Cloud-Point Extraction and Flame Atomic Absorption Spectrometric Determination of Valsartan in Pure Form and Its Pharmaceutical Preparations

Mohammed Fadel Hamad, Shahla Jamal Shakkor*

Department of Chemistry, College of Science, University of Kirkuk, Kirkuk, Iraq.
**Corresponding author, Email address: shahla.jamal@uokirkuk.edu.iq*

KEYWORDS

Valsartan; Spectrophotometer; P-Bromoaniline; Triton X-114, Cloud Point Extraction. Flame Atomic Absorption

ABSTRACT

To determine Valsartan in pure form and its pharmaceutical preparations, a new method using UV-Vis and Flam atomic absorption spectrophotometry (FAAS) has been used. This is done by cloud point extracting (CPE) method using active surface Triton X-114 as a non-ionic surfactant. The (CPE) method involves the formation of two complex, the first is based on the formation of a complex between valsartan and para-bromoaniline in the presence of para-dimethyl amino benzaldehyde (Mannich complex) at 438 nanometers , While the second complex is formed between valsartan and Fe(III) at 441 nanometers , and another method (FAAS) was applied to estimate Valsartan using second complex . A number of conditions were established such as the volume of a non-ionic surfactant, temperature , effect of time on complex formation, reagent volume, and metal ion concentration . the optimal conditions used being the same in UV_Vis and FAAS where 75 °C was the best temperature for cloud point extraction . Ethanol was the best solvent for extracting the two complexes, and Beer's law range was 0.8 _7.2 µg/ml for (UV_Vis) and 0.5-4.5 µg/ml for (FAAS), The samples' average recoveries were found to range between 99.88-101.042%. The relative standard deviation (RSD) for1.6 µg/mL of VAL was < 2.5% The limits of detection and quantification were 0.004210 and 0.01047 µg/mL respectively. The method has been validated and successfully applied to pharmaceutical valsartan preparations, and from the obtained results and recovery ratios, we found it to be a good, highly sensitive, inexpensive, non-toxic, and environmentally friendly method.

1. Introduction

VAL is a white powder with the molecular formula $C_{24}H_{29}N_5O_3$. It belongs to the class of angiotensin II receptor blockers (ARBs)[(1)]. These drugs work by selectively binding to angiotensin II (AT1) receptors in the body. This binding prevents another molecule called angiotensin II from binding to these receptors. Angiotensin II often causes blood vessels to constrict, which raises blood pressure. By preventing angiotensin II from binding to (AT1) receptors, valsartan prevents this effect and helps to lower blood pressure[(2)]. In general, the physiological effects of valsartan lead to a reduction in blood pressure. by blocking the various effects of angiotensin II . Lowering aldosterone levels by reducing and minimizing aldosterone production. Helps to eliminate excess sodium and water, which contributes to lowering blood pressure[(3)] Decreased heart activity: Valsartan reduces the stimulation of the heart muscle, which helps to lower the heart rate and thus reduce the pressure on the heart.

Increased sodium excretion: Valsartan prevents the reabsorption of excess sodium, leading to its elimination through urine. This reduces the volume of fluids in the body and consequently lowers blood pressure [(4)]Valsartan is minimally distributed outside the plasma and is highly bound to plasma proteins. Due to the presence of carboxyl groups, valsartan is soluble in the neutral pH range and is predominantly found in its ionized form. In the steady state, the volume of distribution is 171 liters [(5)]. Valsartan has a melting point of 105-110°C. Its molecular weight is 435.59 g/mol Its IUPAC (International Union of Pure and Applied Chemistry) name is 4-[2-(2H-tetrazol-5-yl)phenyl]benzoic acid. Valsartan does not require metabolism in the body to be effective. There are several spectroscopic methods for determination of valsartan including spectrophotometric[(6-7-8_9_10_11)] , Chromatographic[(12-13)], Liquid chromatography-mass spectrometry (LC-MS), [(14,15)] Electrochemical methods[(16)]

Instruments Used

UV-Visible double beam(T92+Spectrophotometer Range (190-800)nm, China), Sensitive balance(Sartorius BL210 SAG Gottingen – Germany), Heater HPL-248 China, Computer DEL, Windows 7, Uv probe 2.34 China, water bath, centrifuge, Ice bath

Chemical materials

The crude material for Valstartan was obtained from the state Company for Drugs Industry and Medical Appliances (SDI), Samarra, Iraq. The purity of the materials was approved as proven by the supplier. As for the chemical materials that were used in the research were of a high degree of purity

Chemical materials and reagents used:

Valsartan solution (500 ppm)
It was prepared by dissolving 0.05 mg of pure valsartan powder in methanol and it was completely dissolved, then supplemented with distilled water in a 100 ml bottle. It was considered a standard solution from which the remaining diluted solutions were prepared.

Para-bromoaniline reagent solution ($3X10^{-2}$ M)

This solution was prepared by dissolving (0.5 mg) of the above reagent powder in (10 ml) of ethanol. The dissolution was complete, then the volume was completed to this mark in a 100 volume bottle with 100 ml distilled water.

Para-dimethylaminobenzene aldehyde reagent solution ($3X10^{-2}$ M)
It is prepared by dissolving (0.4470 mg) of the above reagent powder, then add it a little in (10 ml) of ethanol and the dissolution was complete, then complete the volume to one mark in a 100 volume bottle with distilled water.

. Hydrochloric acid solution (1 M)
It is prepared by adding 8.47 ml of hydrochloric acid solution (11.8 ml) to a small amount of distilled water in a volumetric bottle (100 ml), then complete the volume related to the distilled water.

Valsartan pharmaceutical preparations (100 mg/ml)
5 valsartan pills were crushed. Each pill contains 80 mg of valsartan. The weight of five pills was taken as 1.016 mg, and 0.4 mg was taken from them and dissolved in an amount of methanol. After filtering the mixture, the sediment underwent multiple methanol washes. Next, transfer 25 milliliters of the ready solution into a 100 milliliter bottle and top it off with distilled water to create a solution with a concentration of 100 micrograms per milliliter.

Surfactant Solution (10%)
Triton X-114 (10% , V/V) was prepared by diluting 10 ml in 100 ml volumetric flask with distilled water

Metal Ion Solution
This solution was prepared by dissolving 0.9000 gm of ammonium ferric sulfate in 1 mL of sulfuric acid with a concentration of 1M, then make up the volume with distilled water in a 100 mL volumetric flask. Then, the solution was left for 24 hours to ensure complete dissolution.

Results & Discussion

General Principle of CPE Method:

Upon adding an organic reagent solution of para-bromoaniline to a valsartan solution, followed by adding para-dimethylaminobenzaldehyde solution and **Triton X-114** a yellow complex (Mannich complex) is formed. This complex is then extracted with ethanol and its absorbance is measured at a wavelength of 438 nm against a blank solution which is shown in **Figure (1) .**

The mechanism of reaction summarized by formation Mannich complex between drug and para-bromoaniline in the presence of para-dimethylaminobenzaldehyde as show in **Figure (2)** .

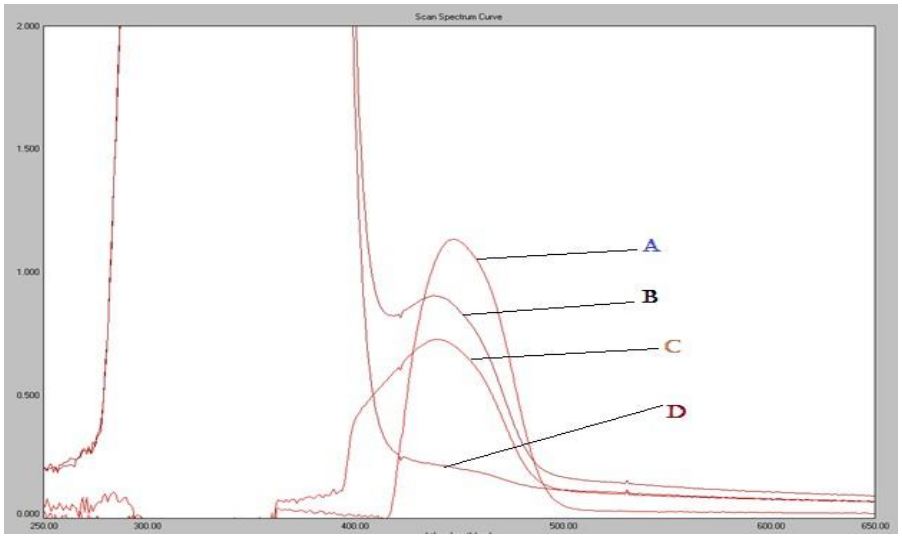


Figure (1): Final absorption spectrum from VAL- Complex
A= Sample & Blank (With CPE) , B= Water & Sample (With out CPE) , C= Sample & Blank (With out CPE) , D= Water & Blank (With out CPE)

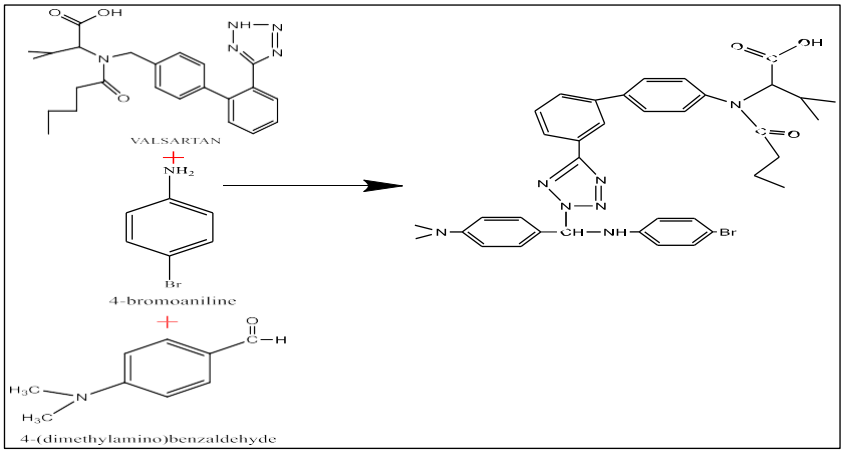


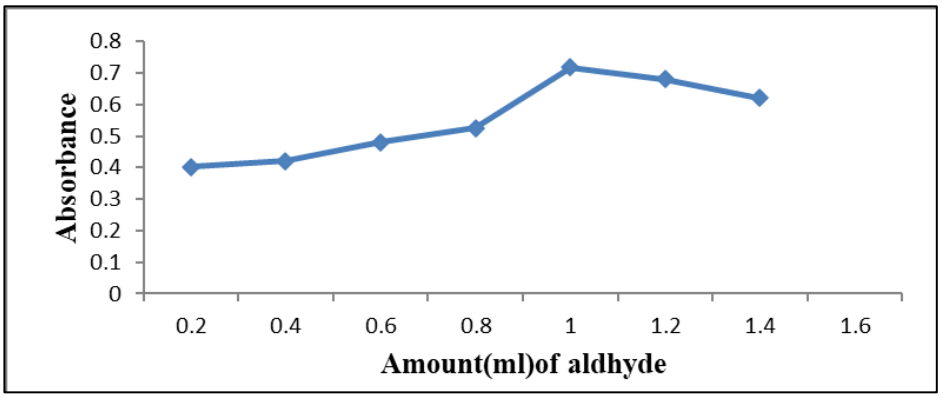
Fig (2) : Mechanism of formation of mannich complex

Study optimal conditions

various factors affecting absorption were studied using a VAL solution with a concentration (100ppm) in a final volume (25ml) and a final concentration (8µg/ml). The absorption of solutions at different wavelengths was measured against its blank solution.

Effect of Reagent

This effect was studied by taking different reagent solutions ($3x10^{-2}$M) with defferent volumess (0.2___2.5) mL in Triton X-114 medium. The absorbance of the solutions was measured at of 438 nm against the blank solution. The results in **Figure(3) and (4)** show that P_bromo aniline is the best reagent and the highest absorption of the colored outpat was given at 1.5ml . which is used in this method



Figure(3): The effect of amino reagent Type

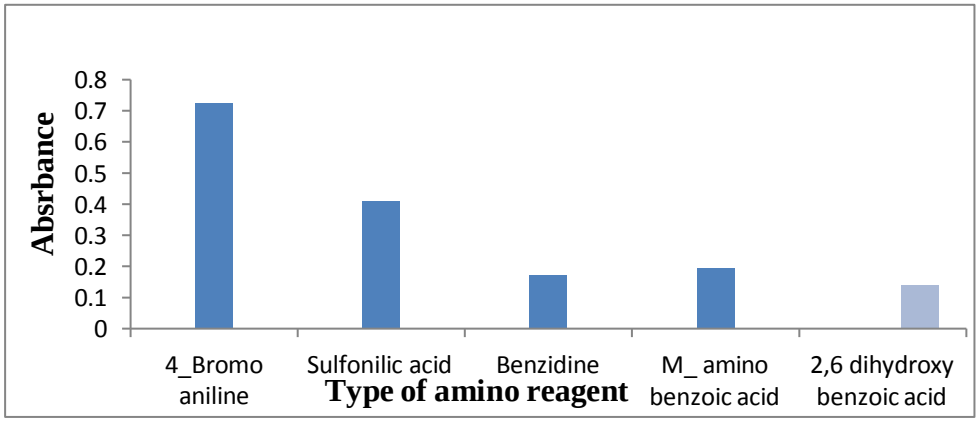


Figure (4): Effect of volume of p-bromoaniline reagent

Effect of paradimethylaminobenzaldehyde amount

This effect of the volume of (para-dimethylaminobenzaldehyde) solution was shown in **figure (5)** by using various quantities (0.2-1.4) of aldehyde solution ($3X10^{-2}$ M) . It was found that the optimum volume of aldehyde solution that gives the highest absorbance is 1 ml, so this volume was adopted in the subsequent steps

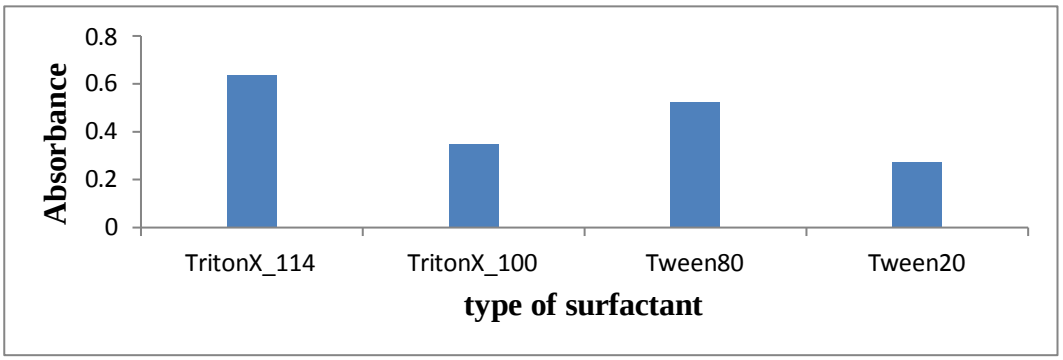


Figure (5): Effect of volume of aldehyde

Effective surfactant

Varions surfactant such as (Tween80, Tween20, TritonX-100, TritonX-114) **with concertration of 10% have been tested at 75Ç in water bath for 25 mint, due to high concentration and volume of surfactant solutions, they must be used under heating .**Then, they were placed in a centrifuge at 6000 rpm for 20 minutes. The phase rich in the effective surface was separated and dissolved in 1 ml of ethanol, and 1.5 ml of distilled water . It was found that TritonX_114 is the best surfactant and 1.4 ml of it gves the highest color intensity **(Figure 6 , Table 1)**

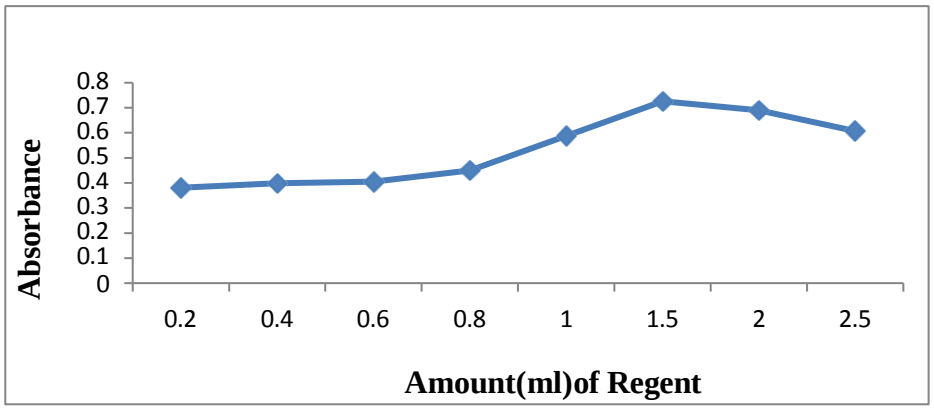


figure (6): Effective surfactant type

Table (1) Effective of surfactant amount

Volume of TritonX_114(ml)	Absorbance of Valsartan
0.2	NO COMPLEX
0.4	NO COMPLEX
0.6	0.275
0.8	0.384
1	0.653

1.2	**0.914**
1.4	**0.989**
1.6	**0.866**
1.8	**0.781**
2	**0.805**

Temperature and Time effect

Temperature and time effect was studied on the product absorption at different temperature (35_95℃) and (5-40) min ,respectively the highest absorption was obtained at 75℃ (figure 7) and 25 minutes is the best time for the Formation of complex (Table 2)

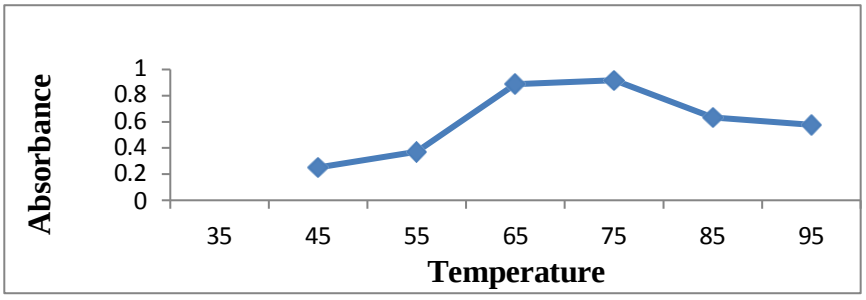


figure (7): Temperature effect

Table (2): Effect of time on the absorbance at the cloud point of valsartan

Time/mint	Absorbance
5	NO COMPLEX
10	0.396
15	0.512
20	0.781
25	**0.897**
30	0.881
35	0.802
40	0.654

Order of Additions

From the results listed in **Table (3)** it is clear that the best sequence of additions, which gives the highest absorption, is the first sequence .
The optimum conditions used for the determination of valsartan are listed in **Table (4)** after completing the study of the effect of the optimum conditions on the absorption intensity of the complex formed in the proposed method.

Table (3): The effect of the order of additions

No	Order of additions	Abs of 8mg/ml of VAL
1	D+ R+ A+T	0.741
2	A+ D+ R+T	0.441
3	R+ A+ D+T	0.074

Table(4): summary of Optimal Conditions(CPE)

Experimental Condition	
Λ_{max}	438(nm)
Amount(ml) of P_dimethyl amino benzaldhyde 3×10^{-2}M	1ml
Amount(ml) of P_Bromo aniline 3×10^{-2}M	1.5ml
Amount(ml) of (TritonX_114 %10V/V)	1.4ml
Order of additions	D+R+A+T
Surfactant	TritonX_114
Temperature	75℃
Time	25mint
Solvent	Ethanol+Water
Time of centrifugation	20 mint
centrifugation	6000 rpm

Approved working method and calibration curve

After determining the optimal conditions for estimating valsartan, as shown in Table (4), the calibration curve was prepared as follows : The method involves adding increasing volumes (0.2 - 1.8 ml) of valsartan solution concentration (100 µg/ml) to a series of 25 ml volumetric flasks. Then, 1.5 ml of p-bromoaniline solution, 1 ml of p-dimethylaminobenzaldehyde solution, and 1 ml of surfactant are added. The mixture is left for 5 minutes to complete the reaction. The solutions were placed in a water bath at 75 °C for 25 minutes to form cloud point , centrifugation was used at 6000 rpm for 20 minutes to separate the aqueous layer . After that, the surfactant _ rich phase is separated and dissolved in 1 ml of ethanol with 1.5 ml of distilled water , then the absorbance is measured at 438 nanometers against the blank solution. The data obtained follows Beer's law in the concentration range of 0.8 to 7.2 µg/ml. The correlation coefficient (R^2) is determined to be 0.9942.

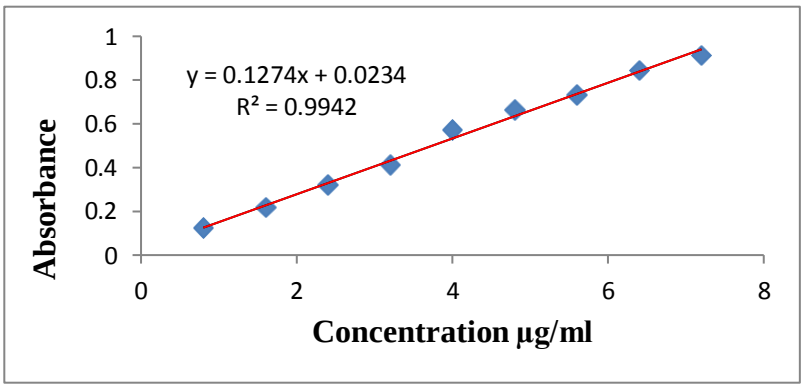


Figure (8): (VAL- complex) Calibration Curve by CPE Method

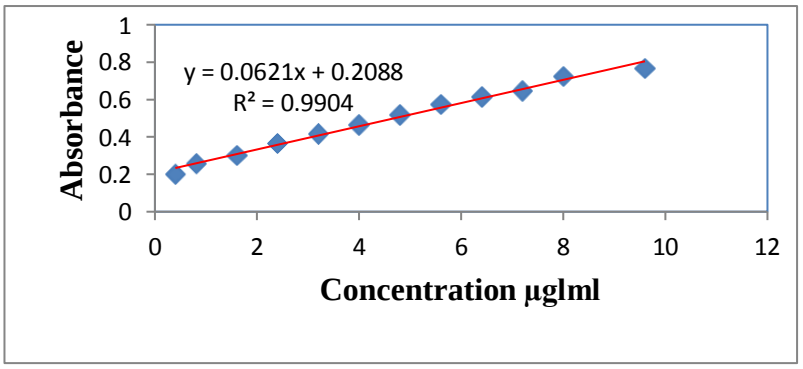


Figure (9): (VAL- complex) Calibration Curve With out CPE Method

Quantitation

After reaching the mentioned experimental conditions were used to plot the standard calibration curves for valsartan by plotting the concentration versus absorbance. The **table (5)** shows the relative standard deviation (RSD) and the average recovery% for six readings of three different concentrations of valsartan drug. To prove the accuracy of the method, the limit of detection (LOD) and the limit of quantitation (LOQ) were calculated, and **table (6)** shows that. The obtained results are within the acceptable range for the minimum requirement of Beer's law.

Table(5): Accuracy and precision

Amount of VAL (µg/ml)	Method	Conc. of VAL (µg/ml)	RE%	Recovery %	RSD %
1.6	With CPE	1.6036	0.2126	100.21	0.0003
	With out CPE	1.6038	0.24883	100.243	2.0373
4	With CPE	3.9992	0.1104	99.98	0.0015
	With out CPE	4.0417	1.0425	101.0425	2.0234
6.4	With CPE	6.4052	0.0832	100.082	0.003
	With out CPE	6.3926	-0.1151	99.8849	1.44127

Table(6): Detection Limit

With CPE*				
SLOP	**T**	**SD**	**LOD(µg/ml)**	**LOQ(µg/ml)**
0.1274	0.4084	0.0001788	0.004210	0.01407
With out CPE**				
SLOP	**T**	**SD**	**LOD(µg/ml)**	**LOQ(µg/ml)**
0.0621	0.27616	0.0026051	0.125850	0.419508

***Average of five determinations**
****Average of Six determinations**

LOD = 3x SD / Slop

LOQ = 10x SD / SLOP

Table (7): The statistical data of VAL estimation with and without CPE

Parameter	Value	
	With CPE	With out CPE
Regression equation	y = 0.1274x + 0.0234	y = 0.0621x + 0.2088
Correlation coefficient, R^2	0.9942	0.9904
Beer's Law Limit (µg/mL)	0.8_7.2	0.4_9.6
Molar absorptivity, ε (L/mol cm	$0.2x10^1$	$2.7x10^4$
Slope, b (mL/µg)	0.1274	0.0621
Limit of detection, LOD (µg/mL)	0.004210	0.125850
Limit of detection, LOQ (µg/mL)	0.01407	0.4195008

Intercept	0.0234	0.2088
r	0.9970	0.9951

Mole – Ratio & Job's Methods

To determine the nature of the resulting product and the rate of binding of VAL to the para-bromoaniline reagent, the two methods of continuous changes (Job's method) and the molar ratio method were applied. In both methods, the concentration of both the VAL solution is (100µg/ml) and the concentration of the para-bromoaniline reagent solution is ($3X10^{-2}$ M). Where in (Job method), different volumes of the drug solution (0.5-4.5 ml), were placed in 25 ml volumetric flask , these volumes were completed to 5 ml by adding different volumes of reagent solution, then the rest of the additions were completed in the optimal sizes according to the method of work, then diluted with distilled water . the absorbance of the solutions was measured at 438 nm. **Figure (10)** shows that the ratio is 1:1 between the drug and the reagent.

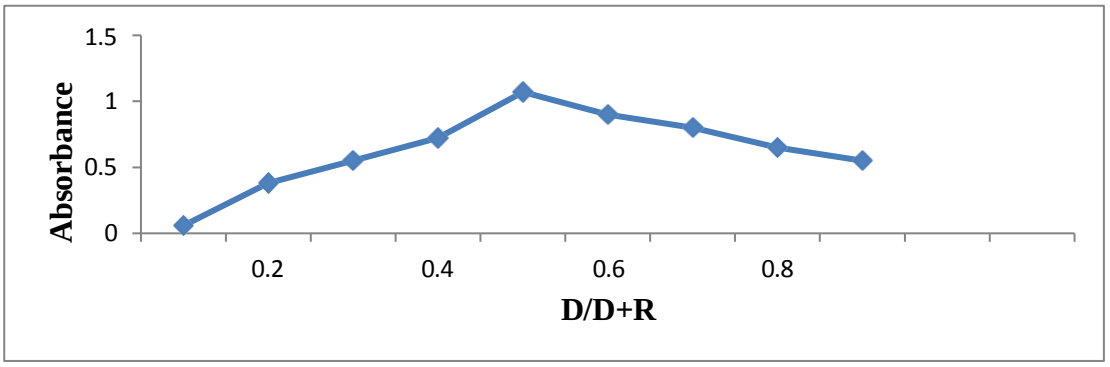


Figure (10): Job's Methods

To ensure that the reaction ratio between VAL and para-bromoaniline is 1:1, the molar ratio method was used, where 2 ml of the drug solution was placed. In a series of volumetric flask 25 ml, different volumes of reagent (0.5-4.5 ml) were added to it, then the rest of the additions were completed in the optimal volumes and diluted with distilled water to the mark, the absorbance of solutions was measured at 438 nm .

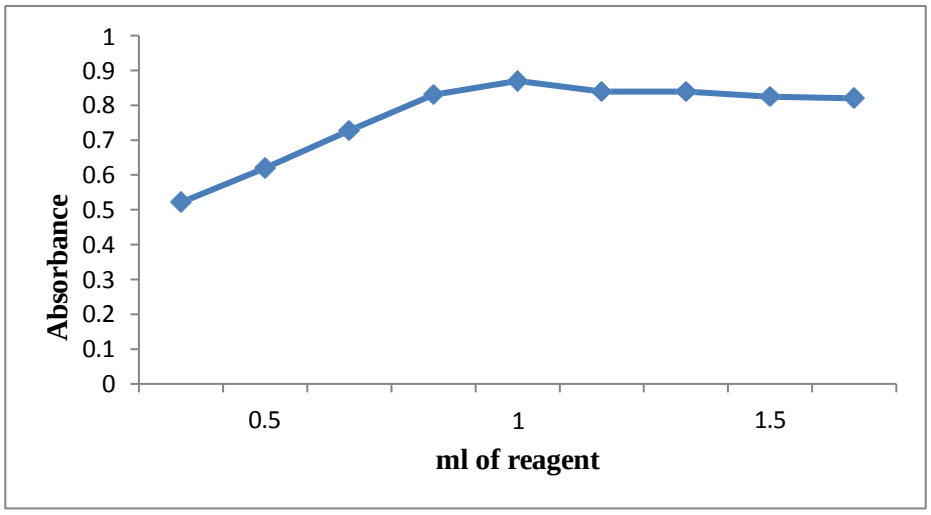


Figure (11): Valsartan molar ratio method

Applications

The proposed method was applied to the pharmaceutical preparation containing valsartan in the form of pills in the following manner.

Estimation of valsartan by direct method

The direct method was studied by taking three different concentrations of a solution of the pharmaceutical preparation (pills) (1.6-4-6.4) mg/ ml with a concentration of 80 mg/ml. These solutions were treated with the same steps that were followed in giving the calibration according to the optimal conditions and measuring the absorption against their blank solutions at 438 nm. The average was calculated for six measurements for each concentration, the relative error and recovery were calculated. The results are shown in the **table (8).**

Table (8): The Estimation of valsartan by direct method

Drug of VAL	Conc. of VAL (found)	RE%	Rec%	Average %
1.6	1.57868	- 1.331	98.668	99.59
4	3.9996	- 0.001	99.99	
6.4	6.4076	0.1203	100.12	

Indirect determination of VAL by Flame atomic absorption spectrophotometry (FAAS)

Another technical method used for estemation of VAL is Falam Atomic Absorption spectrophotometer (FAAS) by indirect measurement the absorbance of Fe(III) in the complex to detect the VAL concentration as in **figure 13** . The complex VAL_(Fe(III) was prepared by using optimum condition of temperature , proper solvent,type ,amount sufactant and time of reaction which are shown in the table(9) then the effect of changing the concentration of Iron ion was studied ,it was found the best concentration of Fe(III) to give maximum absorbance is 2.5 µg/ml of organic layer is enough to get higher absorbance for complex as in **figure 12** .Also we measured the concentration of VAL was measured in pharmaceutical preparations using calibration curve of indirect (FAAS).

Table (9): The optimal conditions for a complex (VAL_Fe(III))

The optimal conditions	
Λ_{max}	441nm
temperature	75℃
time of reaction	25mint
sufactant of Amount	1.4ml
type of sufactant	TritonX_114
The metal	Fe(III)
solvent	Water + Ethanol
Amount of metal	2.5 ml
Centrifugation	6000 rpm
Time of Centrifugation	20 mint

Effect of metal ion concentration

Figure (12) shows the effect of the volume of Fe(III) ion on the absorbance, where (500 µg/mL) of the drug solution was used. It was found that the optimum volume of the metal that gave the best absorbance is 2.5 µg/mL of Fe(III) .

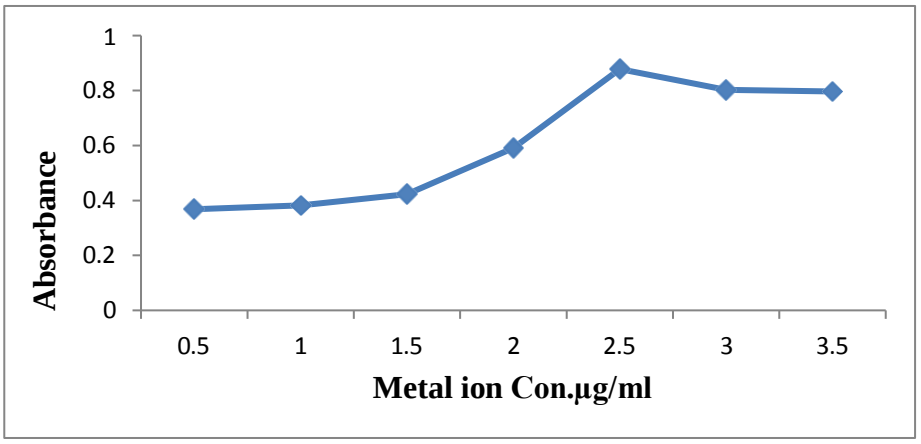


Figure (12): Effect of Optimum concentration Fe(III)ion conc. On absorbance of VAL_Fe(III) complex by FAAS method

Preparation of Calibration Curve for VAL

In order to test the linearity of the method and under the optimized conditions established by VAL-Fe(III) complex procedure **(table 9)** , Calibration graphs were established by plotting absorbance versus concentration of valsartan . of The calibration curve was .Plotting the mean absorbance values of the cloud point versus the concentration (g mL^{-1}) of (VAL-Fe^{+3}) as shown in **Figure(13)**

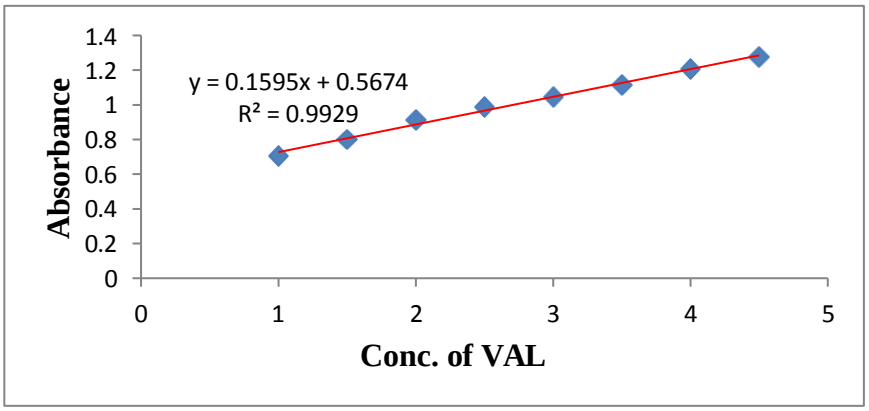


Figure (13): (VAL- complex) Calibration Curve by AAS Method

Comparison between the two methods of the proposed method

To determine a complex, a simple comparison was made between the methods FAAS and UV-VIS approaches, and the statistical parameter of the computation was shown in **Table (10).** The first and second approaches are distinguished by their ease of use, high economic accuracy, and application of the green chemistry requirement. The second approach is distinguished by its high selectivity, economy, and lack of use of hazardous chemicals. Scientist analysts believe that the first approach is preferable due to its best statistical calculation parameter and lack of potential interferences in the UV-Vis area. **Table (10)** compares the two approaches of the suggested method for

Table (10): Comparison between the Two methods of the Proposed method to determination of Complex

Parameter	Complex (VAL-complex) by CPE Method	Complex (VAL-complex) by FAAS Method
Concentration rang (g mL-1)	0.8_7.2	0.5-4.5
Regression equation	y = 0.1274x + 0.0234	y = 0.1595x + 0.5674
Correlation coefficient (R^2)	0.9942	0.9929
Intercept	0.0234	0.5674
slope	0.1274	0.1595
r	0.9970	0.9964

CONCLUSION

In this study, we presented a low-risk, low-cost approach for the pre-concentration and spectrophotometric detection of valsartan: the cloud point extraction procedure. It is a simple, sensitive green method. When compared to alternative methods, the method validation produced good findings in terms of linearity, repeatability, and sensitivity. The suggested technique can be used to figure out how much valsartan is in a tablet.

Competing Interests

Authors declare that there are no competing interests.

Reference

[1] N.Siddiqui, A.Husain,L.Chaudhry, M. S. Alam, M. Mitra , and P. S. Bhasin « Pharmacological and pharmaceutical profile of valsartan: a review », ' ***Journal of Applied Pharmaceutical Science.,111*** n° Issue, p. 12-19.(2011)

[2] R. R. Dargad, M. R. Prajapati, R. R. Dargad, J. D. Parekh, « Sacubitril/valsartan: a novel angiotensin receptor-neprilysin inhibitor », **Indian heart journal,** vol. 70, p. S102-S110. (2018).

[3] C. K. SINGH, « SACUBITRIL/VALSARTAN (ENTRESTO): A REVIEW ON DEVELOPMENT OF ANALYTICAL METHODS AND ITS ASSESSMENT IN PURE, BULK FORMULATION, BIOLOGICAL FLUIDS AND PHARMACEUTICAL PREPARATION »,***International Journal of Pharmaceutical Sciences & Medicine (IJPSM)***, Vol.7 Issue. 6, June- pg. 1-38(2022).

[4] F. O. Qasim, A. A. Haji, K. M. Qadir , A. J. M. Ameen « Development and Validation of Stability Indicating Nanodrop 2000c UV-Vis Method for Determination of Valsartan in Pharmaceutical formulations »**,** ***Journal of Pharmaceutical Negative Results,*** p. 919-925. (2023).

[5] S. Ramachandran, B. K. Mandal , S. G. Navalgund « Simultaneous spectrophotometric determination of valsartan and ezetimibe in pharmaceuticals »**,** ***Tropical Journal of Pharmaceutical Research,*** vol. 10, n° 6, p. 809-815. (2011).

[6] H. K. K. Patel, V. C. Jain, Z. Dedania, N. R. Saiyed , R. C. Patel « Development and validation of spectroscopic simultaneous equation method foش simultaneous estimation of Azelnidipine and Valsartan in synthetic mixture »**,** ***World Journal of Biology Pharmacy and Health Sciences,*** vol. 13, n° 2, p. 277-287. (2023).

[7] R. F. Salih, Q. N. Rashid « Spectrophotometric determination of Valsartan in pure form and in its pharmaceutical preparations »**,** ***Al-Qadisiyah Journal of Pure Science,*** vol. 26, n° 4, p. 239-246. (2021).

[8] Shakkor JS, Mohammed N, Shakor SR. Spectrophotometric method for determination of methyldopa in bure and pharmaceutical formulation based on oxidative coupling reaction**.** ***Chem Methodol.*** 2022;6(11):851–60.(University of

Kirkuk)

[9] Jamal Shakkor S. Spectrophotometric Determination of Reduced Nimesulide using 8-Hydroxyquinolinol Reagent in Pharmaceutical Preparations***. Kirkuk J Sci.*** 2015;10(1):143–57. .(University of Kirkuk)

[10] O. Al Wassil, M. E. Omer, A. E. B. Yassin , D. Ahmad « RP-HPLC method devel-opment for quantitation of valsartan in nano-structured lipid carrier formulation and in vitro release studies »***, Dig J Nanomater Biostruct,*** vol. 15, p. 1017-1102. (2020).

[11] M. A. A. Ragab, S. M. Galal, M. A. Korany , A. R. Ahmed « High performance thin-layer and high performance liquid chromatography coupled with photodiode array and fluorescence detectors for analysis of valsartan and sacubitril in their supramolecular complex with quantitation of sacubitril-related substance in raw material and tablets »***, Journal of chromatographic science,*** vol. 56, n° 6, p. 498-509. (2018).

[12] T. N. Raju, D. R. Kumar , D. Ramachandran « Assay of Valsartan and Sacubitril in Combined Dosage Form by RP-HPLC (Method Development and Validation) »***, J Applicable Chem,*** vol. 6, n° 5, p. 1004-1011. (2017).

[13] S. Trefi, Y. Bitar , V. Gilard « Separation and quantification of sacubitril-valsartan combination in tablets by a new ion-pair hplc »***, Research journal of pharmacy and technology,*** vol. 12, n° 3, p. 1017-1022. (2019).

[14] K. CHINTHALA, P. KANCHERLA , P. KUMAR « Bioanalytical Method Development and Validation for Quantitative Estimation of Valsartan by LC-MS/MS in Human Plasma. »***, Asian Journal of Chemistry,*** vol. 29, n° 7. (2017).

[15] B. Sivaram, T. Shyam « Stability-Indicating RP-HPLC Method Development And Validation For Determination Of Sacubitril Impurities In Sacubitril And Valsartan Microsphere Dosage Form. »***, NeuroQuantology,*** vol. 20, n° 9, p. 4969. (2022).

[16] A. Z. Al-Hafidh, A. T. Al-Taee « Electrochemical Behavior of Valsartan, Glibenclamide and their Interaction with Each other Using Square Wave Voltammetry »***, Raf. J. Sci,*** vol. 28, n° 2, p. 64-75. (2019).

لتحديد عقار الفالاسارتان في شكلة النقي وفي مستحضراتة الصيدلانية . تناولت هذه الدراسة استخدام طريقة جديدة وهي استخدام الطيف الضوئي UV_VIS .

وطيف الامتصاص الذري الغير مباشر(FAAS) . تم القيام بذلك باستخدام طريقة استخراج نقطة السحابة (CPE) باستخدام السطح النشط Triton X-114 كمادة سطحية غير أيونية.

تتضمن طريقة (CPE) تفاعلين، الأول يعتمد على تكوين معقد بين فالسارتان والكاشف بروموأنيلين في وجود ثنائي ميثيل أمينو بنزالديهايد (معقد مانيخ) عند ٤٣٨ نانومتر، بينما يتم تكوين معقد بين فالسارتان و Fe(III) في التفاعل الثاني عند ٤٤١ نانومتر، وتم استخدام (FAAS) لتقدير فالسارتان في المعقد الثاني.

تم تحديد عدد من الظروف مثل حجم المادة السطحية غير الأيونية، درجة الحرارة، تأثير الوقت على تكوين المعقد، حجم الكاشف، وتركيز أيون المعدن (مع استخدام الظروف المثلى نفسها في UV_Vis) و FAAS) حيث كانت درجة الحرارة ٧٥ درجة مئوية هي أفضل درجة حرارة لاستخراج نقطة السحابة لمدة ٢٠ دقيقة. كان الإيثانول أفضل مذيب لاستخراج المعقد، وتم اتباع قانون بير في المدى ٠,٨-٧,٢ ميكروغرام/مل لـ (UV_Vis) و ٠,٥-٤,٥ ميكروغرام/مل لـ(FAAS) .

وتراوحت متوسط استرداد العينات بين ٩٩,٨٨-١٠١,٠٤٢%. كان الانحراف المعياري النسبي (RSD)لـ ١,٦ ميكروغرام/مل من VAL أقل من ٢,٥%. كانت حدود الكشف والكمية ٠,٠٠٤٢١٠ و ٠,٠١٠٤٧ ميكروغرام/مل على التوالي. تم التحقق من صحة الطريقة وتطبيقها بنجاح على مستحضرات فالسارتان الصيدلانية، ومن النتائج والنسب المستردة التي تم الحصول عليها، وجدنا أنها

طريقة جيدة وعالية الحساسية وغير مكلفة وغير سامة وصديقة للبيئة.