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ANALYSIS OF STABILITY CONSTANT OF LABETALOL COMPLEXES WITH SOME TRANSITION METAL IONS – A SPECTROPHOTOMETRIC STUDY

[1]Dr. Namita Bhardwaj* and [2]Archana Yadav

[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.

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***Corresponding Author**
Dr. Namita Bhardwaj
Associate Prof. Dr.
C.V.Raman University,
Kargi Road Kota Bilaspur
C.G.

ABSTRACT

The interaction between Co Ni and Copper (II) metal ions with the antihypertensive drug labetalol leads to formation of the binuclear complexes which absorbed maximally at 370, 365 and 350nm respectively. It was characterized by (UV-Visible) double beam spectrophotometer. The stability constant were found in the order Co < Ni < Cu which obey the Irving-William natural order.

KEYWORDS: Complexation, Stability Constant, Antihypertensive, Labetalol.

INTRODUCTION

Stability constant is equilibrium constant for the formation of complex in solution. It is measure of the strength of the interaction between the reagents that come together to form the complex.[1] Transition metal complexes are cationic, anionic or neutral species in which transition metal is coordinated by ligands. Transition metals exhibit different oxidation states and can interact with a number of inorganic or organic molecules or ions (negatively or occasionally a positive ion) functions as ligand.[2] In present study Labetalol drug is used as ligand and it is chemically 2-hydroxy-5-[1-hydroxy-2 [methyl phenyl propyl) amino ethyl] mono hydrochloride. Labetalol is a third generation selective alpha-1-adrenergic antagonist and non-selective beta-adrenergic antagonist with vasodilatory and antihypertensive properties.[3] Labetalol competitively binds to alpha-1-adrenergic receptors in vascular smooth muscle, thereby inhibiting the adrenergic stimulation of endothelial cell function and vasoconstriction in peripheral blood vessels. This agent also binds to beta-receptors in the

bronchial and vascular smooth muscle, resulting in a decrease in adrenergic stimulation. The result is a decrease in resting and exercise heart rates, cardiac output, and in both systolic and diastolic blood pressure, thereby resulting in vasodilation, and negative chronotropic and inotropic cardiac effects.[4]

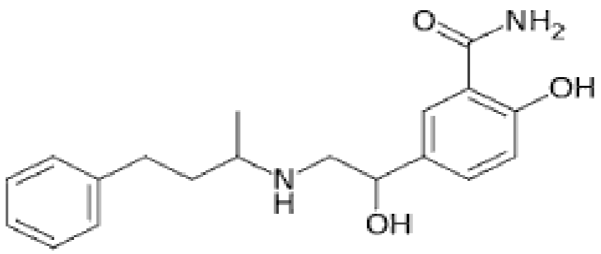

Figure. 1: Structure of Labetalol.

Experimental

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

Labetalol 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.

Preparation of 1×10^{-1} M metal solution[5]

Co $(NO_3)_2 \cdot 6H_2O$ (2.91 g, 20 m mol, M. Wt. = 291.031 $gmol^{-1}$) was dissolved in freshly distilled and dry methanol in a beaker and was made up to the mark in a 100 mL volumetric flask.

Ni $(NO_3)_2 \cdot 6H_2O$ (2.90 g, 20 m mol, M. Wt. = 290.791 $gmol^{-1}$) was dissolved in freshly distilled and dry methanol in a beaker and was made up to the mark in a 100 mL volumetric flask.

Cu $(NO_3)_2 \cdot 6H_2O$ (2.95 g, 20 m mol, M. Wt. = 295.644 $gmol^{-1}$) was dissolved in freshly distilled and dry methanol in a beaker and was made up to the mark in a 100 mL volumetric flask.

Preparation of 1×10^{-1}

M Labetalol[6]

Labetalol (3.64 g, 20 m mol, M. Wt. = 364.87 g mol^{-1}) was dissolved in freshly distilled and dry methanol in a beaker and was made up to the mark in a 100 mL volumetric flask.

METHOD

A series of solutions containing up to 4.0 ml of buffer solution, 1 ml (0.1 M) of the metal ions and 0.3-3.6 ml (0.1 M) of drugs were mixed in 10 ml measuring flask and then diluted up to the mark with water. The mixture was allowed to stand for 10 min. The absorbance was measured at the maximum wavelength (λmax) against a blank solution prepared in the same manner but not contains metal ions. The calibration graphs was prepared by using the same procedure (at least seven concentration points) and were linear passing through the origin[4]. Stoichiometry of labetalol complexes formed in the solution was determined spectrophotometrically applying mole ratio methods. The obtained results revealed the formation of 1:1 (M:L) labetalol complexes with Co, Ni and Cu (II) metal ions. The logarithmic constants (log βn) and the free energy changes (ΔG) of the formed complexes was calculated from the data of mole ratio methods applying equations 1 and 2.[7]

$$\beta_n = \frac{\frac{A}{A_m}}{[1-\frac{A}{A_m}]^{n+1} C_l^n n^2} \rightarrow (1)$$

ΔG = -2.303 RT log ßn..... (2)

RESULT AND DISSCUSION

Spectrophotometric analysis of Labetalol by complexation with Co(II), Ni(II) and Cu(II) ions, was carried out over the wavelength range of 300–800 nm. It was found that Labetalol formed coloured, water soluble complexes with these metal ions. Labetalol complexes in the UV−Vis region exhibits maximum absorption at 375nm, 360nm and 350nm for Co(II), Ni(II) and Cu(II) complexes, respectively, using the same amount of the metal ion as a blank. At these wavelengths the absorption of both Labetalol and metal solutions were negligible. On plotting the absorbance as a function of Labetalol concentration, straight lines were obtained the results are summarized with the other analytical parameters in Table 1. The high values of correlation coefficients and small values of standard deviations indicate the good linearity of all calibration graphs and the confirmatory of Beer's law to absorbance measurements.

Table. 1: Analytical characteristic of Labetalol complexes with Co, Ni and Cu ions.

Metal ion	ʎ max	M/L Ratio	log ßn	- ΔG	Correlation Coefficient	Standard deviation
Co	375	1:1	0.558308	-3292.52	0.984	0.3192
Ni	360	1:1	0.635583	-3748.24	0.982	0.3091
Cu	350	1:1	0.646277	-3811.3	0.980	0.2999

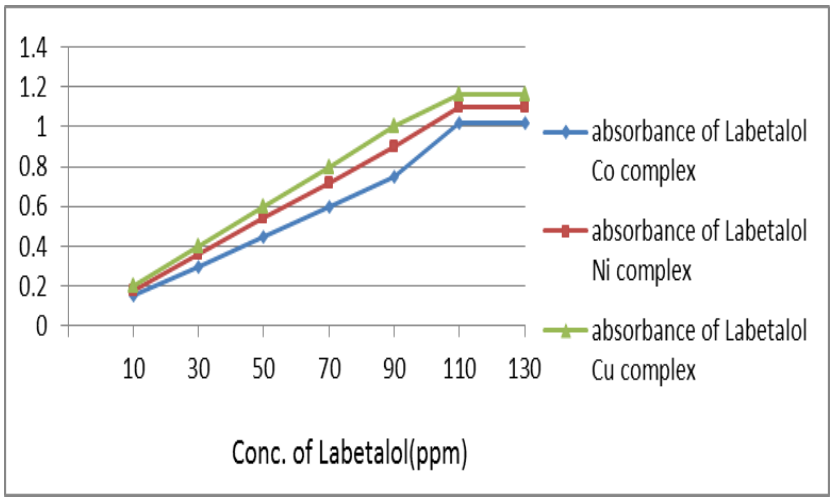

Figure. 2. Absorbance vs concentration plots for Co (II) -Labetalol (λ = 375 nm), Ni (II) – Labetalol (360) and Cu(II)-Labetalol (λ = 350 nm) complexes.

CONCLUSION

Stability constants of these complexes were found in the order Co < Ni < Cu. Thus Cu complexes have the highest value of stability constants with Labetalol, this is found to be in good agreement with Irving and Williams and Mellor and Meley natural order.[8]

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