Stability constant and Thermodynamic parameters of Cu (II) Complex with N-6-Benzylaminopurine as an anticancer compound using Spectrophotometric method

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***Abstract*: In this investigation spectrophotometric studies have been made for the complex formation between Cu (II) with N-6 benzylaminopurine at 25°C and 40°C temperature. In this study firstly we synthesized N-6 benzylaminopurine ligand from adenine, benzaldehyde and formic acid after this we synthesized metal- N6 benzylaminopurine binary complexes by general method.This investigation has been undertaken manly with the view to determine the composition and stability constant of binary metal complexes of Cu (II) with N-6 benzylaminopurine by job's method and view to calculate the thermodynamic parameters. Such as enthalpy change (ΔH) entropy change (ΔS) and free energy change (ΔG) of metal N6 benzylaminopurine complexes. [1]**

***Keywords*: [Cu (II)-N-6 benzylaminopurine] complex, stability constant, Thermodynamic parameter**

Introduction

Nitrogen containing heterocycles show a needed role in studies of the simplexes and compound for particular concepts. This can act as ligand towards metal ions. As co-ordination and bioinorganic chemistry have been producing many complexes and metal containing compounds proved to be medicines. [2] From the survey of Literature. It has been found there are very few references regarding the synthesis, thermodynamic & spectrophotometric studies on the stability constant of transition metal complexes with N-6 Benzyl amino purine as an anti-cancer Compound. The present investigation is to study the binary complex formation of Cu metal using anticancer agent like N-6 benzylaminopurine. [3]

The value of stability constants (log K) and thermodynamic parameters viz enthalpy change ΔH, entropy change ΔS, and free energy change ΔG are to be determined to see the stability of complexes at higher temperature. [4]

The prepared complexes of some of the metals from Cu, Fe, Cd, Zn, Pt, Mn, Co, Cr, Au, Ag and Ni with selected anticancer drugs can be used in treatment of various disease and may give anticancer or antitumor, antibacterial activities in a more effective manner as compared to plane ligand with synthesized complexes.[5,6]

Work was carried out on Cu (II) from proposed metals.

Experimental

1. Method of Synthesis of N6-benzylaminopurine ligand [7]

A mixture of 54.0 gm. of (0.10mole) of adenine, 60.8 gm (0.12mole) of benzaldehyde and 100ml of 98-100% formic acids stirred and heated at refluxing temperature 120°C for one week. The formic acid is evaporated under reduced pressure and the resulting viscous material is treated with 800ml of either. The product turns solid and the mixture is filtered from the hot mixture and recrystallized from absolute ethanol. The yield of product is 47.6 gm.

1. Preparation of Stock Solution of Cu (II):-
A solution of Cu (II) N6-benzylaminopurine was prepared by dissolving 0.0672 g of $CuCl_2.2H_2O$ in 250 ml distilled water,
2. Preparation of N-6 benzylaminopurine solution:-
A solution of N6- benzylaminopurine was prepared by dissolving 0.450 gm of n6-benzylaminopurine in 1000 ml distilled water.
3. Method of synthesis of Cu (II)-N-6 Benzylaminopurine metal-ligand complex:
The following general procedure was adopted for the synthesis of all the complex.
The ligand N-6 benzyalminopurine (2.11g, 0.01mol) was dissolved in ethanol (30ml), and was mixed with a solution of the metal salt of $CuCl_2.6H_2O$ (0.85g, 0.005mol) in ethanol (20ml). This solution was the boiled under reflux for about 2 hours, and the resulting complex obtained was filtered, washed with ethanol, chloroform and ether. The complex was finally dried in vacuum over anhydrous $CaCl_2$.

Table 1. Physical and Analytical data of the metal (II) complexes. [8]

Metal	Ligand	Complex	Colour of ligand	Colour of complex
Cu(II)	**N-6 Benzylaminopurine**	**Cu(II)-N-6 Benzylaminopurine**	**Off White**	**Blackish Brown**

4. Determination of stability constant by continuous variations method (Job's method): [9, 10]
Procedure:

i. **Selection of filter:** pipette out 5ml of 0.002M metal (II) solution along with 5ml of 0.002M N6-benzylaminopurine ligand solution in a stoppered test tube. Mix well and measure the absorbance of the solution against distilled water as blank using different filters. Select the filter giving maximum absorbance.

ii. **Determination of mole ratio of the complex**: prepare in stoppered test tubes a series of mixture of 0.002M metal(II) solution and 0.002M N6-benzylaminopurine ligand solution in following manner

Table 2. Ratio solution of concentration of ligand and metal complex.

Metal ions solution in ml	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Ligand solution in ml	**9**	**8**	**7**	**6**	**5**	**4**	**3**	**2**	**1**

Using the filter selected preciously measure the absorbance of each mixture. The measurements for optical density were made an after adjusting the appropriate pH (7.30±0.1) and appropriate wavelength at 0.1M ionic strength (KNO_3) at 25°C and 40°C temperature. The pH of each solution maintain by using the buffer solution. Plot a graph of absorbance against molar composition of the mixtures.

5. Determination of stability constant: The stability constant of a complex can be determined from job's curve. We adopted extinction coefficient method. In this method plot a graph of absorbance against the concentration of metal (II) solution and determine the molar absorptivity of the complex. From the various mixtures prepared for the determination of mole ratio of complex, select the mixture having maximum absorbance: calculate present in the solution.

Table 3. Observation Table for λmax. [Cu (II)-N-6 Benzylaminopurine]
pH = 7.30 ± 0.01, μ = 0.1 M KNO_3

S.No.	Wavelength(nm)	Absorbance	
		25°C	**40°C**
1.	320	2.015	2.180
2.	340	2.025	2.186
3.	360	2.037	2.200
4.	380	2.053	2.261
5.	400	2.066	2.338
6.	420	**2.075**	2.410
7.	440	2.072	**2.452**
8.	460	2.062	2.430
9.	480	2.056	2.420
10.	500	2.052	2.391
11.	520	2.050	2.380
12.	540	2.047	2.362
13.	560	2.041	2.360
14.	580	2.032	2.356
15.	600	2.030	2.347
16.	620	2.018	2.342

λmax at 25°C = 2.075
λmax at 40°C = 2.452

Table 4. Observation table for determination of mole ratio of complex.

[Cu (II)-N-6 Benzylaminopurine]

S.No.	Ratio	Vol. of Metal solution(ml)	Vol. of solution(ml)	Total volume(ml)	25°C (λmax = 420)	40°C (λmax = 440)
1	1:9	9	1	10	1.990	2.000
2	2:8	8	2	10	2.005	2.100
3	3:7	7	3	10	2.026	2.221
4	4:6	6	4	10	2.056	2.380
5	5:5	5	5	10	2.075	2.452
6	6:4	4	6	10	2.053	2.442
7	7:3	3	7	10	2.027	2.330
8	8:2	2	8	10	2.012	2.289
9	9:1	1	9	10	2.010	2.210

Table 5. Observation table for concentration of solution of series.

[Cu (II)-N-6 Benzylaminopurine]

Total volume maintain by buffer solution.

S.No.	Vol. of Metal solution(ml)	Vol. of Ligand solution(ml)	Vol. of solution(ml)	25°C (λmax = 420)	40°C (λmax = 440)
1	1	9	10	2.008	2.206
2	2	8	10	2.015	2.013
3	3	7	10	2.022	2.020
4	4	6	10	2.028	2.021
5	5	5	10	2.032	2.030
6	6	4	10	2.044	2.042
7	7	3	10	2.052	2.050
8	8	2	10	2.058	2.065
9	9	1	10	2.066	2.064

Graph 1. To calculate the λmax for complex formed between Cu (II) ion and N-6 Benzynaminopurine at 25°C.

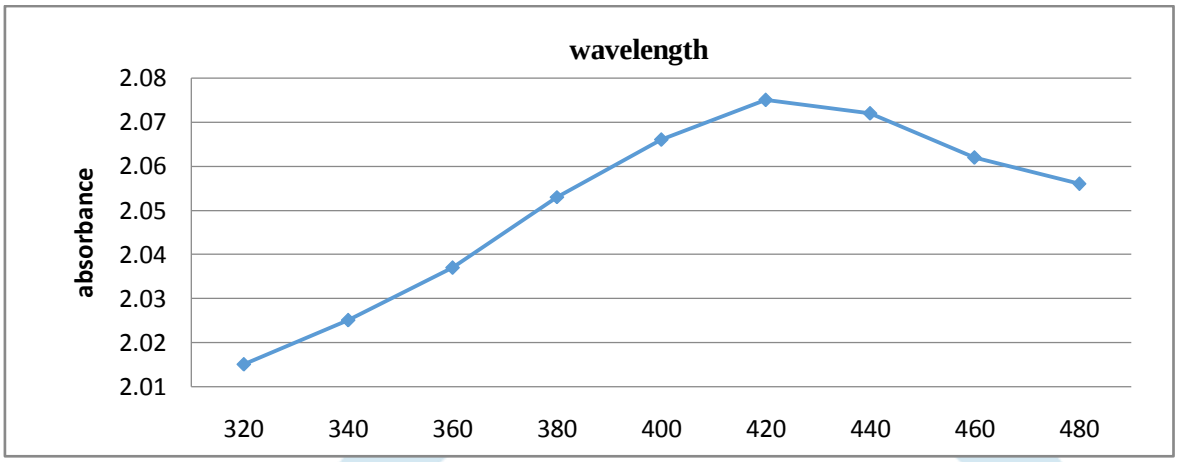

Fig. 1 λmax for Cu (II)-N-6 Benzylaminopurine at 25°C

Graph 2. To calculate the λmax for complex formed between Cu (II) ion and N-6 Benzynaminopurine at 40°C.

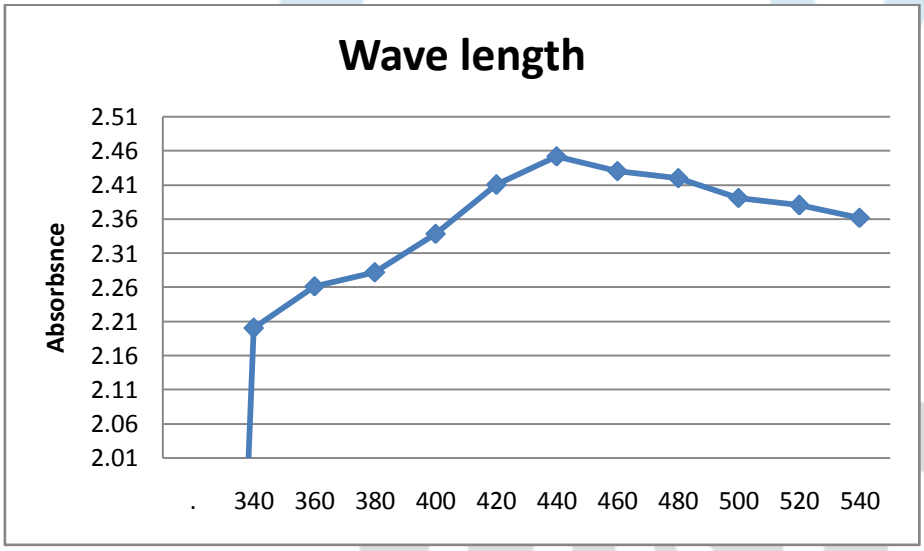

Fig. 2 λmax for Cu (II)-N-6 Benzylaminopurine at 40°

Graph 3. Absorbance against concentration of Cu (II) ion with N-6 Benzynaminopurine at 25°C.

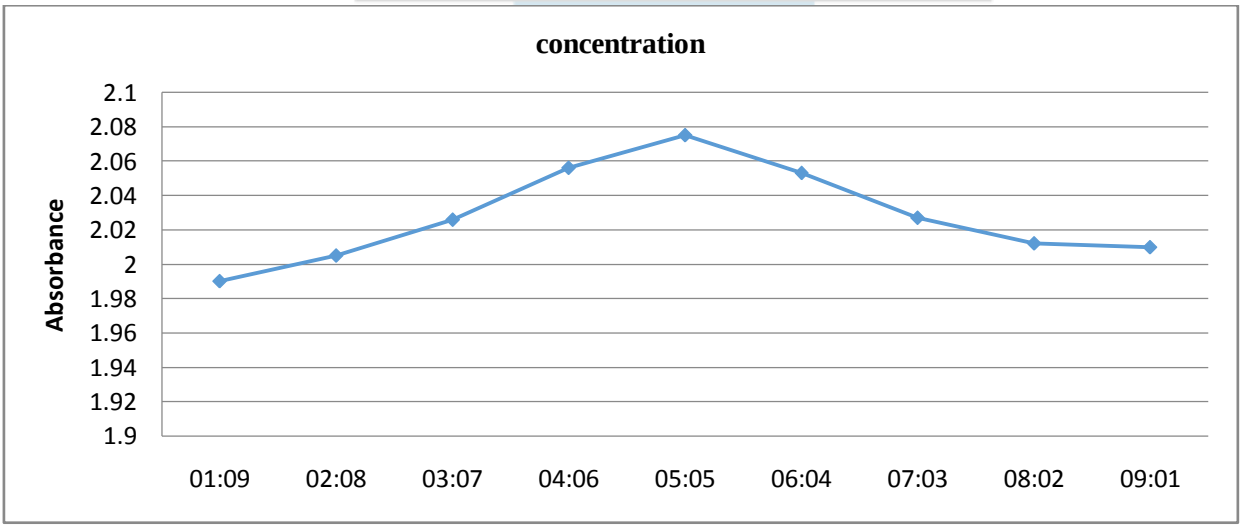

Fig. 3. Cu (II)-N-6 Benzylaminopurine at 25°C

Graph 4. Absorbance against concentration of Cu (II) ion with N-6 Benzynaminopurine at 40°C.

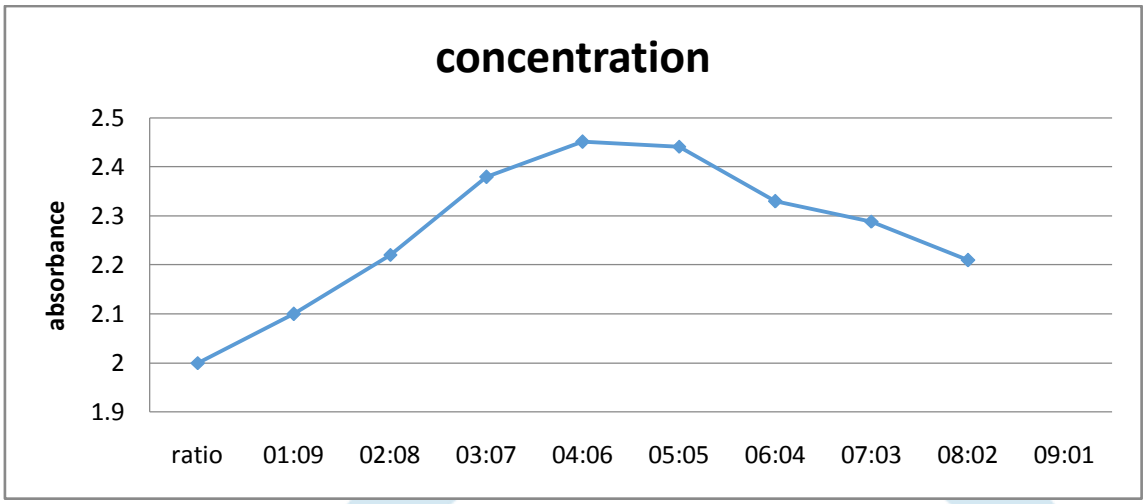

Fig. 4. Cu (II)-N-6 Benzylaminopurine at 40°C

Graph 5. Absorbance against concentration of Cu (II) ion with N-6 Benzynaminopurine for stability constant at 25°C.

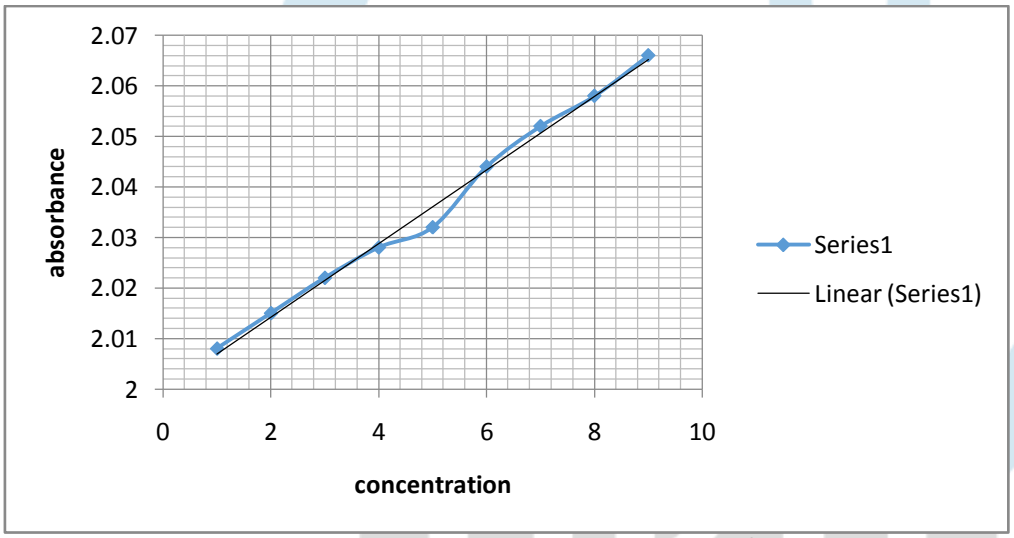

Fig. 5. stability constant for Cu (II)-N-6 Benzylaminopurine at 25°C

Graph 6. Absorbance against concentration of Cu (II) ion with N-6 Benzynaminopurine for stability constant at 40°C.

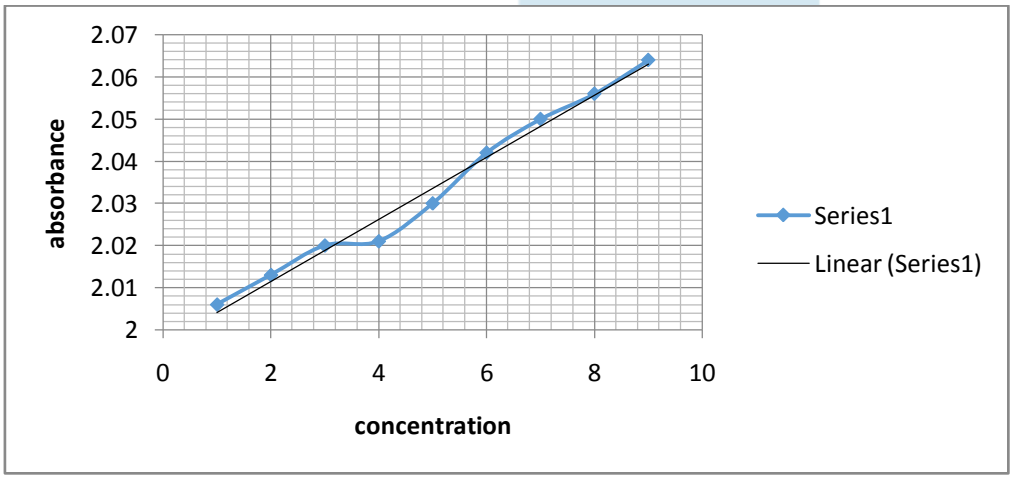

Fig. 6. Stability constant for Cu (II)-N-6 Benzylaminopurine at 40°C

Result

The spectophotometric method were applied to the study of complexes of metal (Cu) with N-6 benzylaminopurine and stability constants and thermodynamic parameters were determined at pH= 7.30 ± 0.01 at constant ionic strength

(μ = 1.0) at 25° C and 40° C temperatures.

The formation of (Cu (II)-N6BAP), complex have been studied spectrophotometrically at an absorption maximum of 680nm respectively at 25°C and 640nm respectively at 40°C temperature. The value of stability constant log K and thermodynamics parameters such as enthalpy change (ΔH), free energy change (ΔG) and entropy change (ΔS) have also been determined. Both the stoichiometry as well as the stability constants of the complexes in solution has been determined using continuous variation method (Job's method).

Table 6. Stability constant of binary complexes of metal at 25° C and 40° C [11]

METAL	LIGAND	STABILITY CONSTANT log K	
		Log K_1 25° C	Log K_2 40° C
Copper	N-6 Benzylaminopurine	3.613	3.287

Table 7. Thermodynamics Parameters of binary system [12]

SYSTEM	STABILITY CONSTANT	-ΔH K Cal mol^{-1}	-ΔG K Cal mol^{-1}	-ΔS Cal deg^{-1}
		40° C -25° C Different 15°C	25°C/40°C	25°C/40°C
Cu(II)-N-6 Benzylaminopurine	3.613	09.277	4.927	14.5973
	3.287		4.708	14.5971

Conclusion

In this investigation spectrophotometric studies have been made for the complex formation between Cu (II) with N-6 benzylaminopurine at 25°C and 40°C temperature. The study was also carried out at 40°C to determine the stability constant and thermodynamic parameters. The value of thermodynamic parameters confirmed that the complexes are not stable at higher temperature. The stability constants (log K_1) and (log K_2) decreased with increased in temperature conforming that complexes are not more stable at higher temperature. Sufficiently larger negative value of ΔG showed that spontaneous formation of the complexes, spontaneously increased with temperature. Negative value of ΔH indicated the exothermic nature of the metal-ligand interaction. The ΔS values for the ligand complexes are negative, confirming that the amount of disorder in complex formation is very little.

The stability constant values were found is in biologically active range for Cu^{2+} metal ion. These stability constant values could be quite informative for a biochemist during drug design or drug discovery. It is the major implication of present study.

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