Chemical Technology: An Indian Journal

Research Article | Vol 17 Iss 2

Polarographic Study and Thermodynamic Parameters of Bioinorganic [Zn (II)-Antibiotics-Phenacetin] Ternary System

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Received: April 08, 2022, Manuscript No. tsct-22-60777; **Editor assigned:** April 11, 2022, PreQC No. tsct-22-60777;
Reviewed: April 25, 2022, QC No. tsct-22-60777; **Revised:** June 07, 2022, Manuscript No. tsct-22-60777;
Published: June 14, 2022, DOI: 10.37532/ 0974-7443.2022.17(2).430

Abstract

Thermodynamic parameters *viz.* enthalphy change (ΔH), free energy(ΔG) and entropy change (ΔS) and kinetic parameters such transfer coefficient (α), degree of irreversibility ()λ, diffusion coefficient (D) and standard rate constant (*k*) and stability constan (logβ) of Zn(II) complexes with neomycin, chlortetracyclin, oxytetracyclin, tetracyclin, penicillin-V and penicillin-G as primary ligan and phenacetin as secondary ligand were determined polarographically at pH = 7.30 ± 0.01 and an ionic strength of μ = 1.0 M NaClO at 25°C. The study showed that the complexes are not stable at higher temperature.

***Keywords:** Thermodynamics; Kinetic parameters; Stability constants; [Zn(II)-antibiotics-phenacetin] complexes*

Introduction

Antibiotics are well known naturally occurring compounds which are produced mostly by plant organisms [1]. These antibiotics are used in several diseases in plants, animals and human being [2-4]. The in-vitro activity has been found to be effective with even lower concentration of these antibiotics, on the other hand, paracetamol is a biologically active drug used as antipyretic agent to bring down the body temperature in high fever, therefore, and the complex study of these drugs with Zn has great importance. A literature survey reveals that there are no references available about ternary complexes of Zn with selected antibiotics and phenacetin, so, authors have undertaken the present study and report the mixed ligands complexation of Zn with neomycin, chlortetracyclin, oxytetracyclin, tetracyclin, penicillin-V and penicillin-G as primary ligands and phenacetin as secondary ligand with the view to determine the values of thermodynamic parameters and finally with these data, the position of transition state has also been pointed out.

Materials and Methods

Antibiotics and drug paracetamol used from the Fluka products and there solutions were prepared in double distilled water. The concentration of Zn(II) in all analytes was 0.5 mM while 1.0 M $NaClO_4$ was used to maintain the ionic strength as well as used as supporting electrolyte. NaCl-agar-agar plug together with sintered disc were used in Latinine-Lingane cell which connect the

Citation: Kesharwani AK, Khan F. Polarographic Study and Thermodynamic Parameters of Bioinorganic [Zn (II)-Antibiotics-Phenacetin] Ternary System. Chem Tech Ind J. 2022;17(2):430

polarographic cell with SCE [5,6]. The resistance of cell was lower than 200 ohms as to make no correction for IR.

The concentration of primary ligands varied from 0.5 mM to 30 mM at two constant concentration of phenacetin at 0.025 M and 0.050 M at pH=7.30 ± 0.01 at 25°C. The p^H of the analytic was maintained by using the requisite amount of $HClO_4$ and NaOH (both B.D.H.) solutions. Potassium dihydrogen phosphate-sodium hydroxide buffer was used to stabilize the p^H of the analyte at 7.30 ± 0.01.

A manual polarograph (AJCO electronics, Poona) with PL-50 polyflex Toshniwal galvanometer was used to record the current voltage data. The capillary (5.00 cm long and 0.04 mm in diameter) characteristics were $m^{2/3}$. $t_{1/6}$ = 2.40 $mg^{2/3} S^{-1/2}$ at 60.02 cms (calculated) effective height of mercury. An Elico (LI-120) p^H-meter was used to record the pH of the analytes. The C-V data for the analytes were recorded after passing the pure hydrogen gas. All the measurements were carried out at 25°C.

Results

Zn(II) gave a well-defined two electron quasireversible waves in 1.0 M $NaClO_4$ at p^H range 7.10 to 8.50 at 25°c, but p^H=7.30 was selected to investigate the complex formation in human blood p^H range. The 0.001 % solution of Tritone- X 100 was used as suppressor. Devries and Kroon method was used to determine the number of electrons involved in the reduction processes [7].

The values of $E_{1/2}$ quasireversible of Zn (II) was found -1.010 V *vs* SCE which by Gellings method gave $E_{1/2}$ reversible = -0.985 V [8]. Similarly $E_{1/2}$ reversible from $E_{1/2}$ quasireversible for complexes of Zn(II) with neomycin, chlortetracyclin, oxytetracyclin, tetracyclin, penicillin-V, penicillin-G as primary ligands and phenacetin as secondary ligand for different concentration of primary ligands (varried from 0.5 mM to 30 mM) and secondary ligand (at a fixed concentration at 0.025 M and 0.050 M) were determined. In all these cases it has been observed that irreversibility increases with increase of the ligand concentration. Zn formed 1: 1 and 1: 2 complexes with phenacetin and the stability constants [9-13] are given in (Table 1).

TABLE 1. **Stability constants of [Zn-antibiotic-phenacetin] complexes.**

Ligands	$Log\beta_{01}$	$Log\beta_{02}$	$Log\beta_{10}$	$Log\beta_{20}$	$Log\beta_{30}$	$Log\beta_{11}$	$Log\beta_{12}$	$Log\beta_{21}$
Phenacetin	1.92	2.95	-	-	-	-	-	-
Neomycin	-	-	3.60	6.51	9.101	4.70	7.55	9.96
Chlortetracyclin	-	-	4.40	7.61	9.502	4.91	7.75	10.00
Oxytetracyclin	-	-	4.50	7.81	9.860	5.01	7.70	10.12
Tetracyclin	-	-	4.80	8,01	9.909	-	8.00	10.20
Penicillin-V	-	-	4.91	-	10.110	5.30	8.36	10.40
Penicillin-G	-	-	4.96	8.12	10.140	5.38	-	10.60

Polarography of [Zn(II)-penicillin-G-phenacetin] complexes

The half wave potential increased with increase of concentrations of secondary ligand *i.e.* phenacetin to the [Zn-antibiotics] system showed ternary complex formation. The values of stability constants are given in (Table 2). The polarographic characteristics & $F_{ij}[X\ Y]$ values for the [Zn(II)-penicillin-G-phenacetin] system are given in (Table 2) and plot of $F_{ij}[X\ Y]$ *vs* [penicillin-G] is given in (Figure 1).The plots of $[(E-0.0591/n)\{\log (i_d - i)/i\}]$ *vs* i for Zn and its complexes are given in (Figures 1,2).The quasireversible waves for Zn(II) and its complexes were confirmed by the slope of current voltage curves and kinetic parameters which are given in (Table 3).

TABLE 2. **The polarographic characteristics & $F_{ij}[X\ Y]$ values for the [Zn(II)-penicillin-G-phenacetin] system.**

Phenacetin=0.025 M (Fixed)								**Phenacetin=0.050 M (Fixed)**						
Pen.-G X 10^{-3} M	**$(E_{1/2})^r$- V *vs* SCE**	**$\Delta E_{1/2}$ V**	**log**	**F_{00} [X,Y] x 10^2**	**F_{10} [X,Y] x 10^5**	**F_{20} [X,Y] 10^9**	**F_{30} [X,Y] x 10^{10}**	**$(E_{1/2})^r$ - V *vs* SCE**	**$\Delta E_{1/2}$ V**	**log**	**F_{00} [X,Y] x10^2**	**F_{10} [X,Y] x 10^6**	**F_{20} [X,Y] x10^9**	**F_{30} [X,Y] x 10^{10}**
0	0.985	-	-	-	-	-	-	0.985	-	-	-	-	-	-
0.5	1.0596	0.0746	0.00068	3.357	6.6414	1.1339	1.3803	1.0665	0.0819	0.00068	5.9123	1.1677	2.1292	1.3803
1	1.0764	0.0914	0.01137	12.4162	12.3799	1.1408	1.3307	1.084	0.099	0.01137	22.4658	2.2392	2.1361	1.3307
2	1.0938	0.1088	0.02088	48.1637	24.0639	1.1546	1.3819	1.1015	0.1165	0.02088	88.1318	4.4029	2.1499	1.3909
3	1.1042	0.1192	0.028	108.108	36.0239	1.1684	1.3505	1.1119	0.1269	0.028	197.8998	6.5942	2.1637	1.3543
4	1.1116	0.1266	0.03353	193.0759	48.2599	1.1822	1.3909	1.1193	0.1343	0.03353	352.5978	8.8131	2.1775	1.3852
5	1.1174	0.1324	0.04227	303.9208	60.7769	11,961	1.3613	1.2591	0.1401	0.04227	553.0788	11.0601	2.1914	1.3832
6	1.1212	0.1362	0.05003	407.7795	73.5659	1.2099	1.3807	1.1298	0.1448	0.05003	800.1318	13.3343	2.2052	1.3343
8	11,298	0.1448	0.05579	799.8755	99.9799	1.2376	13905	1.1374	0.1524	0.05579	1437.377	17.9663	2.2329	1.3542
10	1.1358	0.1508	0.06058	1,275,055	127.501	1.2653	1.3311	1.1432	0.1582	0.06058	2270.983	22.7091	2.2606	1.3934
20	1.1549	0.1699	0.06058	5634.274	281.711	1.4037	1.3718	1.1618	0.1768	0.07037	9616.693	48.0831	2.399	1.3323
30	1.1665	0.1815	0.07037	13908.99	463.631	1.5422	1.3203	1.1729	0.1879	0.08019	22868.5	76.2281	2.5375	1.3832
log A = 0.5606 log C =9.0519								log A =0.8684 log C =9.3268						
log B =4. 9876 log D =10.1400								log B = 5.0136 log D =10.1400						

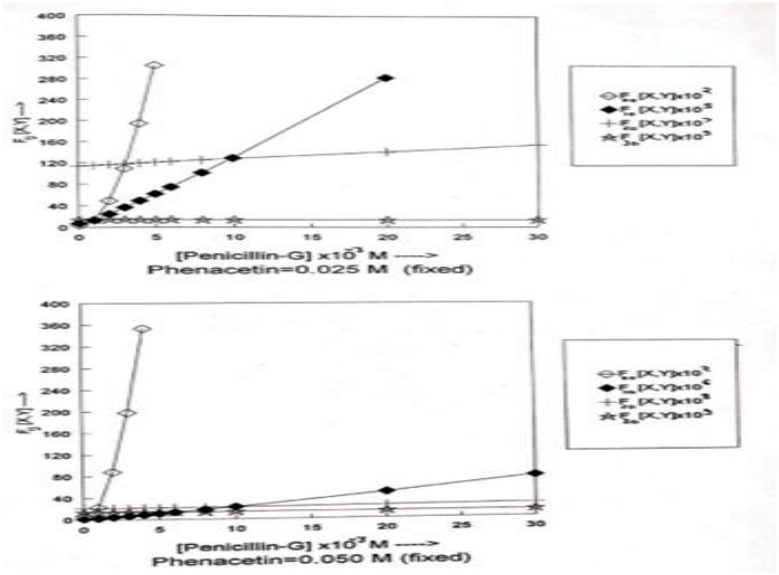

FIG.1. **Plot of F_{ij} [X, Y] versus [Penicillin-G] for [Zn-penicillin-G-phenacetin] system.**

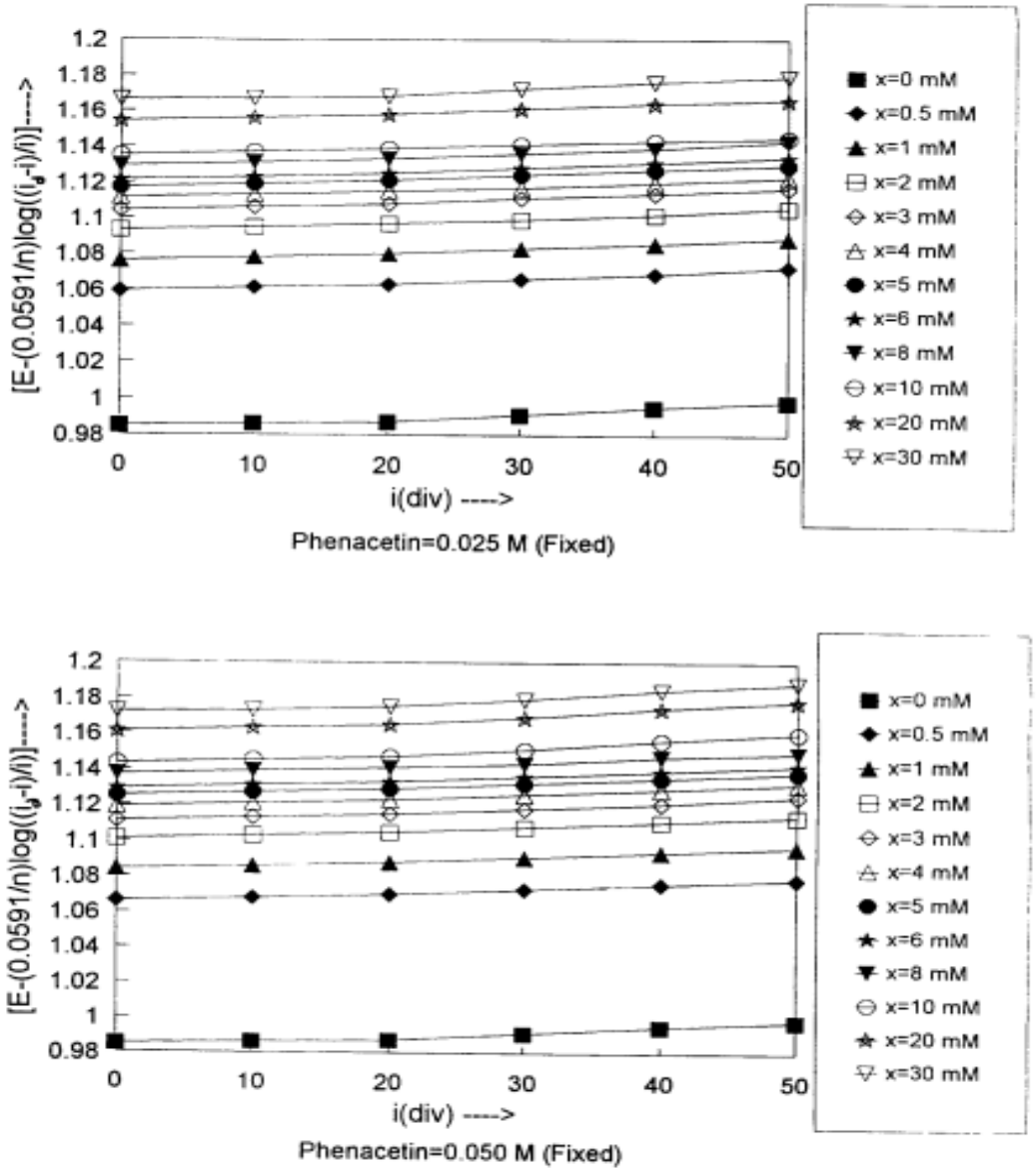

FIG.2. **Plot of [- E - (0.0591/n) log {(i_d-i) / i}] versus I for [Zn-penicillin-G-phenacetin] system.**

Kinetic parameters of [Zn(II)-penicillin-G-phenacetin] complexes

The kinetic parameters such as standard rate constant (k), degree of irreversibility (l) and charge transfer coefficient (a) for the [Zn(II)-penicillin-G-phenacetin] complexes were given in (Table 3). The parameter Z, which is measure of degree of irreversibility, is given by the following equation 10

$$Z=\text{antilog}\,[(nF/2.303).RT.(E_{1/2}\ r\text{-}E)]+\log(i_d - i)/i.$$

The values of standard rate constant (*k*) of Zn and its complexes are found to be order of 10^{-3} cm. sec^{-1}, confirmed that the electrode processes are quasi reversible and the reduction of the electro active species at the surface of the electrode is not fast. The charge

transfer coefficient (α), which can be regarded as the fraction of the applied potential, either assists or hinders the process under consideration; also have the expected values. The values of α comes about 0.500 confirming the transition state lies in the midpoint of dropping mercury electrode and mercury solution interface.

TABLE 3. **Kinetic parameters such as standard rate constant (k), degree of irreversibility (l) and charge transfer coefficient (a) for the [Zn(II)-penicillin-G-phenacetin] complexes.**

Zn(II) = 0.5 m M; u=1.0 M $NaClO_4$; pH = 7.30 + 0.01; temp. = 25^0c												
Phenacetin = 0.025 M (Fixed)							**Phenacetin = 0.050 M (Fixed)**					
Pen.-G X 10^{-3} M	**$(E^{1/2})^v$ - V *vs* SCE**	**Slope mV**	**α**	**λ $sec^{-}_{1/2}$**	**$D^{1/2}$ X $10^{-3}Cm^2$ sec^{-1}**	**k X 10^{-3} cm sec^{-1}**	**$(E^{1/2})^V$ - V *vs* SCE**	**Slope mV**	**α**	**λ $sec^{-}_{1/2}$**	**$D^{t/2}$ x10^{-3} cm^2sec^{-1}**	**k X 10^{-3} cm sec^{-1}**
0	1.01	37.5	0.487	1.18	4.39	5.18	1.01	37.5	0.487	1.18	4.39	5.18
0.5	1.08	40	0.465	1.18	4.32	5.09	1.086	37.5	0.496	1.11	4.32	4.79
1	1.095	40	0.519	1.11	4.25	4.71	1.104	37.5	0.519	1.05	4.25	4.46
2	1.114	42.5	0.487	1.11	4.18	4.63	1.123	40	0.519	1.11	4.18	4.63
3	1.125	40	0.487	1.66	4.11	6.82	1.133	40	0.472	1.66	4.11	6.82
4	1.131	37.5	0.472	1.86	4.04	7.51	1.14	40	0.465	1.66	4.04	6.7
5	1.14	40	0.487	1.48	3.98	5.46	1.147	40	0.465	1.57	3.98	6.24
6	1.143	37.5	0.487	1.57	3.91	6.13	1.153	40	0.472	1.48	3.91	5.78
8	1.152	40	0.487	1.48	3.84	5.68	1.16	40	0.465	1.57	3.84	6.02
10	1,157	40	0.45	1.66	3.77	6.25	1.17	45	0.501	1.32	3.77	4.97
20	1.179	'42.5	0.45	1.4	3.7	5.18	1,187	45	0.501	1.48	3.7	5.47
30	1.189	42.5	0.487	1.48	3.7	5.47	1,196	42.5	0.487	1.48	3.63	5.37

Thermodynamic parameters of [Zn(II)-antibiotics-phenacetin] complexes

Theromodynamic parameters such as enthalpy change (ΔH), free energy change (ΔG) and entropy change (ΔS) of the complexes have been determined at $25^{\circ C}$ and $35^{\circ C}$ by using the following equations.

$$\Delta H = 2.303\ RT_1 + T_2\ (\log K_2 - \log K_1)\ (T_2 - T_1),$$

$$\Delta G = -\ 2.303\ RT \log K,$$

$$\Delta G = \Delta H - T\Delta S$$

The values of ΔS, ΔG and ΔH are given in the (Table 4). From these values it is clear that ΔS are more negative at higher temperature while the values of ΔG are less negative at higher temperature confirmed that the complex are not stable at higher temperature. The negative values of ΔH ensured that the reactions are exothermic in nature.

TABLE 4. **Thermodynamic parameters (the values of DS, DG and DH) for [Zn(II)-antibiotics-phenacetin].**

System	**Stability Constants**			**ΔH Kcal Mol^{-1}**			**-ΔG K Cal Mol^{-1}**			**-ΔS Cal deg^{-1} Mol^{-1}**		
	log β_{11}	Logβ_{12}	logβ_{21}	logβ_{11}	logβ_{12}	logβ21	log β_{11}	logβ_{12}	logβ_{21}	log β_{11}	logβ_{12}	logβ_{21}
	25°C and 35°C			(35°C-25°C)			25°C and 35°C			25°C and 35°C		
Zn-Neomycin-	4.7	7.55	9.96	25.2	21.42	17.64	6.409	10.296	13.582	63.057	37.329	13.617
phenacetin	4.1	7.04	9.54				5.778	9.922	13.445	63.058	37.331	13.62
Zn-Chlortetracycline-	4.91	7.75	10	24.78	20.16	17.22	6.695	10.568	13.637	60.687	32.187	12.023
phenacetin	4.32	7.27	9.59				6.088	10.246	13.516	60.688	32.188	12.025
Zn-Oxytetracycline-	5.01	7.9	10.12	24.36	18.9	16.8	6.832	10.773	13.8	58.818	27.272	10.067
phenacetin	4.43	7.45	9.72				6.243	10.5	13.699	58.821	27.273	10.068
Zn-Tetracycline-	-	8	10.2	-	16.8	16.38	-	10.909	13.909	-	19.768	8.291
phenacetin	-	7.6	9.81				-	10.711	13.826	-	19.769	8.292
Zn-Penicillin-V-	5.3	8.36	10.4	23.94	14.7	15.96	7.227	11.4	14.182	56.083	11.073	5.966
phenacetin	4.73	8.01	10.02				6.666	11.289	14.122	56.084	11.074	5.967
Zn-Penicillin-G- phenacetin	5.38	-	10.6	23.1	-	15.54	7.336	-	14.455	52.899	-	3.641
	4.83	-	10.23				6.807	-	14.418	52.9	-	3.642

Stability constants of the [Zn (II)-antibiotics-phenacetinl] complexes

Stability constants for [Zn (II)-antibiotics-phenacetin] complexes are given in (Table 1). Stability of the complexes can be compared by the value of mixing constant (log Km) which is given by the following equation.

$\log Km = \log b_{11} - 1/2 [\log b_{20} + \log b_{02}]$

The values of log Km for the complexes [Zn(II)-neomycin- phenacetin], [Zn(II)-chlortetracyclin- phenacetin], [Zn(II)-

oxytetracyclin- phenacetin], [Zn(II)-penicillin-V- phenacetin] and [Zn(II)-penicillin-G- phenacetin] are -0.030, -0.370, -0.370, +3.825, -0.155 respectively. The value of log Km for [Zn(II)-tetracyclin-paracetamol] is not calculated because [Zn(II)-tetracycline-phenacetin] complex is not found in this case.

Ternary complexes with negative values of log Km are less stable than their parent binary complexes and those with positive log Km are more stable than their parent binary complexes.

The value of stability constants (from Table 1) of neomycin complexes showed that this antibiotic formed the complexes of lowest stability amongst all the selected primary ligands because there is steric hindrance between metal and various groups present in the neomycin. In the complexes of chlortetracyclin, oxytetracyclin and tetracyclin, bonding takes place with metal ion through the oxygen of amide group and the oxygen of carbon atom. All tetracyclins have the same structures but they differ only in the group R_1 and R_2. The chlortetracyclin complexes is less stable than oxytetracyclin complexes, can be explained as the basis of the presence of electronegative chlorine atom at R_1 in chlortetracyclin while oxygen atom in OH group of R_2 in oxytetracyclin. Due to higher electronegativity of chlorine it attracts electrons very rapidly from groups present in the chlortetracyclin while oxygen does not attract electron as rapidly as chlorine, and so in case of chlortetracyclin there is higher electronic disturbance than in oxytetracyclin causes the less stability of chlortetracyclin complexes than oxytetracyclin complexes. The p^K values of these drugs are also support this order of stability.

Discussion

Since there is no such electronegative atoms are present in case of tetracyclin, results no electronic disturbance in tetracyclin and so it forms highly stable complexes amongst all the selected tetracyclins.

In case of penicillin-V and penicillin-G, oxygen atom of carboxylic group and ring nitrogen may take part in formation of complex with Zn. High stability of penicillin-G complexes than penicillin-V is supported by besic strength of these drugs. In case of penicillin-G the value of log K is 4.77 while in case of penicillin-V it is found 3.98.

As a result of lesser steric hindrance in penicillin complexes than other antibiotics, penicillin complexes are highly stable than other.

The trend of stability of the complexes is neomycin <chlortetracyclin <oxytetracyclin < tetracyclin < penicillin-V <penicillin-G.

The stability constants of the complexes of Zn with antibiotics are of great importance in pharmaceutical sciences. The values of stability constants obtained are not high, so Zn toxicity in-vivo can be reduced by using these drugs .

Conclusion

The overall view for the water analysis parameters is complicated in terms of maintaining best quality of water on our planet. Imbalance in one of them creates misbalance in other parameters. Thus, we have to take extreme care to preserve the natural resource of water in its purest form.

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