Spectrophotometric Determination of Captopril in Pharmaceutical Formulations based on Ion-Pair Reaction with the Red Congo

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Abstract

A simple and sensitive spectrophotometric method has been proposed for the determination of captopril. The method is based on ion coupling between Congo Red and captopril, giving an intense violet color at 15°C. The colored product is quantified by spectrophotometry at 596 nm. Optimization of experimental conditions is described. The method was used to estimate 1-60 µg/ml of captopril. The accuracy of the method is achieved by mean recovery (97.446%) and accuracy is supported by relative standard deviation values (0.06-0.965%). The sensitivity of the method is indicated by the molar absorptivity (5757.92) L mol-1 cm-1The results of the method are compared with the formal method. The interaction of common drug additives was also studied. The proposed method is successfully applied for the determination of captopril in pharmaceutical.

Keywords: Captopril Spectrophotometric, Congo Red, Ion-pair.

DOI: 10.47750/pnr.2022.13.S07.006

INTRODUCTION

An effective oral blood pressure medication also used to treat another type of congestive heart disease [(1)], captopril contains a terminal thiol group that acts as a free radical [(2)]. Active ACE inhibitor [(1)], chemical formula C9H15NO3S, molecular mass 217.29 g/mol, Figure, shows the chemical structure of the drug (Captopril). Captopril has been extensively studied in the treatment of patients with mild to moderate hypertension and severe hypertension that do not respond to conventional regimens of diuretics, adrenergic receptors, and vasodilators [(3)]. Indications (hypertension, left ventricular dysfunction after myocardial infarction, diabetic nephropathy) and adverse side effects of captopril include cough, angioedema, agranulocytosis, hyperkalemia, taste change, teratogenicity, postural hypotension, acute renal failure and cytopenia. Eggs except for postural hypotension. Occurring due to the rapid and short action of captopril, most of the listed side effects are common to all ASE inhibitors. Of these, coughing is most commonly caused by elevated bradykinin levels [(4)].

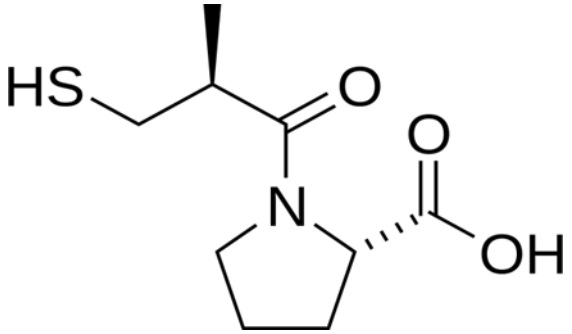

Figure 1: Captopril.

Many methods have been reported for the estimation of CAP in its pure form or pharmaceutical preparations. These methods include spectrophotometry Use of H-point[(5)] for simultaneous determination of captopril and hydrochlorothiazide in some pharmaceutical images where wavelengths of 221.5 and 230.3 nm were used. 104.37% and a relative standard deviation of 2.46% Taking advantage of redox reactions [(6)], a new and sensitive method was developed for the determination of the drug under study, in which the redox reaction occurs between the drug and Cu(II)-2,9-dimethyl-1phenanthroline (neocuproine), and then the Cu(I) compound was estimated)) -Neocuproin with a wavelength of 458 nm, and the results showed a broad linear concentration response of CAP with a detection limit of 0.2 µg/ml and a quantitative limit of 0.8 µg/ml. The proposed method was applied to analyze the commercial

preparations of the pharmaceutical companies producing the drug where the recovery rate was 99.0 - 101.5% and with a relative standard deviation of less than 2.0%. The UHPLC technique[8] was used in the determination captopril in some of its pharmaceutical forms, where the best working conditions were as a C18-type separating column and an equal mobile phase of methanol, Milli-Q water and trifluoroacetic acid in a ratio of 55:45:0.05 V/v/v, respectively, at a rate of Flow 0.1 ml/min. The components were detected at a wavelength of 220 nm and the method was sensitive, accurate and fast. The electrode method [7] was developed using a modified liquid carbon ion electrode using copper hydroxide nanoparticles to determine the drug under study in some of its pharmaceutical forms (tablets). It was found that the linearity was 0.7-70 µm with a detection limit of 12 nm, so the method is good for quantification. And. However, spectrophotometric methods are still more spread than other techniques due to their simplicity and inexpensive equipment. In this work, we developed an easy and sensitive spectrophotometric method for assaying CAP in its pharmaceutical.

Equipment and Materials

Devices The devices used in this study, with the make and model, are shown in Table (1-1).

Table (1-1) used equipment

Origin	Module	Instruments
Japan	Shimadzu 1900i	UV-Vis Spectrophotometer
German	Elma Sonic p	Ultra Sonic
Japan	Shimadzu AU	Electronic Scale

Chemicals

The reagents and materials used in this research are of high purity and are shown in Table (2-1).

Table (2-1) Reagents and Chemicals Used

Chemical name	Chemical formula	Pure%	origin
Captopril	$C_9H_{15}NO_3S$	98.92%	SDI
Congo Red	$C_{32}H_{22}N_6Na_2O_6S_2$	97%	German

Prepare the Solutions

1. Standard solution Captopril (500 µg/ml)

0.05 g of Captopril was weighed and dissolved with distilled water and the volume was completed to 100 mL in a volumetric vial so that the concentration became 500 µg/mL working solution.

2. Reagent solution, Congo red (200 µg/ml)

Prepare by dissolving 0.02 g of Congo Red in a given volume of distilled water and complete the volume in a 100 ml volumetric vial.

Pharmaceutical Solid:

1. A Captopril with a concentration of 500 µg/ml

10 tablets of the preparation (Aceprotin) produced by the General Company for Pharmaceutical Industries and Medical Appliances Samarra - Iraq SDI, were taken using ceramic slurry, and the average weight of one tablet contains 50 mg captopril, to prepare a solution of 500 µg/ ml, was taken in a volumetric bottle of 100 ml and fill volume up to mark with distilled water.

Discussion

1. Preliminary exams

When 2 mL of Congo red dye at a concentration of 200 µg/mL is added to 0.8 mL of captopril at a concentration of 500 µg/mL, the solution is violet. Then it was diluted with distilled water up to the mark in a 10 ml volumetric bottle, and then the resulting spectrum of the colored product was measured, which gave the highest absorption at the 596 nm wavelength versus the placebo solution.

A- Effect of the amount of Reagent

The effect of the reagent quantity of Congo red dye on absorption at a concentration of 200 µg/ml was studied by adding different concentrations (3µg/ml-50µg/ml) to 0.8 ml of captopril at a concentration of 500 µg/ml, and the volume was filled with distilled water up to 10 ml in a volumetric vial. 10 ml, then the absorbance of all solutions was measured at 596 nm wavelength against their sham solutions and the results are shown in Table (3-1)., 2 ml was also used in subsequent experiments.

Table (3-1) Effect of the size of the Congo Red on absorption

Concentration of CongoRed (µg/ml)	Absorbance
3	0.1995
5	0.2538
10	0.3721
15	0.4845
20	0.5749
25	0.6691
30	0.7623
35	0.8532
40	0.9321
45	0.8011
50	0.7001

B- Effect of Reagent time

The time required for captopril to conjugate red dye was studied by taking a volumetric flask of 10 ml capacity, containing 0.8 ml of captopril at a concentration of 500 µg/ml, adding 2 ml of Congo red at a concentration of 200

µg/ml, and leaving the solutions for different periods of time. Then it was diluted with distilled water to 10 ml, and the absorbance of all solutions was measured at a wavelength of 596 nm against their dummy solutions and the results are shown in Table (4-1).

Table (4-1) Effect of ion transfer time on absorption

Time(min)	Absorbance
0	**0.932**
5	**1.051**
10	**1.167**
15	**1.22**
20	**1.01**
25	**0.99**
30	**0.98**

Note from Table (4-1) that 15 minutes is sufficient to complete the ion transfer process and it was adopted in subsequent experiments.

C- Effect of the Temperature of Reagent

Then the complex absorbance was measured The product at the moment of reaction and in the temperature range 7-35 ° C is clear from The results of this study are shown in the table (improving absorption peaks, which are according to laboratory temperature (20), while the absorption of the colored product decreases when increasing. note Temperature. so it was relied on laboratory temperature.

Note from Table (5-1) that

Temperature (°C)	Absorbance
0	**0.583**
7	**0.729**
10	**0.941**
15	**1.221**
20	**1.465**
25	**1.368**
30	**1.201**

Temperature (20 ^{oC}) is sufficient to complete the charge transfer process and it was adopted in subsequent experiments.

D-Effect of PH of complex

A study was conducted to select the best acidity function, with different pH values ranging from 4.03 to 10.40, and the absorption values of the compound formed at each of these values were recorded as shown in Table (6-1). The results of this study showed that the addition of the acid led to a decrease in the absorption of the colored product, so it was not used, and the addition of the base affected the absorption value of the formed compound, so the base was not added. Do without it, so don't rely on acid and base.

Note from Table (6-1) that the acidity function (PH)

Addition	Volume(ml)	Absorbance	pH
HCl (0.01)M	0.9	0.87	**4.03**
	0.6	1.07	**5.54**
	0.3	1.11	**6.31**
Without	-	1.462	**6.8**
NaOH (0.01)M	0.3	0.0648	**0**
	0.6	0.0640	**8.82**
	0.9	0.0636	**9.90**
	1.2	0.0529	**10.40**

At point 6.8 is sufficient to complete the charge transfer process and was adopted in subsequent experiments.

3-Finl absorption spectrum

The wavelength of the highest absorption under optimal working conditions for the determination of captopril was confirmed by measuring the absorption spectrum of the resulting solution. Figure (1-1) was obtained and the wavelength of the highest absorption was found to be 596nm, as shown in the initial.

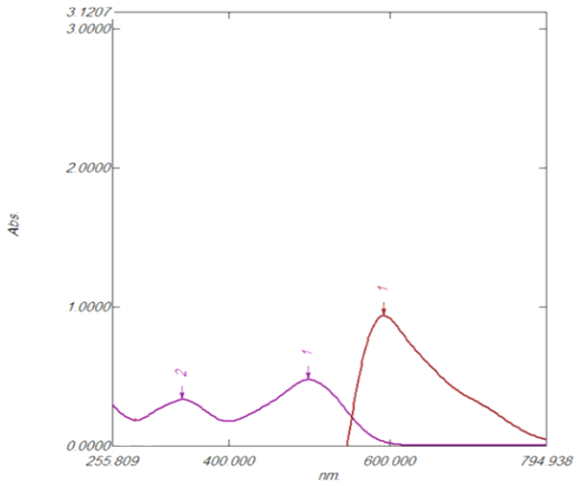

Figure 1-1 final absorption spectrum of Complex

1. Represents the new complex compound at 596 nm
2. Refers to the spectrum of Congo red dye at 498 nm

4 -Approved working method and calibration curve preparation Procedure

After determining the optimal conditions for captopril determination, the standard curve was prepared as follows:

Increase volumes (1.2-0.02ml) by 500 µg/mL. Captopril solution was added to a series of 10 ml volumetric flasks and 0.8ml was then added. 200µg/ml Congo Red reagent

was added, supplemented the volume to the mark with distill water, the solutions were left for 15min and the absorbance for all solutions was measured at 596nm against the sham solution.

Figure (2-2) represents the standard curve following Beer's law for a range of concentrations between 1-60µg/mL of Captopril, the molar absorbance of the method was (5757.92 L mol -1 cm-1), and the Sandel significance is 0.3773µg. cm-2, which indicates that the standard curve has a high specification.

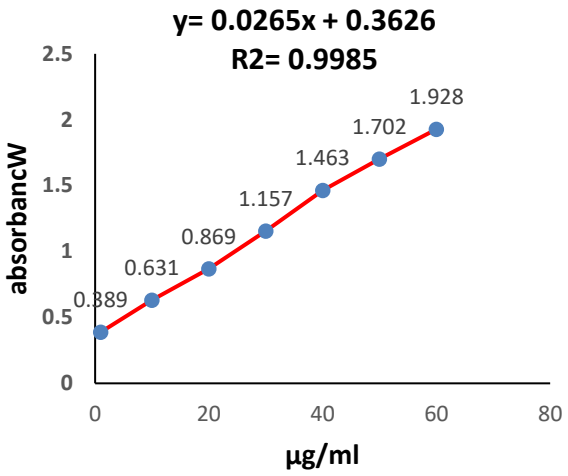

Figure (2-2) calibration standard curve for the determination of Captopril

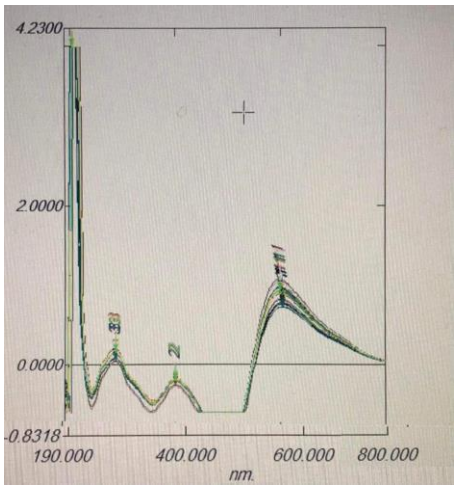

Figure (2-3) Absorption spectrum of concentrations between 1-60 µg /ml of Captopril with reagent

5-The accuracy and compatibility of the method

The accuracy and compatibility of the proposed method for the estimation of Captopril and compatibility under the optimum conditions indicated in the method work by calculating the recall and the relative standard deviation of different concentrations (10, 20, 30,40,50) µg/ml by taking an average of six readings for each, and the recall rate was 100.312%, and the relative standard deviation does not exceed 0.66%, meaning that the method has high accuracy and the results are shown in Table (7-1).

Table (7-1) accuracy and compatibility of the method

Conc. of captopril taken mg/ml	Conc. of Captopril found mg/ml	Rec %	RSD %
10	10.128	101.28	0.965
20	19.109	95.54	0.959
30	29.977	99.92	0.552
40	41.524	103.81	0.063
50	50.505	101.01	0.78

6 -Limit of detection

The limit of detection (LOD) and the quantitative limit (LOQ) were calculated for the determination of Captopril at the wavelength of 557 nm, by measuring the absorption of the lowest concentration taken from the calibration curve, which is 1 µg/ml, six times and under the same conditions. The results are shown in Table (8-1) and can be expressed as The detection limit has the following relationship:

Table (8-1) limit of detection and quantitative limit for Captopril

Concentration µg\ml	$\bar{X}$	S	L.O.Q µg\ml	L.O.D µg\ml
1	**0.389**	**0.0102**	**0.0786**	**0.2358**

7 -The nature of the resulting product

The continuous changes method [Job's method] was used to find out the reaction rate of Captopril with the Congo Red reagent. below:

Some number of solutions were prepared to contain different volumes of Captopril ranging from 0.9-0.1 ml and from the Congo Red reagent was 0.1-0.9 ml at a concentration (200µg/ml) for each in a final volume of 10 ml, and the rest of the solutions were added The solutions were under the same optimal conditions for the working method, and the absorption of the formed product against the mock solution was measured at the wavelength of 596nm. Figure (4-1) shows that the reaction ratio of Captopril with the reagent is 1:1.

Table (9-1) Absorption of the binding ratio of the product

VD	VR	Absorbance	VD/VD+VR
0.1	0.9	0.0641	0.1
0.2	0.8	0.2002	0.2
0.3	0.7	0.2998	0.3
0.4	0.6	0.3693	0.4
0.5	0.5	0.3721	0.5
0.6	0.4	0.2942	0.6
0.7	0.3	0.2062	0.7
0.8	0.2	0.1201	0.8
0.9	0.1	0.0651	0.9

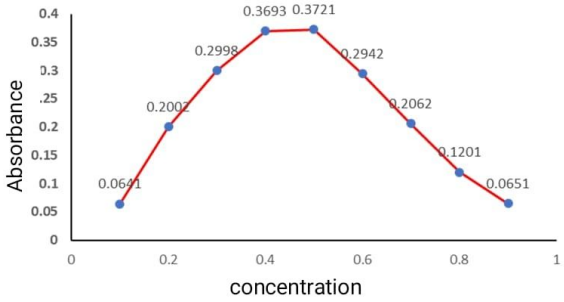

Figure (1-4) Continuous Changes Curve (Joepe's Method) for the Product

8 -Application of the developed method for the determination of Captopril in pharmaceutical preparations

First: the direct method

Determination of Captopril in 50 mg Aceprotin tablets by the direct method

To find out the success of the developed method, it was necessary to apply it to pharmaceutical preparations containing Captopril, different volumes (0.2,0.4,0.6 ml) of the 50mg solution prepared on the page (4) were taken to obtain concentrations (10, 20, 30) µg/ml, were treated according to the optimal working method, and the absorbance (average of six readings) was measured for each solution against the sham solution at the wavelength of 596nm, and the reactivity and RSD were calculated and the results are shown in Table (10-1).

Table (10-1) Determination of Captopril in Aceprotin tablets by the direct method

Conc. of Drug taken µg/ml	A	Conc. of drug found µg/ml	Rec %	RSD %
10.000	0.604	10.203	102.03	0.259
20.000	0.847	19.513	97.56	0.166
30.000	1.125	30.164	100.4	0.012

The results of Table (10-1) confirm the success of the proposed method for the determination of Captopril in the in Aceprotin tablets.

Second: Standard add-on method

To determine the efficiency of the proposed method and to prove that the developed method is free of interference, the standard additive method was applied in the determination of Captopril in pharmaceutical preparations. The method included adding fixed amounts (0.2ml) of Aceprotin tablets at a concentration of 500 µg/mL prepared on the page (4), in two series of volumetric bottles of 10 mL capacity, then adding increasing volumes (0.7,0,6,0.5,0.4, 0.3, 0.2, 0.1 and 0.8ml) of the pure standard solution of a concentration of 500 µg/ ml, and one of the bottles was left without addition, and the solutions were treated higher with the same method used when preparing the calibration curve, then the absorption (average of six readings) was measured for each solution against its sham solution at the wavelength of 596nm, and the results are shown according to Table (11-1) and shapes.

Table (11-1) method of standard additions

Captopril			
Conc. taken (µg/ml)	**Conc. found (µg/ml)**	**Rec %**	**RSD %**
10	9.82	98.2	0.0850

The results of Table (11-1) show that the standard additions method is in good agreement with the direct method within the acceptable range of error, which indicates that the method is satisfactory and free of interferences.

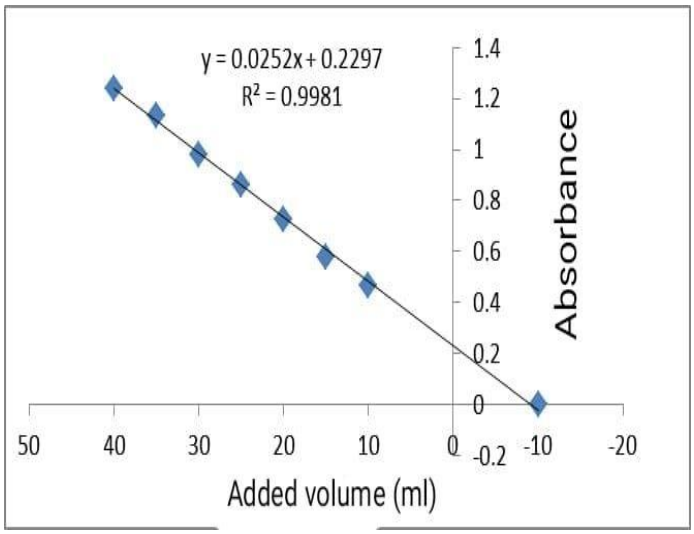

Figure (1-5) Standard additives for the determination of Captopril in ACEPROTIN

9-Conclusions

The ion pair method was used to determine CAP in its pure drug and pharmaceutical form Aceprotin. This method is based on the reaction of CAP with Congo red reagent to form a violet complex. The highest absorption was given at the wavelength 596 nm, and the obtained results showed the values of percentage recovery, relative standard deviation, limit of detection, quantitative limit of accuracy and precision of the method, which indicates the success of the proposed method in the determination. from CAP.

10 -Method comparison

The proposed method was compared with another spectroscopic method and Table (12-1) shows the results of that comparison.

Table (12-1) comparison of the proposed method with another spectroscopic method

Other [14] Method	Present Method	Parameters
507	596	λmax(nm)
2-60	1-60	Beer's (µg/ml) law range
R.T	º10	T(ºC)
10	15	Development time(min.)
red	purple	Color of the dye
1:1	1:1	Nature of the dye
Syrup	Tablets	Application of the method
1500	5757.92	ε(L/mol.cm)
2.050	0.962	RSD%

Conclusion

Statistical Attached

1- Standard Deviation SD[9]

$$S = \sqrt{\sum \frac{(Xi - X)}{n-1}} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots$$

when-:

Arithmetic mean: X

Xi: readings

: nThe number of readings

2- Relative standard deviation [10]

$$\mathbf{RSD\% = \frac{S}{X} * 100}$$

when-:

S: Standard deviation

Arithmetic mean: X

3. L.O.D and quantitative limit L.O.Q [11]

$$\mathbf{L.O.D = \frac{3.3 * S * Conc.}{X}} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots$$

$$\mathbf{L.O.Q = \frac{10 * S * Conc.}{X}}$$

when-:

S: standard deviation

X: the arithmetic mean of a series of readings

Conc.: lowest concentration in the titration curve

4- Recursion %[12]

$$\mathbf{Rec\% = \frac{Xi}{u} * 100} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots$$

when-:

Xi: Practically calculated value

u: theoretically calculated value

5- Molar Absorption Coefficient[13]

ε =Mw x slope x 1000

When-:

M.Wt: The molecular weight of the substance to be estimated (g/mol)

6. Sandal's factor[13]

$$\mathbf{S = \frac{M.Wt}{\varepsilon}}$$

when-:

S: Sandel's modulus (µg.cm-1)

M.wt: the molecular weight of the substance to be estimated (g/mol)

$\boldsymbol{\varepsilon}$: molar absorption coefficient

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