Spectrophotometric method for the determination of Captopril in pharmaceutical formulations

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Abstract:

A simple, rapid and sensitive spectrophotometric method has been developed for the determination of captopril in aqueous solution. The method is based on reaction of captopril with 2,3-dichloro 1,4- naphthoquinon(Dichlone) in neutral medium to form a stable yellow colored product which shows maximum absorption at 347 nm with molar absorptivity of 5.6×10^3 $L.mole^{-1}. cm^{-1}$. The proposed method is applied successfully for determination of captopril in commercial pharmaceutical tablets.

Key word: Spectrophotometry; Captopril; Dichlone; 2,3-dichloro 1,4-naphthoquinon

Introduction:

Arterial hypertension is one of the diseases with major prevalence in the world, being known that one in six habitants is affected by this health problem. Although it is caused by still unknown factors, some risk factors contribute to the development of this pathology, like family history, age, high salt intake, obesity, sedentariness, alcoholism and stress.[1]

The first drug planned to be used for arterial hypertension treatment was captopril,1-[(2S)-3-mercapto-2-methylpropionyl]-L-proline (Figure 1), which belongs to the class of angiotensin-converting enzyme (ACE) inhibitors. This drug interacts with ACE due to its similarity with a dipeptide and the sulphydryl group also plays an important role, linking covalently to the zinc atom in the enzyme active site. This drug is widely used mainly for arterial hypertension treatment, but also in diabetic nephropathy and congestive cardiac insufficiency. [2,3]

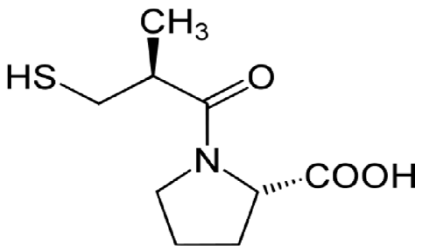

Fig. (1). Molecular structure of captopril.

Several types of analytical procedures have been proposed for the analysis of captopril in pharmaceuticals formulations. These procedures include colorimetry[4- 9] ,fluorimetry [10] ,capillary electrophoresis [11],high-performanceliquid chromatography (HPLC)[12-15],polarography [16], voltammetry [17],coulometry[18],amperometry[19], conductometry [20], Potentiometry[21- 23] and flow injection methods[10, 24, 25] . Some of theses procedures are not simple for routine analysis and required expensive or sophisticated instruments. In this work a simple analytical producer is described for captopril determination .

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Materials and methods:

Apparatus

All absorption measurements were made on a Shimadzu UV-210A double-beam spectrophotometer supplied with a digital printer DP80Z and matched 1-cm optical silica cells.

Reagents

All reagents used were of analytical grade and obtained from Fluka and BDH companies. captopril was provided from State Company for Drug Industries and Medical Appliances, Sammara-Iraq, SDI.

Dichlone(1×10^{-3}M)solution : This solution is daily prepared by dissolving 0.0227 g of dichlone in ethanol and the volume completed to the mark in 100 ml volumetric flask with the same solvent.

Ethanol: Absolute (99-100%) is used.

Captopril(100ppm)solution: solution is prepared daily by dissolving 0.01g of captopril in distilled water and made up to volume in 100ml volumetric flask.

Captopril tablets solution: The contents of 10 tablets (25mg) were weighed and the powder was mixed. The accurately weighed portion of the powder equivalent to one tablet was dissolved in amount of ethanol. The solution was filtered into a 100ml calibrated flask, the residue was washed with water and the filtrate was diluted to the mark with distilled water.

Results and Discussion:

Absorption spectra

Captopril reacted with 2,3-dichloro 1,4- naphthoquinon in neutral medium to form a stable yellow coloured product having a maximum absorption at 347 nm against reagent blank (Fig. 2).

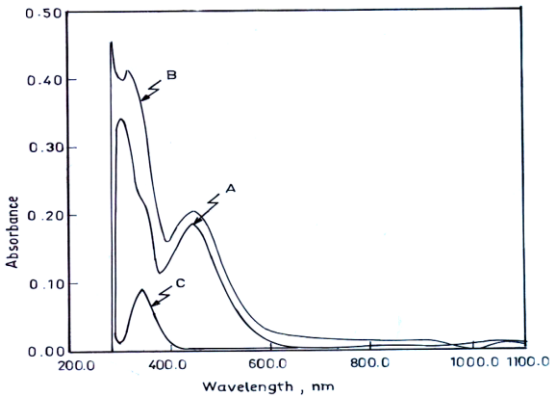


Fig.(2). Absorption spectra of 300µg captopril / 25ml treated according to the recommended procedure and measured against (A) reagent blank, (B) distilled water and (C) reagent blank measured against distilled water.

Study of the Optimum Reaction Conditions

The various parameters affecting and related to the above mentioned coloured product have been studied and optimum conditions have been selected.

Effect of the pH

The effect of the pH on the determination of captopril with dichlone was examined by varying it from 1.00 to 14.00. The absorbance of the reaction was close to 0 in acidic and basic solutions, In order to keep the high sensitivity for the determination of capotril , pH 7.0 was chosen for subsequent experiments.

Effect of reagent concentration

The effect of changing the reagent concentration on the absorbance of solution containing a fixed amount of the drug was studied. It was found that the absorbance increased rapidly with the increase in the amount of dichlone, and became maximal and constant when the amount of dichlone was 2.0 ml or greater. Thus, 2.0 ml of dichlone solution was chosen.

Table (1): Effect of reagent concentration

Dichlone(1×10^{-3}M)ml	Absorbance
1	0.134
2	0.240
3	0.245
4	0.253

Effect of the temperature

The absorbance of the reaction was determined at different temperatures ,The reaction time found to be a 15-min. With the temperature increasing, the absorbance gradually decreased after 25°C. Therfore the room temperature was chosen as the optimum and also the reaction was found to be stable for further 45 min.

Table (2): Effect of temperature on absorbance.

Temp °C	Absorbance									
	Time (min)									
	0	5	10	15	20	25	30	35	40	50
0	0.013	0.025	0.030	0.037	0.048	0.050	0.126	0.124	0.061	-
25	0.075	0.097	0.120	0.255	0.253	0.251	0.252	0.251	0.250	0.248
40	0.05	0.060	0.064	0.062	0.060	0.067	0.064	0.064	0.062	-

Effect of surfactants

The effect of amount of different types of surfactants (cationic, anionic and non-ionic) on the colour intensity of captopril complex with dichlone reagent has been tested. The experimental data show no useful results. Therefore, they have not been incoporated in subsequent steps.

Recommended procedure

Transfer an increasing volumes of the 100 µg/ml captopril into 25ml volumetric flask to cover the range (20 – 300**)** µg. Then 2ml of (1×10^{-3} M) Dichlone were added. The volumes are completed to the mark with distilled water and the absorbance is measured at 347 nm against the reagent blank prepared in the same manner but without Captopril.

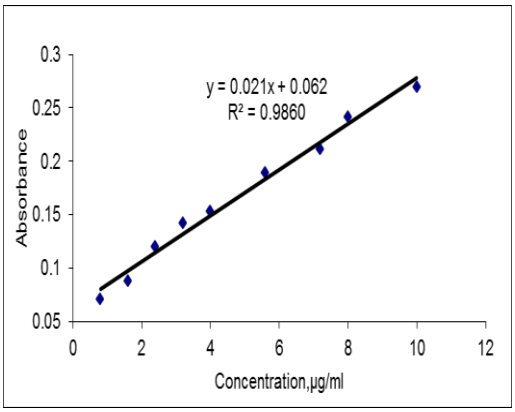


Fig. (3) Calibration graph for captopril.

Effect of excipients

The effect of some species commonly present in captopril pharmaceutical formulations (lactose, glucose, sucrose, starch, stearic acid, magnesium stearate and microcrystalline cellulose) was evaluated in molar quantities showing that the usual amounts in pharmaceutical formulations doesn't interfere in captopril determination by the proposed procedure.

Accuracy and precision of the method

To check the accuracy and precision of the method, captopril has been determined at three different concentrations with three replicates. The results, described in Table 3, indicate that the method is accurate and precise.

Table (3): Accuracy and precision of the method

Amount of Drug taken, µg	Relative error, % *	Relative standard deviation, % *
100	+ 0.87	±1.17
200	+0.48	±0.53
300	-0.76	±1.39

*Average of three determinations

Nature of the product

The nature of the coloured products was studied by applying Job's method (Figure 4).The results show that the mole ratio of captopril to dichlone was 1:1

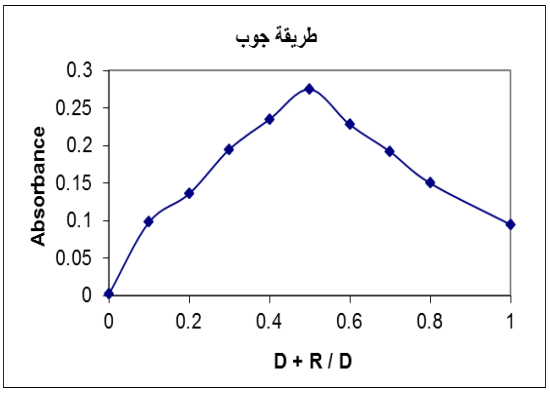
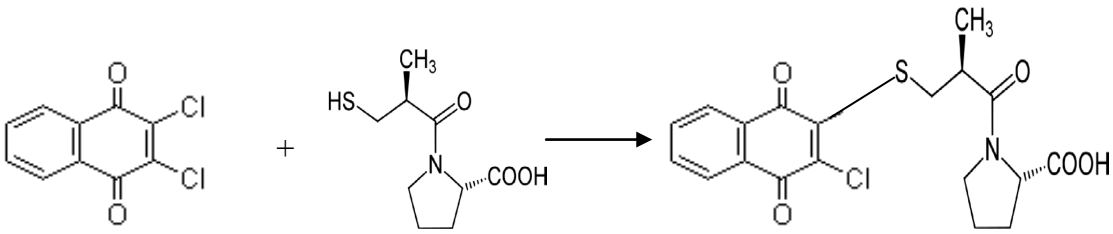


Fig (4.) : Job's method for captopril - dichlone product

Therefore, the formation of the product may occur as follows:



Analytical application

Different volumes of the solution of captopril in it's tablet solution were transferred to cover the concentrations 4, 6, 8 µg/ml of captopril and preceded with recommended procedure. The data are given in Table 4.

Table (4): Determination of captopril in its pharmaceutical preparation by the proposed method

Pharmaceutical perparation	Amount added (µg/ml)	Recovery*(%)	Average recovery (%)
Tablet	4	98.03	101.9
	6	104.04	
	8	103.73	

* Average for five determination

Conclusion:

Simple, rapid and inexpensive spectrophotometric method for the assay of captopril has been developed. The method has been successfully applied to the determination of captopril in tablet, the common excipients do not interfere with the proposed method.

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طريقة طيفية لتقدير الكابوتريل في المستحضرات الدوائية

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الخلاصة:

تم تطوير طريقة طيفية بسيطة وسريعة وحساسة لتقدير الكابوتريل في المحلول المائي . تعتمد الطريقة على تفاعل الكابوتريل مع 3,2 –ثنائي كلورو4,1 نفثوكوينون في محيط متعادل لإعطاء ناتج ملون مستقر يظهراعلى امتصاص عند 347 نانوميتر والامتصاصية المولارية 5.6×10^{3} لتر.مول$^{-1}$.سم$^{-1}$ تم تطبيق الطريقة وبنجاح في تقدير الكابوتريل في مستحضره الصيدلاني بشكل حبوب.