



Spectrophotometric investigation on complex formation of captopril with palladium(II) and its analytical application

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Abstract: The formation of the complex between captopril and palladium(II) chloride in Britton–Robinson buffer solution was studied. It has been established that captopril reacts with palladium(II) chloride in the pH range 2.14–9.10 to form a yellow water — soluble 2:1 complex with maximum absorbance at 380 nm. By applying different spectrophotometric methods, the conditional stability constant of the complex at the optimum pH of 4.03 and ionic strength $\mu = 0.5$ M was found to be $10^{8.25}$. The molar absorptivity was 1.875×10^3 l mol⁻¹ cm⁻¹. Beer's law was obeyed in concentrations up to 5×10^{-4} M captopril. The detection limit was 2.17 μ g ml⁻¹ and the relative standard deviation varied from 1.24 to 1.68%. The proposed method was found to be suitable for the accurate and reproducible analysis of captopril in water and in tablets.

Keywords: *Captopril; palladium(II) chloride; complexometry; spectrophotometry.*

Introduction

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

Čaplar and co-authors [4] studied the physico-chemical and analytical characteristics of captopril. A comparative study of three different spectrophotometric methods for the determination of captopril in pharmaceutical formulations based on reaction of the SH-group with Ellman's reagent, the Fe(III)-phenanthroline system and the N-ethylmaleimide reagent was described [5]. Several electrochemical methods have been reported for the determination of captopril in pharmaceutical formulations and biological fluids, including potentiometry [6, 7], conductometry [8], conductometry and amperometry [9], stripping voltammetry [10] and HPLC [11, 12] methods.

There are no data on the use of metal ions as analytical reagents for the determination of captopril. The present paper reports the results obtained during a study of the reaction of captopril with the palladium(II) ion, as the basis for its determination in water and in dosage forms.

Experimental

Reagents

Captopril (standard substance) (Zorka, Šabac), palladium(II) chloride (pro analisi, Merck) and Zorkaptil tablets (Zorka, Šabac) each containing 50 mg of captopril were used. All other chemicals were of analytical grade (Merck). Double-distilled water was used.

Solutions

A freshly prepared 2×10^{-3} M aqueous solution of captopril (standard substance) was used as the stock solution.

A palladium(II) chloride standard solution (2.08×10^{-2} M) was prepared by dissolving palladium(II) chloride in water to which 0.60 ml of concentrated hydrochloric acid had been added, by warming the mixture in a water-bath. The solution was cooled and diluted to volume with water in 250-ml calibrated flask; the solution was then standardized gravimetrically by precipitation with dimethylglyoxime [13]. Standardization of the palladium(II) chloride solution is not necessary for the determination of captopril alone.

The ionic strength (μ) of the final solutions used for the spectrophotometric determination was kept constant at 0.5 M by addition of 2.5 M potassium chloride.

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Britton–Robinson buffer solutions [14] of the pH range 2.14–9.10 were prepared by mixing 0.04 M orthophosphoric, boric and acetic acids with the appropriate volume of 0.4 M sodium hydroxide and sufficient 2 M potassium chloride to bring the ionic strength to 0.2 M. The pH of each buffer solution was determined.

Apparatus

A Pye Unicam SP-6-500 UV–vis spectrophotometer (Cambridge, UK) with 10-mm quartz cells was used. A Radiometer PHM 62 pH-meter, calibrated with appropriate standard buffer solutions, was employed. The pH values were determined with a saturated calomel–glass electrode system.

Procedure for calibration curve

A 10^{-2} M palladium(II) chloride solution (0.5 ml) and 2.5 M potassium chloride (2 ml) were placed in a 10-ml volumetric flask and an aliquot of captopril stock solution (0.05–2.50 ml) was added. The pH was adjusted by adding 5 ml of Britton–Robinson buffer (pH 4.03) and the solution was diluted to volume with water and mixed; and absorbance was measured after 5 min at 380 nm against a reagent blank.

The method was then applied to the assay of captopril in tablets. The captopril was extracted from tablets with water and diluted to 2.3×10^{-3} M; an aliquot (0.90 ml) of this solution was treated by the same procedure as described for the calibration curve.

All measurements were made at room temperature ($25 \pm 0.5^\circ\text{C}$).

Results and Discussion

Absorption spectra

Captopril reacts with palladium(II) chloride to produce a yellow complex that is soluble in Britton–Robinson buffer in the pH range 2.14–9.10. Absorption spectra were recorded over the range 300–500 nm. The complex gave an absorption peak at 380 nm (Fig. 1, curve 2) which was therefore used for the analytical determination.

Under the same conditions captopril does not absorb at this wavelength. Since the palladium(II) chloride has a low absorbance (Fig. 1, curve 1) at the wavelength of the maximum absorbance of the complex, all measurements were performed against a re-

agent blank with a correction for the cell blank, as appropriate.

Reaction conditions

The pH of the reaction mixture influenced the absorbance (Fig. 2) of the complex. The absorbance at pH 2.14–2.97 increases to reach a plateau at pH 3.95–8.00 and then rapidly decreases at higher pH. The shape of the absorption spectra and the position of the absorption maximum of the complex formed with a 5:1 molar ratio of palladium(II) to captopril do not depend on pH, which means that only one type of complex is formed.

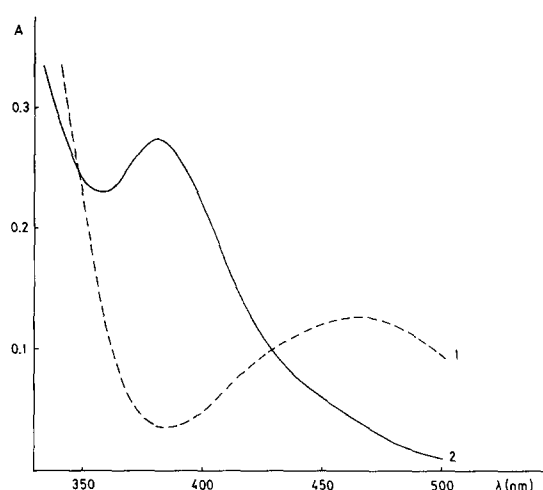


Figure 1
Absorption spectra of palladium(II) chloride (curve 1) and captopril–palladium(II) complex (curve 2). $c_{\text{KPL}} = 1.5 \times 10^{-4}$ M; $c_{\text{R}} = 7.5 \times 10^{-4}$ M; pH 4.03; $\mu = 0.5$ M.

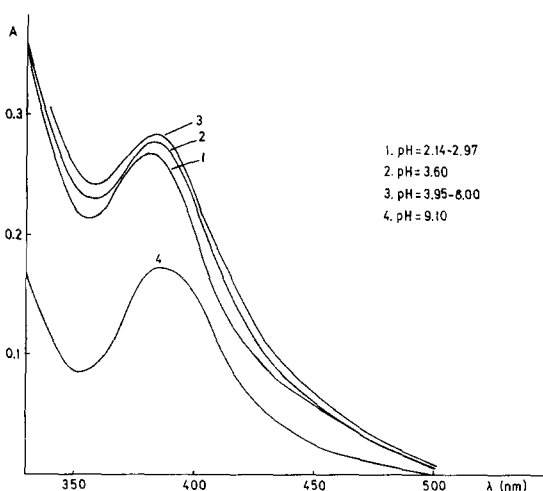


Figure 2
The effect of pH on complex formation. $c_{\text{KPL}} = 1.5 \times 10^{-4}$ M; $c_{\text{R}} = 7.5 \times 10^{-4}$ M; $\mu = 0.5$ M.

A Britton–Robinson buffer of pH 4.03 was used to provide the working pH. At this pH at least a two-fold molar ratio of reagent to analyte is necessary for maximum complex formation; the absorbance did not increase when a further excess of palladium(II) chloride was used. Little influence of ionic strength (0.05–1.00 M) on the course of the reaction was observed.

Under these conditions the complex was completely formed after 5 min and was unchanged up to 24 h.

Composition of the captopril–palladium(II) complex

The composition of the complex was established by the continuous — variation method [15, 16]. The plot reached a maximum at a fraction x_{\max} 0.33 which indicates the formation of 2:1 captopril–palladium(II) complex (Fig. 3). The curves obtained by the molar ratio method [17] show a break point at a captopril: Pd(II) molar ratio of 2:1 (Fig. 4). The results were confirmed by means of Nash's graphical method [18]. A linear dependence was found for $y^2 = f(-x)$ (Fig. 5), where:

$$y^2 = \frac{1}{c_{KPL}^2} \text{ and } x = \frac{A}{(A_0 - A)},$$

where A_0 = absorbance of $PdCl_2$ and A = absorbance of the complex.

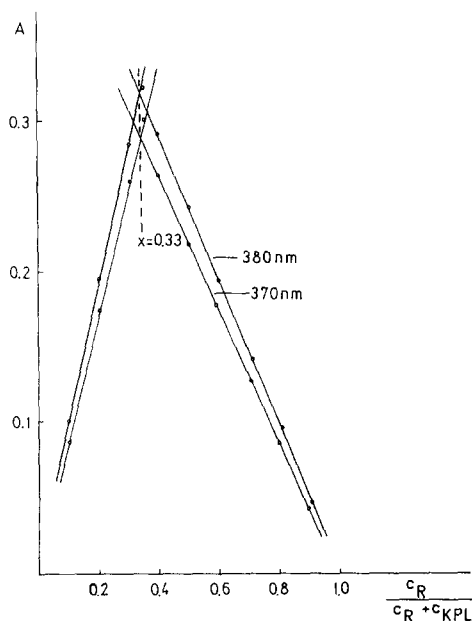


Figure 3
Job's curves of equimolar solutions. $c_{KPL} + c_R = 2.5 \times 10^{-4}$ M; pH 4.03; $\mu = 0.5$ M.

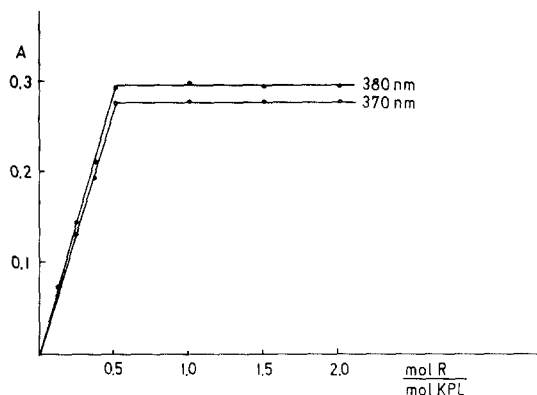


Figure 4
Molar ratio method. $c_{KPL} = 1.5 \times 10^{-4}$ M; pH 4.03; $\mu = 0.5$ M.

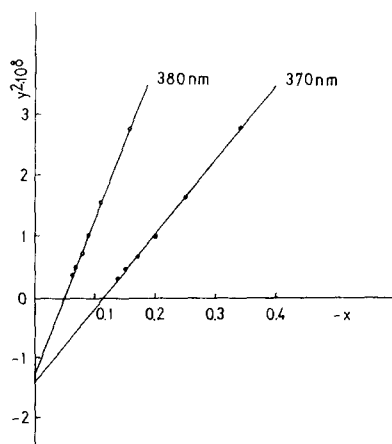


Figure 5
Nash's method. $c_{KPL} = 6 \times 10^{-5} - 1.8 \times 10^{-4}$ M; $c_R = 5 \times 10^{-4}$ M; pH 4.03; $\mu = 0.5$ M.

Conditional stability constant of the complex

By Job's method of non-equimolar solutions [15, 16] the curve for a five-fold excess of reagent was obtained. The conditional stability constant was calculated according to the equation:

$$K' = \frac{(p - 1)^2 (2 - 3x_{\max})}{c_{KPL}^2 [(2 + p)x_{\max} - 2]^3}$$

The values of $\log K'$ are presented in Table 1.

Using the method of Nash [18] (Fig. 5) the values of the stability constant were obtained from the negative intercept on the ordinate (Table 1). The values of $\log K'$ obtained with both methods are in good agreement and indicate the good stability of the captopril–palladium(II) complex.

Table 1
Conditional stability constant (K') of the captopril–palladium(II) complex*

Job's method of nonequimolar solutions			Nash's method	
λ (nm)	x_{\max}	$\log K'$	λ (nm)	$\log K'$
370	0.125	8.39	370	8.10
380	0.125	8.39	380	8.12
Mean $\log K' = 8.39$			Mean $\log K' = 8.11 \pm 0.01$	

* Conditions: pH = 4.03 ± 0.05 ; $\mu = 0.5$ M; $T = 25 \pm 0.5^\circ\text{C}$; $p^+ = 5$ (five-fold excess of reagent).

Table 2
Spectrophotometric determination* of captopril with palladium(II) chloride

Found		Concentration of captopril		
		6.00 $\times 10^{-5}$ M	12.00 $\times 10^{-5}$ M	24.00 $\times 10^{-5}$ M
\bar{x}		5.81	11.59	23.16
SD†		0.08	0.19	0.28
$S\bar{x}$		0.03	0.07	0.11
RSD (%)		1.39	1.68	1.24

* At $\lambda_{\max} = 380$ nm and pH = 4.03 ± 0.05 ; $\mu = 0.5$ M (KCl).

† Inter-assay standard deviation ($n = 7$).

Quantification and precision of the method

Under the optimum conditions described above, the calibration graph was a straight line over the range 10^{-5} – 5×10^{-4} M. The molar absorptivity for the complex was 1.875×10^3 l mol⁻¹ cm⁻¹. The regression equation was: $y = 0.0004 + 1854.8x$ with a correlation coefficient (r) of 0.9986 ($n = 7$) indicating good linearity. The lower detection limit was 2.17 $\mu\text{g ml}^{-1}$.

The precision of the method was determined on three different concentrations of captopril. The results presented in Table 2 show that the relative standard deviation varied from 1.24 to 1.68% for captopril concentrations in the range 6.0 – 24.0×10^{-5} M.

Application to a dosage form

When the proposed method was applied to determination of the captopril in Zorkaptil tablets (Table 3) the mean recovery was found to be $102.70 \pm 1.38\%$, which indicates the applicability of the method for the assay of dosage forms.

Excipients in Zorkaptil tablets did not influence the absorbance values even if present in large excess.

The proposed spectrophotometric method which uses palladium(II) chloride as the analytical reagent is rapid and simple and the results are reproducible. The colour is developed after 5 min and is long lasting. As this

Table 3
Content uniformity of captopril in Zorkaptil tablets, each containing 50 mg captopril

Assay no.	Found* (mg)	Recovery
1	51.68	103.35
2	51.68	103.35
3	51.06	102.12
4	52.43	104.85
5	52.89	105.79
6	48.54	97.08
7	52.35	104.70
8	52.37	104.74
9	49.54	99.09
10	50.95	101.92
\bar{x}	51.349	102.70
SD	1.38	
$S\bar{x}$	0.437	
RSD (%)	2.69	

**'Found' represents the mean of three analyses.

method is sensitive, only small quantities of the substance and the reagent are used. In conclusion, the method can be successfully applied to the determination of captopril in water and its dosage form.

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