Thermodynamics Applied in the Mixed Ligand Complexes of [Zn(II)-Antibiotics-Clindamycin] System: A Polarographic Approach

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Abstract

The present communication deals with the stability constant and thermodynamic paratmeters such as change in free energy (ΔG) , change in enthalpy (ΔH) *and change in entropy* (ΔS) *for the Zn(II)-antibiotics clindamycin ternary complex system have been determined use in polarographic measurement in aqueous medium, ionic strength was maintained with $NaClO_4$ (μ= 1.0 M) at two different temperature (25°C and 35°C). In all the systems Zn(II) reduced quasireversibly. Complexes were found in 1:1:1, 1:2:1, and 1:1:2 ratios using neomycin chlortetracycline, tetracycline, oxytetracycline, penicillin-V and penicillin-G as primary ligands and clindamycin as a secondary ligand at pH=7.30± 0.01.The study shows that [Zn (II)- penicillin- G- clindamycin] is more stable then complexes with other above primary ligands. There is no change in the number of speeches formed by increasing the temperature but the stability constant of complex speeches decreased with the rise in temperature.*

Keywords: Stablity Constant,Thermodynamics parameters of [Zn (II)- antibiotics-clindamycin] System.

Introduction:

Antibiotics are natural compounds produced mostly by plant microorganisms. They are used against several fungal and bacterial diseases in plants, animals and human beings .Clindamycin, a semi synthetic derivative of lincomycin is usually more active than the parent compound in the treatment of bacterial infections. The coordinated metal ion in these antibiotics play an important role in maintaining proper structure and or function of these antibiotics metalloantibiotics can interact with several different kinds of biomolecules including DNA, RNA, proteins, receptors and lipids rendering their unique and specific bioactivities.

Antibiotics metal complexes as well as mixed antibiotics metal complexes were found more effective as chemotherapy agents than their parent antibiotics**[1,2]**. In the past some polarographic analytical procedures were listed in numerous pharmacopoeis. It should be a goal of electro analytical chemists around the world to have them listed again. The lower costs, faster results and the possibility for quickly detecting mishandlings by technicians are powerful arguments. To use polarographic methods for analysis of such simple matrices yields results often much faster with a better accuracy and without using organic solvents.

Thermodynamic parameters **[3,4]** such ΔG, ΔH & ΔS of interaction are important to interpret the binding of metal ligand complex. The kind of complex species that can be measured with a DME depends on thermodynamic aspect[**5**]. The knowledge of thermodynamic parameter is of fundamental importance for learning about the spontaneous occurrence of a given process at a given temperature.It would appear, therefore, that a quantitative knowledge of the metal ion complexing tendencies of antibiotics would be of great value. A survey of the literature reveals that no ternary complexes of Zn^{2+} with these antibiotics and clindamycin have been reported polarographically. Therefore the present work has been undertaken for the study.

Material and Methods:

Reagents: All antibiotics employed were of Fluka product and their solutions were prepared in double distilled water. The concentration of metal ion was 0.5 mM. Ionic strength was maintained with $NaClO_4$ at 1.0 M. The concentration of each primary ligands was very from 0.5 mM to 30 mM .Pure hydrogen gas was passed through each test solution before recording C-V data. NaOH and perchloric acid were used to adjust the pH of the test solution at 7.30 ± 0.01. Triton X-100 (sigma) 0.002 % was used as maximum suppressor.

Instruments**:** The polarogram were obtained on a manual polarograph using polyflex galvano meter (PL-50) with a dropping mercury electrode having $m^{2/3}$ $t^{1/6}$ = 2.40 mg $^{2/3}$ $s^{-1/2}$ at 60.02 cms (calculated) effective mercury height was used to obtain the analyte was measured using digital pH meter model (LI-120) all the measurements were made at 35°C.

Polarographic procedure: An aliquot (10 ml) of experimental solution was placed in a dry clean polarographic cell. Saturated calomel electrode (SCE) was used as the reference electrode and was connected to the polarographic cell through KCl Agar-Agar bridge. Oxygen was expelled by passing a slow steam of purified nitrogen into the test solution before recording the polarograms.

Result and Discussion:

In each case simple well defined two electron quasireversible reduction wave observed in 1.0M $NaClO_4$, at pH = 7.30 ± 0.01 was selected to study the complex formation in human blood pH. The diffusion was found to decrease the increase of ligand concentration as a result of the complex formation. The value of stability constants of ternary complexes were calculated by Schaap and Mc Master Method **[7]** at (25°C and 35°C). The nature of the C-V curves of Zn(II) complexes with reported antibiotics were quarsireversible and diffusion controlled**[6].**

In this investigation, the concentrations of antibiotics varied from 0.5mM to 30mM and were added to Zn(II). The half wave potential became more negative with addition of antibiotics to Zn(II) showing complex formation. The $E_{1/2}$ values increased with increase of concentration of clindamycin to

[Zn(II) – antibiotics] system showed the formation of ternary complex [Zn(II) -antibiotics – clindamycin].

The system has been investigated at two temperature viz 25°C and 35°C the thermodynamic functions (ΔG, ΔH and ΔS) has been calculated by following equations **[8,9]:**

$$\Delta H = \frac{2.303\ RT_1T_2\ (\log K_2 - \log K_1)}{T_2 - T_1} \quad \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

$$\Delta G = -2.303\ RT \log K \quad \ldots\ldots\ldots\ldots\ldots\ldots (2)$$

$$\Delta S = \frac{\Delta H - \Delta G}{T} \quad \ldots\ldots\ldots\ldots\ldots\ldots (3)$$

Thermodynamic parameters are very important to understand the temperature effect on the stability of complexes or to interpret the binding of metal ligand complex. The kind of complex speeches that can be measured with a DME depends on thermodynamic aspect.

Table (1): Thermodynamic parameters of [Zn (II)- Antibiotics- Clindamycin] Ternary system.

Systems	Stability Constants			$-\Delta H$ K cal mol $^{-1}$			$-\Delta G$ K cal mol^{-1}			$-\Delta S$ cal deg^{-1} mol $^{-1}$		
	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$	$\log\beta_{11}$	$\log\beta_{12}$	$\log\beta_{21}$
	25°C / 35°C	25°C / 35°C	25°C / 35°C	(35°C - 25°C) For difference of 10°C			25°C / 35°C	25°C / 35°C	25°C / 35°C	25°C / 35°C	25°C / 35°C	25°C / 35°C
[Zn (II) - Neomycin- Clindamycin]	4.363	7.201	9.640	21.002	28.008	17.584	5.949	9.819	13.145	50.513	61.036	14.895
	3.861	6.532	9.220				5.443	9.207	12.995	50.515	61.039	14.898
[Zn(II) -Chlortetracycline -Clindamycin]	4.460	7.315	10.211	18.593	21.532	22.845	6.081	9.975	13.924	41.986	38.781	29.936
	4.015	6.758	9.666				5.660	9.526	13.624	41.989	38.980	29.937
[Zn(II) -Oxytetracycline -Clindamycin]	4.661	7.501	10.465	13.667	26.184	24.379	6.356	10.228	14.270	24.533	53.543	33.922
	4.335	6.875	9.883				6.110	9.691	13.930	24.534	53.546	33.923
[Zn(II) -Tetracycline - Clindamycin]	_	7.952	10.890	_	15.453	16.456	_	10.843	14.850	_	15.469	5.389
	_	7.582	10.497				_	10.687	14.795	_	15.471	5.391
[Zn(II) -Penicillin V - Clindamycin]	5.112	8.102	10.903	11.854	19.187	15.876	6.971	11.048	14.868	16.385	27.312	3.382
	4.670	7.644	10.524				6.583	10.774	14.833	16.389	27.314	3.385
[Zn (II) -Penicillin G - Clindamycin]	5.322	8.309	_	25.004	19.656	_	7.257	11.330	_	59.553	27.939	_
	4.726	7.840	_				6.661	11.050	_	59.555	27.941	_

The thermodynamic parameters of the [Zn(II)-antibiotics-clindamycin] complexes were given in **table 1.** It is clear from the thermodynamic parameters **[10]** of complexes that, the stability constant (logβ) decreased with increased of temperature, confirming that complexes are not stable at higher temperature and increasing stability suggesting lower temperature favors the chelation process. It can be seen that negative value of ΔG indicates the spontaneity of the complex. **table 1** shows that the values of ΔG is less negative at higher temperature and ΔS is more negative at higher temperature confirmed that the complex are not stable at higher temperature. The ΔH is negative in all complexes. The negative ΔH suggests that Zn(II) – antibiotics-clindamycin is exothermic. It means greater the amount of heat released in reaction , more stable are the reaction products. The change in entropy (ΔS) is negative in all complexes. The negative value of ΔS corresponds to a more ordered complex and this implies a small value of the steric factor.

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