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Complexation Study of Antihypertensive Drug Captopril with Some Transition Metal Ions

[1]Namita Bhardwaj[*] and [2]Aarti Singh

[1]Associate Prof. Dr. C.V. Raman University, Kargi Road Kota Bilaspur C.G.
[2]Research Scholar Dept. of Chemistry, Dr. C.V. Raman University Kargi Road Kota, Bilaspur

ABSTRACT: The present work involves the physicochemical study of the interaction of some transition metal ions Fe(II), Co(II), Ni(II), and Zn(II) with anti hypertensive drug Captopril. Captopril is a potent, competitive inhibitor of angiotensin-converting enzyme (ACE) and used in the treatment of hypertension. Stoichiometry of Captopril complexes formed in the solution was determined spectrophotometrically applying the continuous variation and mole ratio methods. The logarithmic constants (log βn) and the free energy changes (ΔG) of the formed complexes were calculated from the data of continuous variation (Issa *et al.,* 1975) and mole ratio methods Captopril complexes in the UV-Vis region exhibit maximum absorption at 300,330,350 and 450nm for Fe(ll), Co(ll),Ni(ll),and Zn(ll) complexes respectively using same amount of metal ion as a blank.

INTRODUCTION

Captopril is a potent, competitive inhibitor of angiotensin-converting enzyme (ACE), the enzyme responsible for the conversion of angiotensin I (ATI) to angiotensin II (ATII). ATII regulates blood pressure and is a key component of the renin-angiotensin-aldosterone system (RAAS). Captopril used in the treatment of hypertension[1].

Stability constant is equilibrium constant for the formation of complex in solution. It is measure of the strength of the interaction between the reagent that come together to form the complex. One of the most spectacular effect of complex formation is the change of spectral properties. The reason for light absorption by the complexes are the excitation of electrons of the both the metal ions and the ligand due to their interaction. Owning to interaction of the central metal ion and the ligand a charge transfer from the ligand to metal ion may occur on irradiation[2]. This phenomenon is the reason for so called charge transfer spectra in the visible and near ultraviolet region[3]. The present work involves the synthesis characterization and study of the interaction of some transition metal ions Fe(II), Co(II), Ni(II), and Zn(II) with anti hypertensive drug Captopril.

** To whom correspondence be made:*
E-mail: nbnillisweet@gmail.com

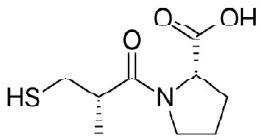


Figure 1: 01 Structure of Captopril

MATERIAL AND METHODOLOGY[4]

Apparatus

A Systronic UV/Vis spectrophotometer with 1 cm quartz cells was used to measure the absorbance. The pH measurements were made with systronic pH meter model 371 All measurements were performed at room temperature (30 ±0.01°C).

Reagents

Captopril was purchased from Sigma Aldrich as hydrochloride form. Metal nitrates and other chemicals used were of analytical grade purchased from Merck Germany. Metal salts were taken in an accurate amount and were not further standardized.

1) Preparation of (0.1 M) Ferrous sulphate hexahydrate solution

   [$FeSo_4 * H_2O$]

   To make 100 ml ferrous sulphate solution of 0,1M 2,8gm of ferrous sulphate hexahydrate

and 1 ml concentrate H_2SO_4 was dissolved in distilled water and made up to the mark in 100 ml volumetric flask.

2) Preparation of cobalt nitrate [$Co(NO_3)_2 * 6H_2O$]

To make 100 ml cobalt nitrate solution of 0.1 M 2.91 gm of cobalt nitrate was dissolved in distilled water and made up to the mark in 100 ml volumetric flask.

3) Preparation of Nickel nitrate [$Ni(NO_3)_2 * 6H_2O$]

To make Nickel nitrate solution of 0.1M 2.91 gm of nickel nitrate was dissolved in distilled water and made up to the mark in 100ml volumetric flask.

4) Preparation of Zinc nitrate hexahydrate[$Zn(NO_2)_2 * 6H_2O$]

To make Zinc nitrate hexahydrate solution of 0.1M 2,97 gm of Zinc nitrate hexahydrate was dissolved in distilled water and made up to the mark in100 ml volumetric flask.

5) Preparation of Buffer Solution

To make buffer solution of P^H 9.2 one buffer tablet was dissolved in 100ml distilled water.

6) Preparation of 0.01M drug Solution

To make 25ml Captopril drug solution 20 tablet was dissolved in methanol and distill water made up to the mark in 100 ml volumetric flask.

Method

A series of solution containing up to 4.0 ml of buffer solution, 1 ml (0.1M) of metal ions and 0.2-2.8 ml (0.01M) of Captopril was mixed in 10 ml measuring flask and then diluted up to the mark with water the mixture was allowed to stand for 10 min[5]. the absorbance was measured at the maximum wavelength (λ max) against a blank solution prepared in the same manner but not contain metal ions. The calibration graphs were prepared by using the same procedure (at least seven concentration points) and were linear passing through the origin stoichiometry of Captopril complexes formed in the solution was determined spectrophotometric ally applying the continuous variation and mole ratio method[6]. The obtained results revealed the formation of 1:1 (M: L) Captopril complexes with all metal ions. The logarithmic constant (log β_n) and the free energy changes (ΔG) of the formed complexes were calculated from the data of continuous variation and mole ratio methods applying equation (1 and 2)[7]

$$\beta_n = \frac{\frac{A}{A_m}}{1-\left[\frac{A^{n+1}}{A_m}\right]} c^n n^2 \qquad (1)$$

$$\Delta G = -2.303\ RT \log \beta_n \qquad (2)$$

Where β_n is the stability constant of the metal chelate, A is the absorbance at ligand concentration CL. Am is the absorbance at full color developed n is the order of the complex formed. T is the absolute temperature and R is the gas constant.

RESULT AND DISCUSSION

The stability constant values for complexation of antihypertensive Captopril with Fe (ll), Co(ll),Ni(ll) and Zn(ll) ions by spectrophotometric method have been presented in Table (1.01). Captopril complexes in the UV-Vis region exhibit maximum absorption at 300,330,350 and 450nm for Fe(ll), Co(ll),Ni(ll),and Zn(ll) complexes respectively using same amount of metal ion as a blank. These longer wavelengths peaks have been used in all subsequent measurements of the absorbance. At these wavelengths the absorption of both Captopril and metal solution were negligible.

On plotting the absorbance as a function of Captopril concentration. straight lines were obtained up 92.00 and 95.10, 100.50, 110.10 µg ml^{-1} using Fe(II), Co, Zn and Ni(II), respectively,

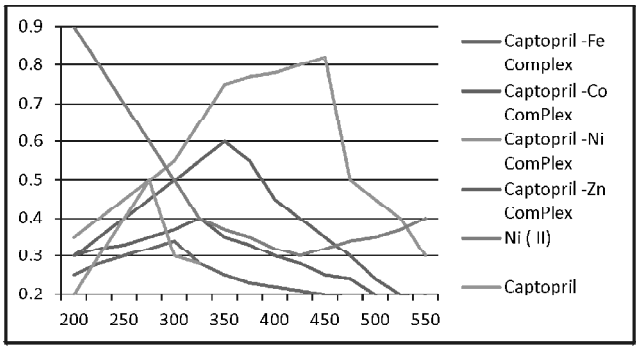
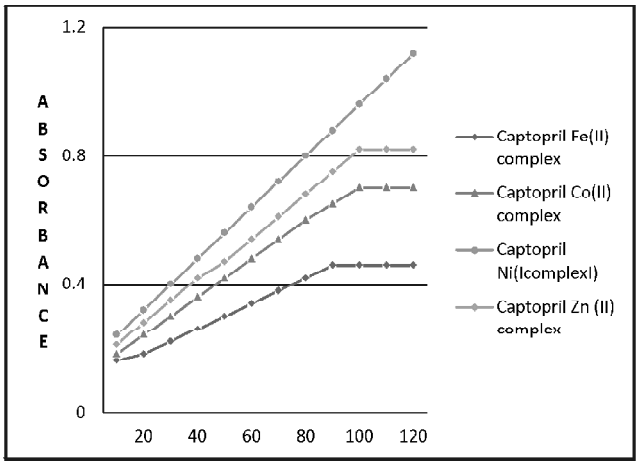


Figure 1: The electronic absorption spectra of Captopril, its complexes and Ni $(No_3)_2$



in presence of borate buffer[8]. The complexes of this drug with all the metal ions indicate the formation of 1:1 complexes. Graphs were obtained in presence of borate buffer.

The complexes of this antihypertensive drug Captopril with all the metal ions indicate the formation of stable complexes. The stability constant values for metal Captopril complexes have been found to be in order Fe(ll)<Co(ll)<Zn(ll)<Ni(ll)[9]. Thus Ni complexes have highest value of stability constant with Captopril. The values of free energies of formation of the complexes have found negative. This indicates that the complex formation is spontaneous[10].

Table 1
Spectrophotometric analytical characteristics of Captopril complexes with Fe(II), Co(II), Zn(II), and Ni(II) ions.

METAL ION	*λ max (nm)*	*U.L. Beer (μg ml^{-1})*	*M / L ratio*	*log βn*	*(- ΔG)*
Fe	300	92.0	1:1	0.48	2852
Co	330	97.1	1:1	0.72	4243
Zn	350	102.5	1:1	0.81	5421
Ni	450	110.1	1:1	0.90	6064

CONCLUSIONS

The Captopril - metal complexation represents a research field of increasing progress. Pharmaceutical profile like solubility, antihypertensive activity of Captopril can be improved by complexation.

Captopril can be determined in pharmaceutical preparation and also in biological samples by complexation with metal ions by spectroflurometric and atomic absorption spectrometric method. Trace metal ions can be determined by using Captopril as a complexing agent. The progress in the field of antihypertensive complexes and their applications will be foundation for the development of the newer antihypertensive drug with enlarged biological activity.

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