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Indirect determination of captopril by AAS

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Abstract

An indirect method is described for the determination of captopril (KPL) in pharmaceutical preparations by atomic absorption spectrometry (AAS). The procedure is based on the complexation of KPL with an excess of Pd(II) ion. The unreacted Pd(II) was resoluted on a cationic ion — exchanger resin, while Pd(II)–KPL sequestrate was not retained. The effluent Pd(II) sequestrade was measured by AAS. The absorbance is found to increase linearly with increasing KPL concentration, because the amount of Pd(II) is related to the concentration of KPL, which is corroborate by the calculated correlation coefficient value of 0.9939. The system obeys Beer's law for 1–40 μg ml^{-1}, S.D. was found to be 0.039 ($n = 5$). The Pd(II)–KPL complex was obtained in the solid phase. Characterization of the complex was performed by elemental analysis, TG, conductance measurements and IR, ^{1}H-NMR spectroscopy.
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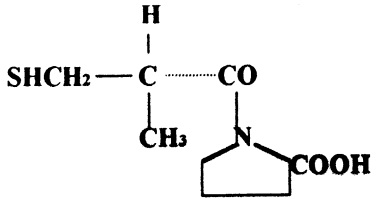
Keywords: Captopril; Atomic absorption spectrometry; Palladium(II) chloride

1. Introduction

Captopril (KPL) (Scheme 1), 1-(3-mercapto-2-D-methyl-l-oxoproppyl)-L-proline (S,S), is used therapeutically as an antihypertensive agent. It acts as a potent, and specific inhibitor of angiotensin-converting enzyme [1–3].



Scheme 1.

The physico–chemical and analytical characteristics of KPL with some references for its quantitation have been collected in an analytical profile [4]. Complex compounds of drugs with different metal ions enable determination of drugs by spectrophotometric methods and provide variable information about biological transformation reactions. Several methods have been reported for the quantitative determination of KPL including electroanalytical [5], high performance liquid chromatography (HPLC) [6], chemiluminescence [7], flourimetry [8], and spectrophotometry [9–11].

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The official method includes the titration of KPL with potassium iodate in acidic medium [12]. There are few data on the use of metal ions as analytical reagents for the determination of KPL, and its complexation properties [13–15]. In previous studies [14,15], it was shown, that KPL forms with Pd(II) ions colored complex of M:L ratio 1:2. The produced color was used for estimation of KPL spectrophotometrically [14], or by flow injection analysis [15]. The application of atomic absorption spectrometry (AAS) involving Pd–KPL complex was not reported in the literature. AAS has been combined with various chromatographic techniques. This method includes ion-exchange chromatography, which is inapplicable during pre-treatment of AAS sample solutions either, for pre-concentration of the analyte element from dilute sample solution or to remove other ions that may exert a chemical or physical interference from the sample solution, so, it introduces some selectivity and amplify the sensitivities of the determination [16,17].

The present investigation reports a new method for indirect AAS determination of KPL combined with ion-exchange chromatography, through complexation with Pd(II) ions. Elemental analysis, IR, and ^{1}H-NMR spectroscopy were used to elucidate the possible structure of Pd(II)–KPL complex obtained in the solid state.

2. Experimental

A Perkin–Elmer AAS model 2380, was used with a hollow cathode lamp of palladium, and a conventional 10-cm slit burner head for air–acetylene flame were used. Conductance measurements were carried out using Metrohm 644 conductometer. A shimadzu TG-50, Shimadzu FTIR-80101A and (DMSO) measurements were recorded on Varian Gemini 200. 200 MHz (^{1}H-NMR) 50-Spectrometer were also used.

2.1. Materials and reagents

All the reagents employed were of high purity. Squibb Egypt Co. Giza, Egypt, supplied KPL (standard substance) and KPL (R) 25 mg, and Capozide 50 mg. Palladium(II) chloride (pro analisi, Merck). Ambereilite-IR-120, of particle size 100–200 mesh (BDH).

A stock solution of KPL (standard substance) of concentration 1×10^{-2} M was prepared by dissolving the accurately weighed amount of the drug in water. More dilute solutions were obtained by appropriate dilution.

A 1×10^{-2} M solution of palladium(II) chloride was prepared by dissolving the required amount of the Proanalisi, Merck product in water in the presence of appropriate volume of sodium chloride (4×10^{-2} M), and warming the mixture in a water bath. The solution was cooled and diluted to volume with water in 50 ml calibrated flask then standardized gravimetrically [18]. Solutions of lower concentrations were obtained by accurate dilution.

Britton–Robinson buffer solutions [19] covering the pH range 2.08–8.00 were prepared by mixing 0.04 M orthophosphoric, boric and acetic acids with the appropriate volume of 0.4 M sodium hydroxide solution. The pH of each buffer solution was determined.

2.2. Calibration of the AAS

Calibration graphs were constructed by performing triplicate measurements of 0, 1, 2,….10 μg ml^{-1} palladium(II), at 244.8 nm, lamp current 5 mA, spectral bandpase; 10 nm, fuel, acetylene; and support, air.

2.3. Analytical determination of KPL

Aliquots containing 25–1000 μg ml^{-1} of KPL were transferred into 25-ml standard flasks. To each flask 2.5 ml of (1×10^{-3} M) Pd(II), atomic absorption standard solution and 5 ml of Britton–Robinson pH 4.5 were added. The reaction mixture was diluted to the mark, warm to 60° and the contents of the chromatographic column is subjected to cation-exchanger (Amberelite 1R-120) 10 cm in length, and 1 cm^2 area, at 0.6 ml min^{-1}. The Pd(II)–KPL complex was then aspirated into AAS under the optimum conditions.

Table 1
Analytical parameters for complexation of KPL with Pd(II) chloride, by AAS

Parameters	Proposed method
Beer's law limits (μg ml^{-1})	1–40
Sandell sensitivity (μg cm^{-2})	0.2814
Slope (specific absorptivity)	0.0035
Intercept	0.0029
Correlation coefficient (r)	0.9939
S.D. ($n = 5$)	0.0391

2.4. Assay of pharmaceutical preparations

An accurately weighed quantity of powdered tablets equivalent to 50 mg of the drug was placed in 50-ml volumetric flask, 30 ml of distilled water was added and the solution was shaken for 5 min to dissolve the drug. The volume was made up to 50 ml and the solution was filtered, and subjected to analysis by applying the previous procedure.

2.5. Preparation of Pd(II)–KPL complex

The solid Pd–KPL complex was prepared by mixing 50 ml solutions of palladium(II) chloride (2×10^{-3} M) with 25 ml solution of KPL (2×10^{-3} M). The precipitate obtained was filtered off, washed with distilled H_2O and dried. Elemental analysis and ^{1}H-NMR spectra were carried out.

3. Results and discussion

3.1. Indirect AAS-determination of captopril

Captopril reacts with palladium(II) chloride at pH 4–8 to form a water-soluble 2:1 complex [14]. The produced complex was resoluted on a cationic-exchange resin (Amberelite IR-120) and aspirated on the AAS. The signals of palladium ions are linearly proportional to KPL concentration over the range of 1–40 μg ml^{-1} under the experimental conditions described for drug determination. Standard calibration curve for KPL was constructed by plotting absorbance versus KPL concentration. Conformity with Beer's law was evident in the concentration range 1–40 μg ml^{-1} of the final dilution, the regression line equation of the drug are tabulated in Table 1. The correlation coefficient (0.9939) indicating good linearity. In order to determine the accuracy, and precision of the method, solutions containing three different concentrations of KPL were prepared and five absorbance measurements were performed on each reaction product. The measured standard deviation (S.D.) and relative standard deviation (R.S.D.) (Table 2) can be considered satisfactory.

Captopril has also been determined by AAS method-involving ashing followed by adding a known excess of barium chloride, and the precipitated barium sulfate was centrifuged. The excess barium chloride in the decanted solution was determined by AAS [13]. However, this method is not highly sensitive, and the steps required for the preparation of the sample solutions, do seem to be quite time-consuming and has the disadvantage that the presence of sulfur-containing compounds such as hydrochlorothiazide, can interfere. In the air–acetylene flame the AAS signal of palladium(II) is depressed in the presence of Al, Co, and Ni at all concentrations [20]. The absence of these species in KPL samples lead to the absence of

Table 2
Precision and accuracy in the determination of pure drug

Drug	Added (μg ml^{-1})	Found ± S.D. (μg ml^{-1})[a]	R.S.D. (%)	Confidence limits ($P = 0.05$)
KPL	10	9.94 ± 0.07	0.70	9.94 ± 0.09
	20	20.10 ± 0.09	0.45	20.10 ± 0.11
	30	29.99 ± 0.108	0.36	29.99 ± 0.13

[a] Average of five determinations.

Table 3
Determination of KPL in tablets

Drug	Sample number	AAS-method	Official method
Capoten (25 mg)	1	100.91 ± 0.27, $t = 1.622$, $f = 1.235$	100.67 ± 0.30
	2	99.70 ± 0.22, $t = 0.387$, $f = 2.25$	100.00 ± 0.33
	3	99.90 ± 0.25, $t = 0.989$, $f = 2.982$	100.12 ± 0.43
Caposide (50 g)	4	99.8 ± 0.2, $t = 0.676$, $f = 0.100$	100.01 ± 0.63
	5	99.5 ± 0.38, $t = 0.527$, $f = 0.555$	99.35 ± 0.51
	6	98.92 ± 0.4, $t = 0.824$, $f = 0.490$	99.10 ± 0.28

their interference on AAS determination of Pd(II).

In the proposed method, which uses Pd(II) as the analytical reagent for the determination of KPL, a cationic-exchanger resin was found to be the most suitable one for such study. This may be due to the competitive effect with other interfering anions present in the medium. Employing cationic-exchanger resin, no interference will occur and good results will be obtained. The method was applied to the determination of KPL content in some of its formulations. The excipients present were not a problem because they did not interfere. Table 3 shows that the results of the assay of KPL in its formulations are in excellent agreement with the labeled contents and with those obtained by the standard method of Pharmacopoeia [12]. The proposed method is simpler and less time-consuming than the official method. For the formulations examined the results obtained by the reference and AAS methods were compared by applying the F-test and the t-test at the 95% confidence level. The calculated F and t values did not exceed the theoretical ($F = 6.39$, $t = 2.306$), which indicates that there is no significant difference between the two methods.

3.2. Site of chelation

On the basis of the analytical data obtained, Table 4 the palladium(II) KPL complex can be formulated as a mono-anionic bidentate ligand towards the Pd(II) ion. This is supported by the low conductance value of the complex (10^{-3} M) in DMF ($0.9 \times 10^{-2}\ \Omega^{-1}\ cm^2\ mol^{-1}$) indicating that the complex is a nonelectrolyte. The TGA thermogram of the complex shows a weight loss (5.93%) at 75–90°C corresponding to two molecules of water, this can be considered as a support for the consistent with the suggested formulae.

3.2.1. IR and ^{1}H-NMR spectra

The bonding of KPL to Pd(II) ion was investigated by comparing the IR, and ^{1}H-NMR spectra of $[Pd(KPL)_2 \cdot 2H_2O$ complex with those of the free ligand.

3.2.1.1. IR-spectra. The IR-spectrum of the displays bands at 2560, 1750, 1640, and 1475 cm^{-1} assigned to ν_{SH}, ν_{COOH}, and $\nu_{C=O}$ (amide), and hetero nitrogen, respectively. The IR spectra of the $[Pd(KPL)_2] \cdot 2H_2O$ shows a band corresponding to the ν_{SH} at the same frequency as that of the ligand. The bands corresponding to stretching vibrations of hetero nitrogen shifted to a lower frequency by 50 cm^{-1} indicating its coordination, and also ν_{OH} which is situated in the spectrum of the ligand disappeared, and ν_{COO^-} is shifted to lower frequency by 25 cm^{-1} in the spectrum of complex compound. The above arguments indicate that the ligand behaves as a monobasic bidentate ligand.

3.2.1.2. ^{1}H-NMR spectra. The ^{1}H-NMR spectra of the complex in DMSO (d6) using TMS as internal standard reveals the following.

The signals of CH_3 group in the spectrum of the ligand situated at 1.1 ppm, whereas CH_2 groups of the side chain, and cyclic chain are observed at 1.9 and 2.4 ppm, respectively. The CH is observed at 3.6 ppm. The signals of δ_{OH}

and δ_{SH} are observed at 4.5 and 12.6 ppm, respectively. This is supported by the fact that on deutration of the last two signals with D_2O the signals disappeared.

On comparing the ^{1}H-NMR of the ligand with that of the complex the following can be pointed out.

1. ν_{OH} of the COOH group disappeared in the spectrum of the complex compound.
2. Small shift is observed comparing the spectra of the ligand and the complex compound.
3. A new signal is observed in the spectrum of complex at 4.3 ppm, which can be attributed to coordinate H_2O.

The magnetic susceptibility measurements showed that the complex is diamagnetic indicating that the complex exhibits square planar geometry.

Based on the above discussion the following structure is suggested.

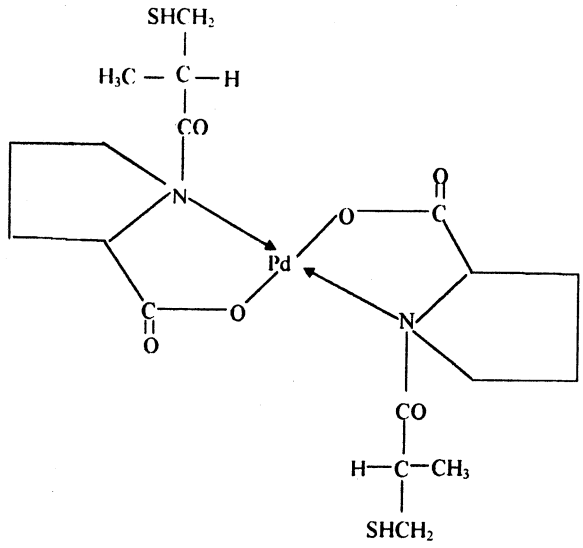

Table 4
Analytical and spectral data of $[Pd(KPL)_2]\cdot 2H_2O$ complex

Assignment	Free ligand	$[Pd(KPL)_2]\cdot 2H_2O$ complex
Analytical data		
Color		Orange
%C[a]		37.6 (37.7)
%H[a]		5.9 (5.2)
%N[a]		4.87 (5.0)
%Pd[a]		18.46 (18.5)
%Loss in weight[a]		6.27 (6%) Loss of 2 mol of H_2O at 75–90°C
$\wedge$ (Ω^{-1} cm^2 mole^{-1})		9×10^{-4}
IR: (cm^{-1})		
ν_{SH}	2560	2560
ν_{COOH}	1750	1725
$\nu_{C=O}$	1640	1600
$\nu_{N\text{-hetero}}$	1475	1425
^{1}H-NMR (ppm)		
δ_{CH_3}	1.10	1.3
$\delta_{CH_2\ side}$	1.95	1.9
$\delta_{CH_2\ cyclic}$	2.70	2.55
δ_{CH}	3.60	3.7
δ_{COOH}	4.30	–
δ_{SH}	12.50	12.5
δ_{H_2O}	–	4.25

[a]Calculated (found).

4. Conclusion

The pre-concentration of Pd(II) ion on amberelite IR-120 is based upon the formation of stable palladium(II)–KPL complex. The developed analytical procedure based on the combination of the amberelite IR-120 ion-exchange chromatography and atomic absorption spectrometry offer the advantages of good accuracy, increased sensitivity, selectivity and were faster and simpler than most of the methods reported for this compound. Therefore, it is useful for the quality control of KPL in pharmaceutical dosage forms since there is no interference from the common excipients that might be found in commercial preparations.

The study threw light on the complexation properties of KPL where a diamagnetic square planar complex is formed with palladium(II).

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