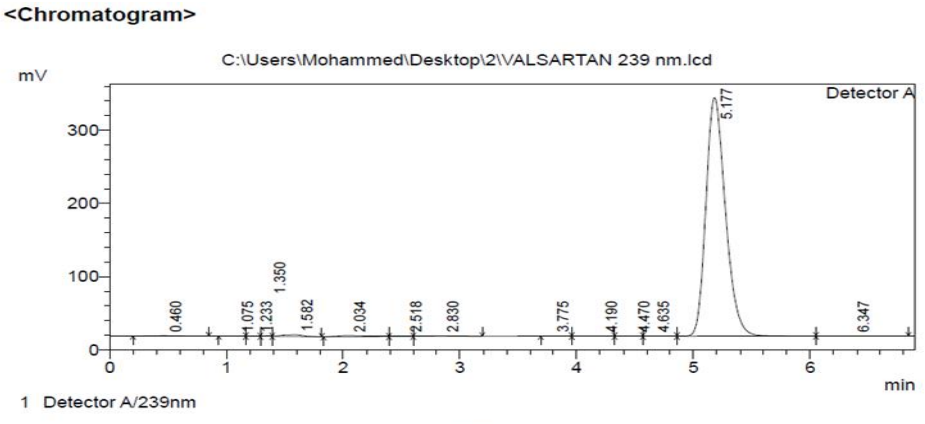


Figure 3: The effect of wavelength on drug separation (VAL).

Effect of mobile phase

In this study, acetonitrile was used as an organic modifier, as the percentage of this modifier that was used in a mobile phase was evaluated. The optimum composition of the mobile phase was determined to be 50:50 (acetonitrile:methanol:triethylamine), Table (3), which leads to good separation at an optimum wavelength of 239 nm. The HETP values of the drug change independently with the change in the percentage of the rate in the mobile phase, which leads to the ease of choosing the optimal ratio. Figure (4) shows the chromatogram of the drug at the optimal ratio of the mobile phase

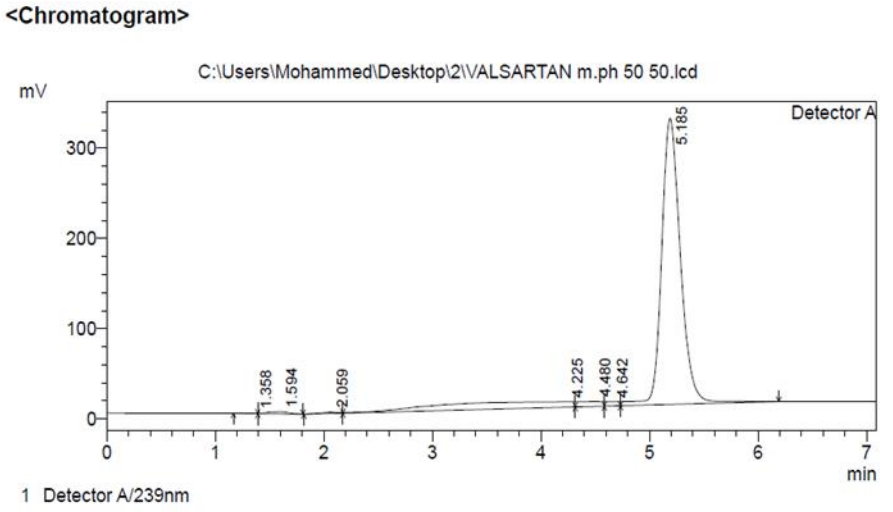


Figure (4): The effect of the mobile phase composition on the separation of the drug

Table (3): HETP values and theoretical plate count according to mobile phase composition

Mobile phase (v/v)	Drug	Parameter	
		N	HETP
30: 70	VAL	4120	36.40
50: 50		4391	34.163
70: 30		4041	37.11

The effect of the acid function

The improvement of the acidity function was studied in VAL analysis over the range (1.8-3.8), Figure (5), pH = 2.4 was chosen as the best acidity function because it gives a good and clear separation, Table (4)

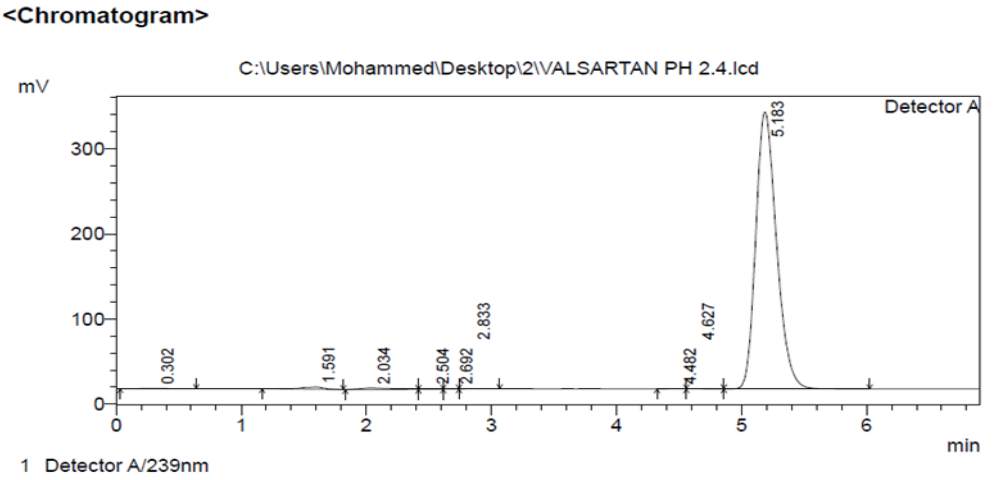


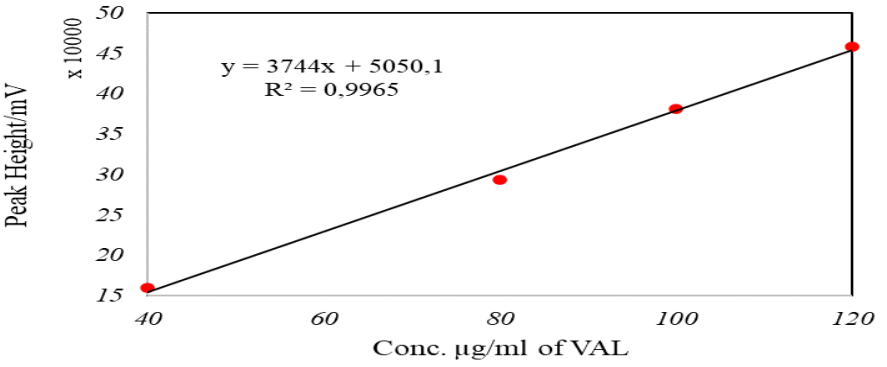
Figure (5): The chromatogram of the drug under study at the best acidity function

Table (4): tR, N and HETP values for the best acidity function

pH	Drug	Parameter		
		t_R	HETP	N
1.8	VAL		37.23	4028
2.4		5.183	33.433	4487
3.8			36.39	4122

Calibration curves

According to the best experimental conditions, the linearity was tested for a range of concentrations (0.1-500) µg/ml of valsartan. Calibration curves for the drug were built by plotting the peak height and peak area against its concentrations as shown in Figure (6) and it was found that the drug was linear (40-120 µg/ml). Table (5) shows the regression equation, estimation coefficient, detection limit and quantitative limit.



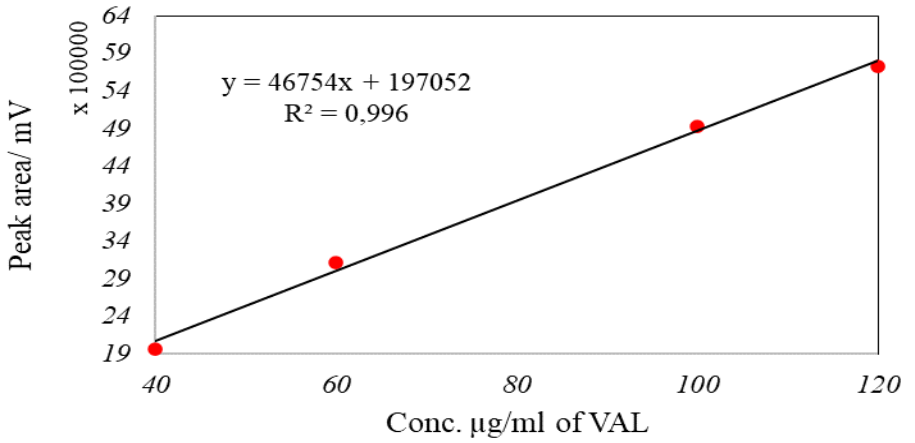


Figure 6: Titration curves for valsartan

Table (5): Results of the calibration curves of the drug under optimal conditions by HPLC technology

Drug	Linearity ($\mu g.mL^{-1}$)	Response	r^2	Slope	Intercept	LO D ($\mu g.mL^{-1}$)	LOQ ($\mu g.mL^{-1}$)
VAL	40-120	Peak Height	0.9965	3744	5050.1	7.4393	22.3179
		Peak Area	0.996	46754	197052	8.4555	25.3665

Accuracy and precision The accuracy was studied by calculating the percentage recovery and the harmonic by calculating the relative standard deviation, for the results of the studied drug. Three different drug concentrations were selected within the linear range of the calibration curve, Table (6), the results of accuracy and agreement indicate that the proposed method is good for quantitative determination.

Table (6): Accuracy and compatibility of the proposed method

Drug	Conc Taken ($\mu g.mL^{-1}$)	Sample Conc. calculated from peak height or peak area	
		Mean*	Rec %
VAL	40	41.34	103.35
	100	100.63	100.63
	120	121.02	100.85

*Average of three measurements.

Application of the method

The proposed method has been successfully applied to estimate valsartan in some of its pharmaceutical forms, which are available in the local market, by direct method by straight line equations. Pharmaceutical solutions were prepared with different concentrations of the drug, and then injected four times in the HPLC system at the optimum conditions that were chosen. The amount of drug was

calculated and the results obtained were recorded as in Table (7). The good agreement between these results and the percentage recovery values within the permissible range shows that the application of the proposed method is successful for the determination of valsartan in its pharmaceutical preparations and that there is no interference with the existing drug additives.

Table (7): Results of applying the method to some pharmaceutical preparations

Sample	Conc. taken (µg.mL^{1}) Of VAL	Conc. calculated from peak height or peak area	
		Conc* found (µg.mL^{1})	Recovery %
EXFORGE/ Tablets (5mg AML, 160mg VAL)	80	79.36	99.2
VALSAR-AM/ Tablets (5mg AML, 160mg VAL)	80	80.08	100.1
Amlodipine & Valsartan/ Tablets IP (5mg AML, 160mg VAL)	80	80.24	100.3

*Average of three measurements.

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