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RESEARCH ARTICLE

Kinetics of Catalytic Oxidation of Carbenicillin: A Degradation Approach for Penicillanic Acid Derivatives (PADs)

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Abstract

Diperiodatocuprate [DPC (III)] was selected to predict the kinetic studies for carbenicillin (CRBC) oxidation in the basic media. The investigation was completed in the presence of $CoCl_3$ as catalyst by using a UV/Visible spectrophotometer at 298K temperature and 0.01 mol-dm^{-3} ionic strength which confirmed a 1:4 stoichiometry between CRBC and DPC (III). Both spectral and elemental analysis was used to identify the final products. Monoperiodatocuperate [MPC (III)] was found to be the primary active species of DPC (III). Pseudo-first order reaction was declared for DPC (III), while fractional order reactions were noticed in case of CRBC (substrate), Co (III) catalyst as well as KOH (alkali). However, for periodate, the reaction was determined to be in negative fractional order. Spectral evidence, determination of various rate constants, and both activation as well as thermodynamic parameters were used to predict plausible mechanism.

Keywords: *Diperiodatocuprate, rate constant, carbenicillin, mechanism, oxidation*

Introduction

One of the commonly consumed classes of antibacterial agents is the so-called β-lactam antibiotics or penicillanic acid derivatives (PADs), which contain a nucleus including a 2-azatidinone (3-lactam) ring that is either connected to a thiazolidine or a dihydro-1, 3-thiazine ring. Compounds whose nuclei contain a thiazolidine ring are noted generically as penicillins, whereas those with a nucleus containing a dihydrothiazine ring are referred to as cephalosporins. Benzylpenicillin (penicillin G), phenoxymethylpenicillin (penicillin V), ampiciliin, oxacillin, amoxicillin, dicloxacillin, and carbenicillin, etc. are some common samples of PADs. Antibiotics or PADs, antimicrobial medications' "silver bullets" are hailed as one of modern medicine's greatest discoveries of the 20th century [1]. However, despite the worldwide consumption of PADs as essential chemotherapeutic agents, they still suffer from some style of shortcomings; therefore, certain members don't respond to certain microorganisms. These PADs are widely consumed in cosmetics, drugs, personal care products (PCPs), hospitals, and sewage for the improvement of our daily life [2-4]. Approximately 30% of these antibiotics or PADs get consumed inside the host body and the remaining non-degraded PADs get discharged into natural water sources in several ways which pollute the entire ecosystem. It has been previously described [5] how antibiotic resistance genes are distributed in the environment. Such contamination in water, air, and soil starts converting them into unfit/unhealthy for drinking purposes by enhancing antibacterial resistance [6-7]. For the deterioration of these emerging contaminants, a number of advanced oxidation processes (AOPs) have been used [8–10]. Hence the degradation of carbenicillin, through catalytic oxidation, will prove an appreciative research work for chemists and drug industries.

Copper, osmium, ruthenium, cobalt, and manganese are common transition metals which catalyze chemical reactions either alone or as binary mixtures. The development of reactive intermediates or highly unstable complexes, substrate oxidation, or free radicals appearance are just a few examples of the redox processes that are involved in Co (III) catalysis, which has garnered a lot of interest [11]. Transition metals can typically be stabilized by chelating with polydentate ligands, such as diperiodatoargentate (III) [12], diperiodatocuprate (III) [13, 14], and diperiodatonickelate (IV) [15] which are utilized as strong oxidants in analytical chemistry and chemical research. The Cu (III): Cu (II) couple plays a significant role in many reactions since both Cobalt (III) and Cu (III) are active intermediate species in multi-electron transfer reactions [16]. DPC (III) synthesis, stability, analytical uses, structural analysis, and analytical applications have all been covered in several research, which were initially created more than 50 years ago [17, 18]. Carbenicillin, a 4th generation antibiotic, is a semi-synthetic analogue of benzyl-penicillin with carboxyl and benzyl groups. The molar mass and formula of carbenicillin are 378.401 g mol^{-1} and $C_{17}H_{18}N_2O_6S$ respectively. FIGURE 1 depicts its structure.

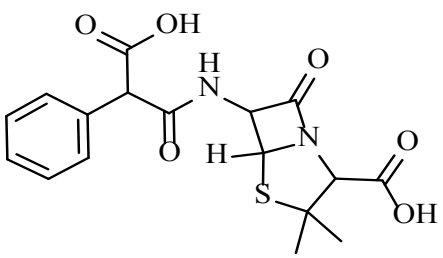


Figure 1. *Structure of Carbenicillin*

Charles B. Smith et al. have described the activity of carbenicillin in vitro and absorption and excretion in normal young men [19]. Kenneth Butler et al. have explained the chemistry of carbenicillin and the mode of its action [20]. Arthur R. English et al. have explained the carbenicillin indanyl sodium, an orally active derivative of carbenicillin [21].

The effects of carbenicillin, cefotaxime, and vancomycin on tobacco and chrysanthemum TCL morphogenesis and Agrobacterium growth have been discussed by Jaime Teixeira da Silva et al. [22]. Kolek Marta et al. have explained the hydrolysis of penicillin G and carbenicillin in pure water through HPLC/ESI-MS reports [23]. T. C. Eickhoff has reported the effect of polymyxin B or gentamycin in combination with carbenicillin in vitro against Pseudomonas aeruginosa [24]. Melvin I. Marks et al. have reported pharmacologic studies of carbenicillin and gentamycin in patients with cystic fibrosis and pseudomonas pulmonary infections [25]. The interactions between carbenicillin or ticarcillin and aminoglycoside antibiotics have been described by H. A. Holt [26]. Pharmaceutical features of the administration of ticarcillin and carbenicillin have been reported by B. Lynn [27]. Rosdahl N. and Thomsen V. F. [28] have already discussed the carbenicillin activity against gram-negative rods in comparison to that of penicillin, cephalosporins, and ampicillin.

The kinetics of uncatalyzed oxidation of Carbenicillin by DPC (III) has been investigated experimentally [29]. As a result, the primary goal is to investigate the kinetics of carbenicillin oxidation and to anticipate a likely process while also determining activation and thermodynamic parameters. Similar to this, accurate calculations have been made for different rate constants, equilibrium constants, and catalytic constants at various four temperatures.

Materials and Methods

Materials and instruments

Throughout the research process, analytically graded chemicals and distilled water were applied. Separate solutions of potassium periodate (Sigma Aldrich) and 0.01 mol dm^{-3} CRBC (Sigma Aldrich, New Zealand) were made. Molarity of KIO_4 solution was obtained using an iodometric technique [30]. An ELICO LI 613 pH meter was used to measure the pH of the solutions. A Varian CARY 5000 UV-VIS spectrophotometer was accustomed to recording electronic absorption spectra in the region of 200-1000 nm. Similarly, FT-IR spectra were recorded by Thermo Nicolet, Avatar 370 FT-IR spectrometer within a region of 4000-400 cm^{-1} with the help of KBr disc. The products' LC-MS

spectra were captured on the positive mode of UPLC-TQD Mass spectrometer between 0 and 1000 m/z.

Synthesis of DPC (III) and CRBC- Co (III) Complex

The oxidizing agent as well as the reagent copper (III) diperiodate [DPC (III)] was prepared [31] and a sintered glass crucible G-4 was applied to filter; a red-brown coloured solution was obtained as filtrate, and 250 ml solution was made after dilution. The iodometric titration ($Na_2S_2O_3$, starch, KI, and KH_2PO_4) was applied to standardize the DPC (III) solution by using the thiocyanate method [32] that helped to determine its concentration. Chemicals like sodium thiosulphate, potassium iodide, potassium persulphate, monopotasium phosphate, and KOH were managed from EMPLURA^R (Merck Life Science Pvt. Ltd. India). Similarly, KNO_3, and $CuSO_4$ were brought from LOBA CHEMIE Pvt. Ltd. India, and the catalyst ($CoCl_3$) was managed from Sigma Aldrich (New Zealand). A UV-visible spectrophotometer verified the existence of DPC (III) which showed absorption bands at 265 nm, 385 nm, as well as the maximum peak at 415 nm. 10 ml CRBC solution of 0.132 mol dm^{-3} and 10 ml DPC (III) solution of 0.528 mol dm^{-3} were mixed along with KOH solution (2.0 ml) of fixed molarity, 1.0 ml of each KNO_3, $CoCl_3$, and KIO_4 solution, stirred for twenty-four hours before re-fluxing and condensation. After cooling for three days, the mixture was filtered; and the purified products were then crystallized again in ethanol until the ethanol evaporated, leaving behind crystals of a greyish tint. Synthesis of the complex was verified by the emergence of peaks in the UV-Visible spectrophotometer. Figure 2 depicts the potential structure of the CRBC- Co (III) complex.

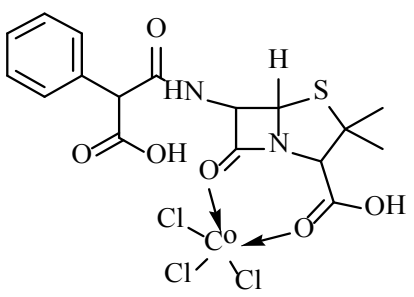


Figure 2. *CRBC- Co (III) Complex*

Kinetic Study Procedure

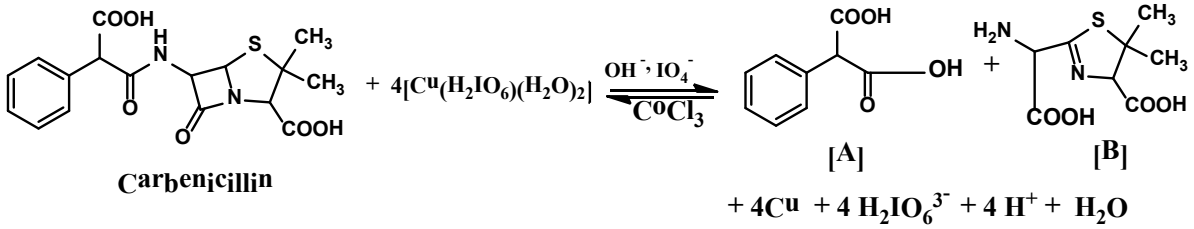
With the help of a micro-pipette, the DPC (III) solution was retained in an extremely dried cuvette which already had pre-fixed concentrated solutions of Co (III), KIO_4 along with KNO_3, and KOH in which CRBC solution of variable concentration was blended gently and carefully. With the aid of a UV-Visible spectrophotometer, absorbance measurements were made quickly and individually while the reaction progressed at 20°C, 25°C, 30°C, and 35°C ± 0.5°C separately within pH range of (9.2-10) and a wavelength of 415 nm. The UV-Visible spectrophotometer was monitored to collect data for DPC (III) at a molar extinction coefficient (€) of 6242.50 dm^3 mol^{-1} cm^{-1}, in decreasing order of absorbance. Using the software Origin 9.6 (2017), values for the parametric statistics regression coefficient (r) and standard deviation or variance (s) were collected. For every concentration of DPC (III), log (Absorbance) against time plots, Figure 5, produced a straight line, allowing rate constants (k_c) to be derived from the slopes.

Results and Discussion

Stoichiometry and Product Analysis

The precise stoichiometry of CRBC: DPC (III) was confirmed by Job's method [33]; it was declared to be 1:4 for CRBC: DPC (III). Various sets of reaction mixtures containing a variable ratio of DPC (III) and CRBC along with an invariable ratio of $CoCl_3$, KOH, and KNO_3 (III) after keeping the reaction mixture for three hours within a closed vessel filled with nitrogen gas atmosphere. Phenyl-malonic acid ($C_9H_8O_4$) and 2-(amino (carboxy) methyl)-5, 5-dimethyl-4, 5-dihydrothiazole-4-carboxylic acid-1-oxide were confirmed as the primary products when CRBC reacted with DPC (III) and Co (III) catalyst in the aqueous alkaline medium which were recovered from ethanol and separated using column chromatography with an eluent of 80% benzene and 20% chloroform over neutral alumina.

The catalyzed reaction between CRBC and DPC (III) in an aqueous alkaline medium [29] can be presented by:



Carbenicillin

Where A = 2-phenylmalonic acid ($C_9H_8O_4$) and B = 2-(amino (carboxy) methyl)-5, 5-dimethyl-4, 5-didydrothiazole-4-carboxylic acid-1-oxide ($C_8H_{12}N_2O_4S$)

Table 1: *Elemental analysis*

Complex/Product	C%	H%	N%	Co%	Cl%	S%	O%
$C_{17}H_{18}Cl_3CoN_2O_6S$	36.85 (37.55)	3.30 (3.34)	5.31 (5.15)	11.02 (10.84)	19.28 (19.56)	5.08 (5.40)	19.15 (18.15)
(A) $C_9H_8O_4$	60.11 (60.00)	4.55 (4.48)	-	-	-	-	35.33 (35.51)
(B) $C_8H_{12}N_2O_4S$	41.53 (41.37)	5.37 (5.21)	12.16 (12.06)	-	-	13.88 (13.81)	27.05 (27.54)

Characterization

Elemental analysis

The Co (III)- CRBC complex ($C_{17}H_{18}Cl_3CoN_2O_6S$), as well as two products A ($C_9H_8O_4$), and B ($C_8H_{12}N_2O_4S$) showed the following % elemental analysis as presented in Table 1.

Spectral analysis

Figure 3 and Figure 4 represent the FT-IR and LC-MS spectra respectively [29].

In FT-IR spectrum, carboxylic OH group shows a peak at 3413.5 cm^{-1}, N-H stretching group at 3380.7 cm^{-1}, methyl stretching group at 1464.4 cm^{-1} & 1386.6 cm^{-1}, carboxylic C=O stretching at 1276.7 cm^{-1} while another peak at 1641.2 cm^{-1} is noticed due to ketonic or carboxylic group. Figure 4 shows the m/z values for the complex and its products. The complex ($C_{17}H_{18}Cl_3CoN_2O_6S$) showed an m/z value at 544 while (m/z) value for 2-phenylmalonic acid was at 182 (m + 2), and that of 2-(amino (carboxy) methyl)-5, 5-dimethyl-4, 5-dihydrothiazole-4-carboxylic acid-1-oxide was at 232 (m+1).

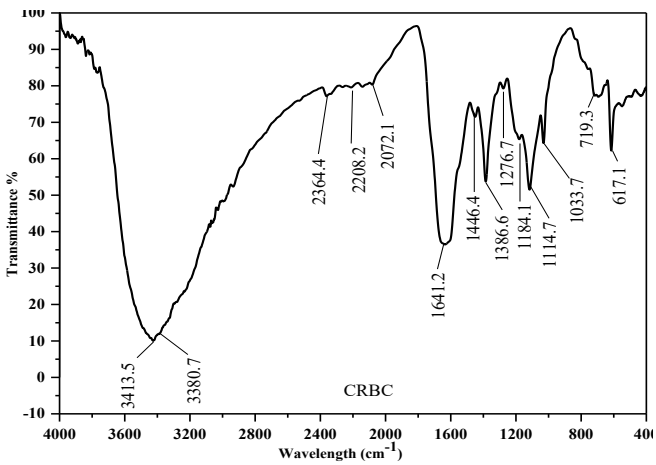


Figure 3: *FT-IR Spectrum for the catalyzed oxidation of CRBC*

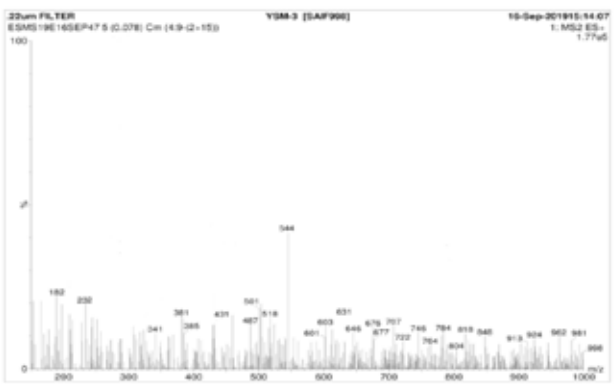


Figure 4: *LC-MS Spectrum for the catalyzed oxidation of CRBC*

Reaction Orders

With variable concentration of CRBC, $CoCl_3$, KIO_4, KOH, and constant concentration of DPC (III), reaction orders were obtained from the slopes of log (absorbance) vs. time, independently for each concentration of DPC (III) [29]. The plots are shown in Figure 5 and Table 2.

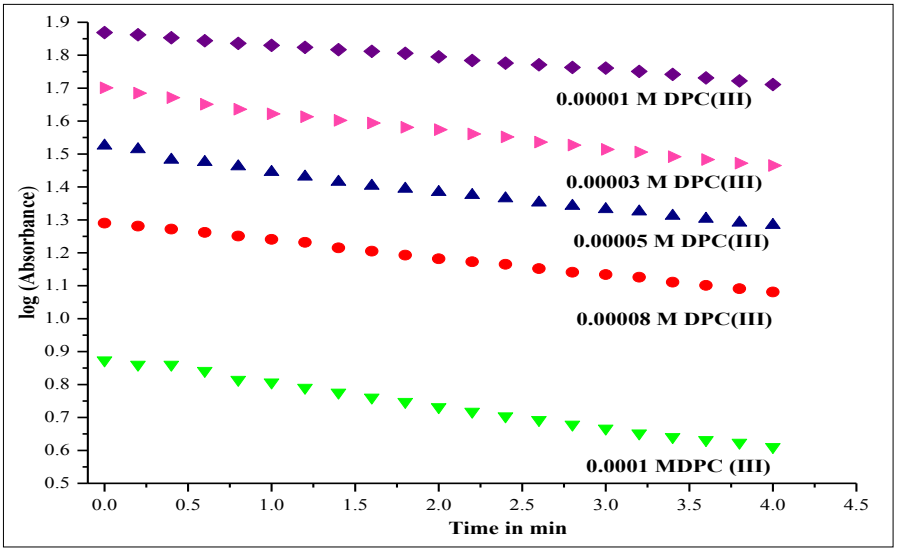


Figure 5: *Order Plot of log (Absorbance) vs. time [for each concentration of DPC (III)]*

Effects of [DPC (III)], [CRBC], and [KOH]

The pseudo-first-order process involving DPC (III) was confirmed by the linearity and nearly parallel

Table 2: *Co (III) catalyzed oxidation of carbenicillin by DPC (III) in an aqueous alkaline medium at 298 K and I = 0.10 / mol dm^{-3}: effect of variation of [DPC]*, [CRBC], $CoCl_3$, KIO_4, and [KOH]*

[DPC] x 10^5 M	[CRBC]x 10^4 M	[OH^-] x10^2 M	[IO_4^-] x10^5 M	[$CoCl_3$] x10^7 M	k_Ux10^4 (s^{-1})	k_Tx 10^3 (s^{-1})	k_Cx 10^3 (s^{-1})
1.0	5.0	0.8	1.0	5.0	1.20	1.47	1.35
3.0	5.0	0.8	1.0	5.0	1.30	1.49	1.36
5.0	5.0	0.8	1.0	5.0	**1.20**	**1.49**	**1.37**
8.0	5.0	0.8	1.0	5.0	1.30	1.48	1.35
10.0	5.0	0.8	1.0	5.0	1.10	1.45	1.35
5.0	**1.0**	0.8	1.0	5.0	0.40	0.50	0.46
5.0	**3.0**	0.8	1.0	5.0	0.80	1.03	0.95
5.0	**5.0**	0.8	1.0	5.0	**1.20**	**1.49**	**1.37**
5.0	**8.0**	0.8	1.0	5.0	1.80	2.01	1.83
5.0	**10.0**	0.8	1.0	5.0	2.30	2.61	2.38
5.0	5.0	**0.2**	1.0	5.0	0.60	0.72	0.66
5.0	5.0	**0.4**	1.0	5.0	0.80	0.98	0.90
5.0	5.0	**0.6**	1.0	5.0	1.00	1.19	1.09
5.0	5.0	**0.8**	1.0	5.0	**1.20**	**1.49**	**1.37**
5.0	5.0	**1.0**	1.0	5.0	1.60	1.85	1.69
5.0	5.0	0.8	**1.0**	5.0	**1.20**	**1.49**	**1.37**
5.0	5.0	0.8	**3.0**	5.0	1.0	1.39	1.29
5.0	5.0	0.8	**5.0**	5.0	0.90	1.05	0.96
5.0	5.0	0.8	**8.0**	5.0	0.70	0.82	0.75
5.0	5.0	0.8	**10.0**	5.0	0.60	0.71	0.65
5.0	5.0	0.8	1.0	**1.0**	1.20	0.46	0.34
5.0	5.0	0.8	1.0	**3.0**	1.20	1.03	0.91
5.0	5.0	0.8	1.0	**5.0**	**1.20**	**1.49**	**1.37**
5.0	5.0	0.8	1.0	**8.0**	1.20	2.07	1.95
5.0	5.0	0.8	1.0	**10.0**	1.20	2.61	2.49

* All solutions were prepared in mole dm^{-3}.

plots of log (Absorbance) vs. time which are in good agreement with Table 2 and Figure 5. Figure 6 represents the plot of (4+ log [CRBC]) vs. (4+ log k_c) vs. and declared that the catalyzed rate constants (k_c) increased as [CRBC] increased, and that the order of CRBC was 0.596 ($r \geq 0.9977$, $s \leq 0.00103$). Similarly, Figure 7 represents the plot of (4 + log k_c) vs. (2 + log [KOH]), and showed an increase in the values of catalyzed rate constants (k_c) as [KOH] increased , and thus the order of reaction with KOH was found to be 0.595 ($r \geq 0.9816$, $s \leq 0.004$).

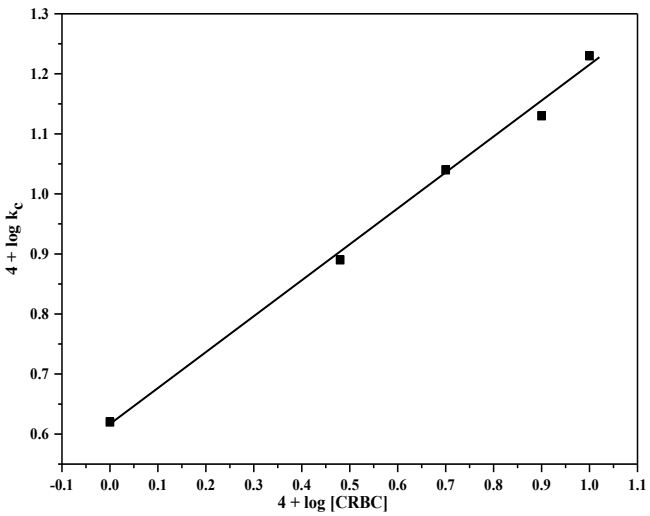


Figure 6: *Plot of 4 + log [CRBC] vs. 4 + log k_c*

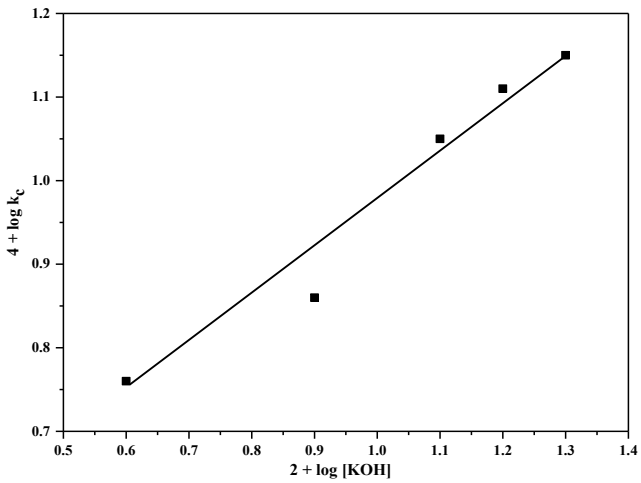


Figure 7: *Plot of 2 + log [KOH] vs.4 + log k_c*

Effects of [Periodate], dielectric constant (D), and ionic strength (I)

The rate constant decreased with a rise in [KIO_4] having an order of -0.488 ($r \geq 0.997$, $s \leq 0.0006$) which is represented in Figure 8 as a plot of 5 + log [KOI_4] vs. (4 + log k_c). The rate of reaction was not significantly impacted by an increase in ionic strength while the rate of the catalyzed reaction was unaffected by the dielectric constant.

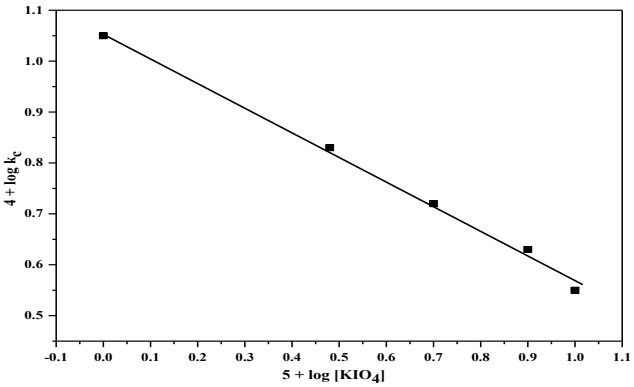


Figure 8: *Plot of 5 + log [KIO_4] vs. (4 + log k_c)*

Effect of Temperature

The temperature effect on carbenicillin oxidation rate was studied at variable temperatures and it was concluded that rate constants increased with a temperature rise. The smallest amount least square method supported to determine activation parameters from i) plots of catalyzed rate constants (Figure 9 and Table 3), ii) catalytic constants (Figure 10 and Table 4), and slow step rate constants (Figure 11 and Table 5). Finally, equilibrium constants were determined from verification plots whose slopes and intercepts supported in the determination of both activation in addition as thermodynamic parameters (Figures 12, 13, 14, and Tables 6, and 7 respectively).

Activation parameters concerning catalyzed rate constant (k_c) for CRBC

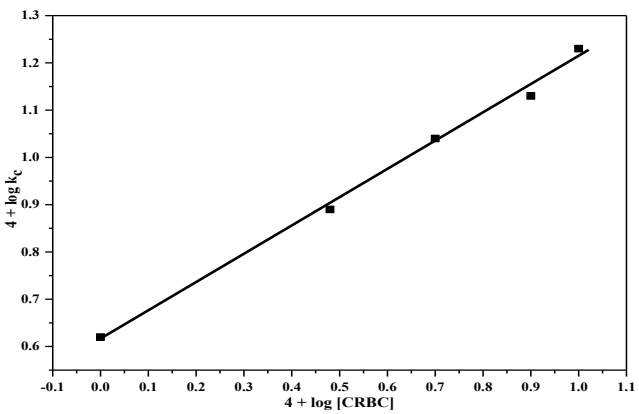


Figure 9: *Plot of 4 + log [CRBC] vs. 4 + log k_c]*

Table 3: *Activation parameters from k_c*

Activation Quantities	Values
Activation Energy	40.84 (k J/mol)
Enthalpy Change	38 ± 1 (k J/mol)
Entropy Change	-169 ± 3 (J/K/mol)
Free Energy Change	87 ± 2 (k J/mol)
Log A	4.3 ± 0.3

Activation parameters concerning catalytic constant (K_c) for CRBC

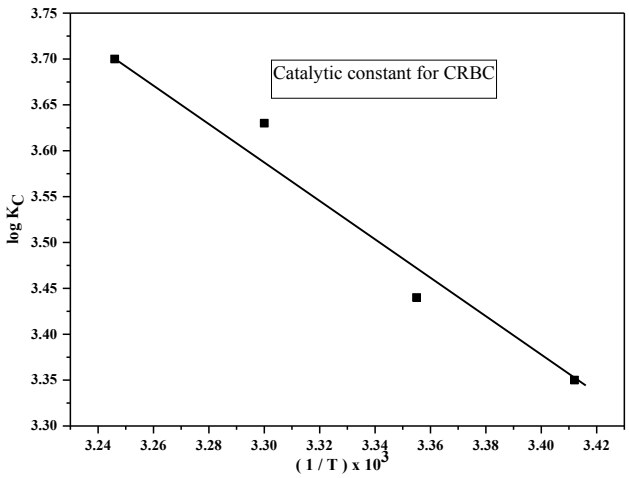


Figure 10: *Plot of (1 /T) x 10^3 vs. log* $\mathbf{K_c}$

Table 4: *Activation parameters from Kc*

Activation Quantities	Values
Activation Energy	43.095 (k J/mol)
Enthalpy Change	40 ± 1 (k J/mol)
Entropy Change	-163 ± 1 (J/K/mol)
Free Energy Change	89 ± $2^{\neq}$ (k J/ mol)
Log A	10.6 ± 0.2

Activation parameters concerning slow step rate constant (k) for CRBC

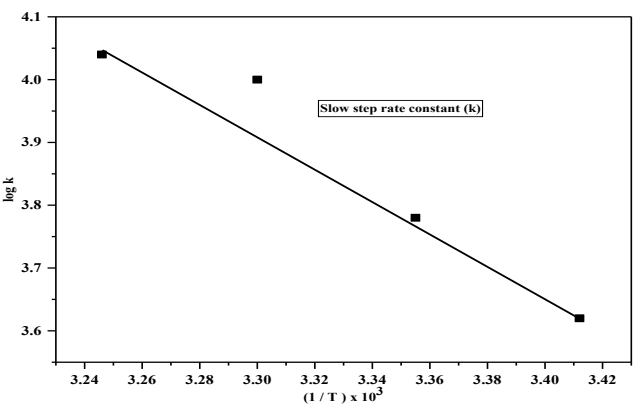


Figure 11: *Plot of (1 / T) x 10^3 vs. log k for CRBC*

Table 5: *Activation parameters from k*

Activation Quantities	Values
Activation Energy	51.53 (k J/mol)
Enthalpy Change	49 ± 2 (k J/mol)
Entropy Change	-8.6 ± 0.8 (J/K/mol)
Free Energy Change	49 ± 2 (k J/mol)
Log A	12.4 ± 0.4

DPC (III) functions both as a robust oxidant as well as a chelating agent at the same time. DPC (III) exists as $[Cu\ (H_3IO_6)_2]^-$ and $[Cu\ (H_2IO_6)\ (H_3IO_6)_2]^{2-}$ as equilibrium state in water due to its solubility where as MPC (III) can exist in the sort of $[Cu\ (H_2IO_6)\ (H_2O)_2]$ as the foremost active species for the current study as confirmed by mechanism.

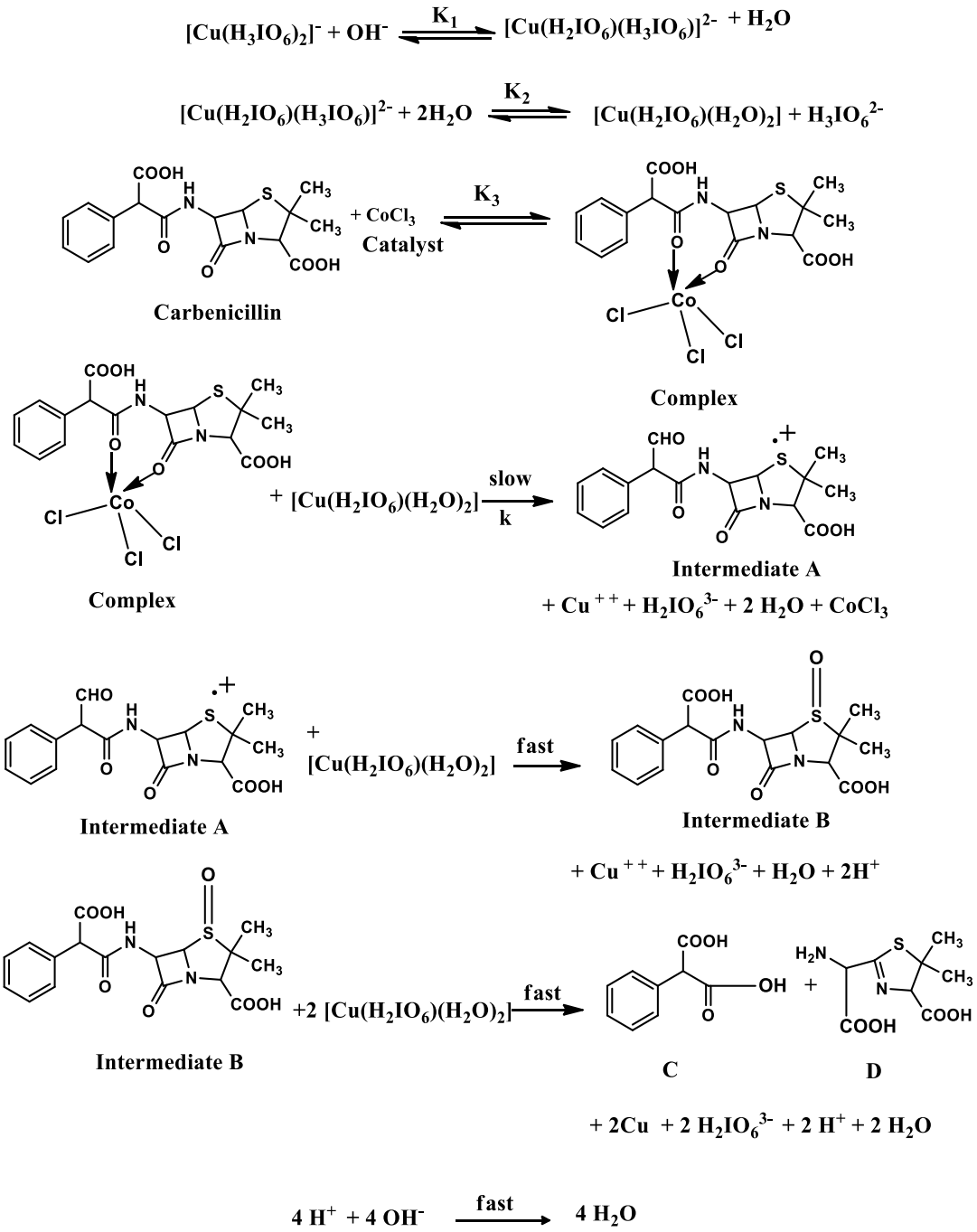
Probable Mechanism of Catalyzed Oxidation of CRBC

An appropriate mechanism (Scheme 1) was proposed with engagement of all reacting species based on experimental evidence. First, DPC (III) combines with the hydroxide ions to produce its divalent anionic form that combines with water to produce MPC (III) and free periodate. The complex formation between the Co (III) catalyst and CRBC is thought to be the cause of the fractional order seen in relation to CRBC. Intermediate (A) is formed when an MPC (III) interacts with that complex by releasing the catalyst which further reacts with fresh MPC (III) to produce a new active intermediate (B) in the second step which finally reacts with another fresh MPC (III) resulting in the production of stable products (C) as 2-phenylmalonic acid ($C_9H_8O_4$), as well (D) as 2-(amino (carboxy) methyl)-5, 5-dimethyl-4, 5-dihydrothiazole-4-carboxylic acid-1-oxide ($(C_8H_{12}N_2O_4S)$).

The below mechanism (**Scheme 1**) supports the derivation of the rate law equation [34] for the catalytic oxidation of carbenicillin as-

$$\text{From Scheme 1, rate} = -\mathrm{d}\frac{[\mathrm{CRBC}]}{\mathrm{dt}} = \mathrm{k(Complex)}$$

$$= \mathrm{k\,K_1K_2K_3}\frac{[\mathrm{CRBC}][\mathrm{OH^-}][\mathrm{Co(III)}][\mathrm{DPC}]}{[\mathrm{H_3IO_6}]^{2-}} \qquad \ldots(1)$$



Scheme 1: *Carbenicillin oxidation by DPC (III) and Co (III)*

The total concentration of DPC can be given as

$$[DPC]_T = [DPC]_f + [Cu(H_2IO_6)(H_3IO_6)]^{2-} + [Cu(H_3IO_6)_2(H_2O)_2]^{2-}$$

$$[DPC]_f \left[\frac{K_1K_2[OH^-] + [H_3IO_6]^{2-} + K_1[OH^-][H_3IO_6]^{2-}}{[H_3IO_6]^{2-}}\right]$$

$$[DPC]_f = \left[\frac{[DPC]_T[H_3IO_6]^{2-}}{K_1K_2[OH]^- + [H_3IO_6]^{2-} + K_1[OH^-][H_3IO_6]^{2-}}\right] \quad \ldots(2)$$

Similarly, $[CRBC]_T = [CRBC]_f + [C]$

$= [CRBC]_f + K_3[CRBC]_f[Co(III)] = [CRBC]_f[1 + K_3[Co(III)]$

Here, **'T'** stands for total molarity and **'f'** stands for free molarity of related species.

Owing to quite lower molarities of AMP and $CoCl_3$

$[CRBC]_T = [CRBC]_f$, $[OH^-]_T = [OH^-]_f$ … (3)

$$\text{And } [H_3IO_6^{2-}]_T = [H_3IO_6^{2-}]_f \quad \ldots (4)$$

$$[Co(III)_T] = [[Co(III)_f] + [C]$$

$$= [Co]_f + K_3[CRBC][Co(III)_f]$$

$$[Co(III)]_f = \left[\frac{[Co(III)_T]}{1 + K_3[CRBC]}\right] \quad \ldots. (5)$$

Substituting values of eqⁿ (2), (3), (4), and (5) in eqⁿ (1), we get

$$\text{rate} = -\frac{d[DPC]}{dt}$$

$$= \frac{kK_1K_2K_3\,[CRBC][Co(III)][DPC][OH]}{K_1K_2[OH]^- + [H_3IO_6]^{2-} + K_1[OH]^-[H_3IO_6]^{2-} + K_1K_2K_3[CRBC][OH]^-} \quad \ldots. (6)$$

After rearrangement, we get

$$\frac{1}{k_{obs}} = \frac{[H_3IO_6]^{2-}}{kK_1K_2K_3[OH]^-[CRBC]} + \frac{[H_3IO_6]^{2-}}{kK_2K_3[CRBC]} + \frac{1}{kK_3[CRBC]} + \frac{1}{k} \quad \ldots (7)$$

Verification plots

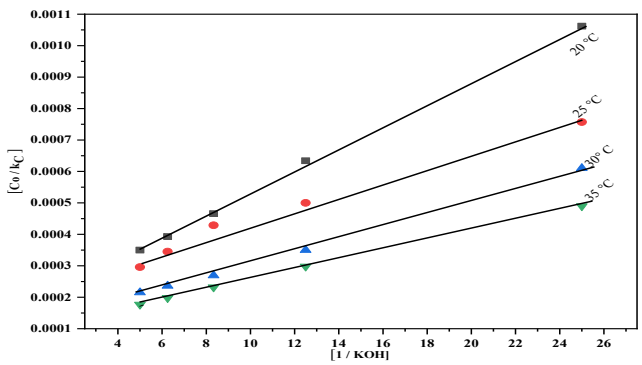


Figure 12: *Plot of 1/[KOH] vs. [Co/k_c]*

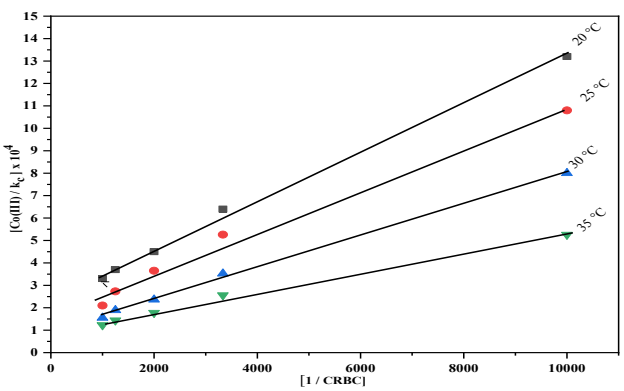


Figure 13: *Plot of 1/[CRBC] vs. [Co/k_c]*

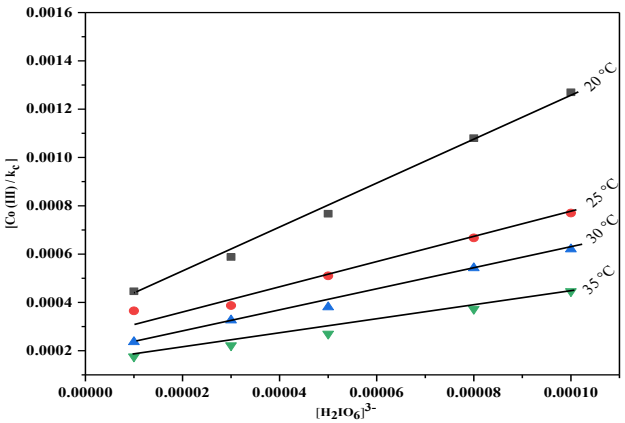


Figure 14: *Plot of $[H_2IO_6]^{3-}$ vs. [Co/k_c]*

The verification plots are shown above in Figures (12, 13, and 14). In accordance with equation (7), the plots of [Co (III)/k_c] vs.1/[KOH] ($r \geq 0.9996, \leq s\ 0.0012$), [Co (III)/$k_c$] vs. 1/[CRBC] ($r \geq 0.998, \leq s\ 0.0085$), and [Co (III)/$k_c$] vs. $[H_2IO_6]^{3-}$ ($r \geq 0.997, s \leq 0.0002$), and are found linearly as shown in Figures 12, 13, and 14 respectively.

Table 6: *Slow step rate constant (k) and equilibrium constants for Co (III) catalyzed oxidation of CRBC*

Equilibrium Constants ↓	**Absolute Temperatures**			
Temperature →	20 °C	25 °C	30 °C	35 °C
k x 10^4	4.1928	6.1349	10.214	11.033
K_1	1.35	2.168	2.638	3.365
K_2 x 10^{-4}	0.905	1.243	1.39	2.20
K_3 x 10^4	5.470	2.734	2.160	1.934

Table 7: *Thermodynamic Parameters for Co (III) catalyzed Oxidation of CRBC*

Thermodynamic Quantities	**Values from K_1**	**Values from K_2**	**Values from K_3**
ΔH°_{298} (k J mol^{-1})	44.41	41.9	-50.91
ΔS°_{298} (J K^{-1} mol^{-1})	154.59	161.24	-103.17
ΔG°_{298} (k J mol^{-1})	-1.66	-6.15	-20.16

Conclusions

Experimental research was completed in an alkaline media on the carbenicillin by DPC (III) that was accelerated by Co (III). For the title study, MPC (III) was confirmed as the primary active species in the form of [Cu (H_2IO_6) (H_2O) $_2$]. Different activation parameters were calculated by using the software Origin 9.6 (2017). Similar to that,

equilibrium constants were determined at various four temperatures and thermodynamic characteristics pertaining to equilibrium constants were also calculated. A comparison between the uncatalyzed and catalyzed oxidation of Carbenicillin showed an overall increment in the rate of Carbenicillin oxidation, in addition to a major increment in numerous rate constants as well as equilibrium constants ($\mathbf{K_1}$, and $\mathbf{K_2}$) while the third equilibrium constant ($\mathbf{K_3}$) showed a slight decrement. Values of thermodynamic parameters increased overall. The values obtained for activation parameters for both the uncatalyzed as well as catalyzed oxidation of Carbenicillin were slightly increased. All experimental evidence, including the results of products, spectral and elemental analysis, mechanism, reaction order plot, and kinetic studies, support and confirm the certainty of overall sequences presented here.

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REFERENCES

[1] G. D. Wright, The antibiotic resistome: the nexus of chemical and genetic diversity, *Nat. Rev. Microbiol.,* 2007, 5, 175-186. (DOI: 10.1038/nrmicro1614)

[2] M. Golchin, M. Khani, M. Sadani, M. Sadeghi, & M. Jahangiri-rad,Occurrence and Fate of Amoxicillin and Penicillin G Antibiotics in Hospital Wastewater Treatment Plants: A Case Study -Gonbad Kavous, Iran, *South African Journal of Chemistry*, 2021, 75, 98-105. (https://doi.org/10.17159/0379-4350/2021/v75a11)

[3] Z. Wang, Xi-Hui Zhang, Y. Huang, & H. Wang, Comprehensive evaluation of pharmaceuticals and personal care products (PPCPs) in typical highly urbanized regions across China, *Environmental Pollution*, 2015, 204, 223-232, ISSN 0269-7491, (DOI: 10.1016/j.envpol.2015.04.021)

[4] D. Fatta-Kasiiinsons, S. Meric, and A. Nikolaun, Pharmaceutical residues in environmental waters and wastewater: current state of knowledge and future research. *Anal Biocanal. Chem*, 2011, 399, 251-275. (DOI: 10.1017/s00216-010-4300-9)

[5] M. Zhuang, Y. Achmon, Y. Cao, X. Liang, L. Chen, H. Wang, B. A. Siame, & K. Y. Leung, Distribution of antibiotic resistance genes in the environment, *Environmental Pollution,* 2021, 285,117402. (DOI: 10.1016/j.envpol.2021.117402)

[6] M. Haenni, C. Dagot, O. Chesneau, D. Bibbal, J. Labanowski, M. Vialette, D. Bouchard, F. Martin-Laurent, L. Calsat, S. Nazaret, F. Petit, A. M. Pourcher, A. Togola, M. Bachelot, E. Topp, & D. Hocquet, Environmental contamination in a high-income country (France) by antibiotics, antibiotic-resistant bacteria, and antibiotic resistance genes: Status and possible causes. *Environ Int*., 2022. (DOI: 10.1016/j.envint.2021.107047)

[7] A. Booth, D. S. Aga, & A. L. Wester, Retrospective analysis of the global antibiotic residues that exceed the predicted no effect concentration for antimicrobial resistance in various environmental matrices, *Environ Int*., 2020. (DOI: 10.1016/j.envint.2020.105796)

[8] A. R. Bracamontes-Ruelas, L. A. Ordaz-Díaz. A. M. Bailón-Salas, J. C. Ríos-Saucedo, Y. Reyes-Vidal, & L. Reynoso-Cuevas, Emerging Pollutants in Wastewater, Advanced Oxidation Processes as an Alternative Treatment and Perspectives, *Processes*, 2022, 10, 1041. (DOI: 10.3390/pr10051041)

[9] R. Andreozzi, R. Marotta, & N. Paxeus, Antibiotic Removal from Wastewaters: The Ozonation of Amoxicillin, *Journal of hazardous materials*, 2005, 122, 243-250. (DOI: 10.1016/j.jhazmat.2005.03.00)

[10] P. P. Marcinowski, J. P. Bogacki, and J. H. Naumczyk, Cosmetic wastewater treatment using the Fenton, Photo-Fenton and H_2O_2/UV processes, *Journal of Environmental Science and Health, Part A*, 2014,49(13):1531–1541. (DOI: 10.1080/10934529.2014.938530)

[11] E. L. Chang, C. Simmers, & D. A. Knight, Cobalt Complexes as Antiviral and Antibacterial Agents. *Pharmaceuticals*, 2010, 3 (6), 1711–1728. (DOI: 10.3390/ph3061711)

[12] C. V. Hiremath, S. D. Kulkarni, and S. T. Nandibewoor, Oxidation of-Leucine by Alkaline Diperiodatoargentate (III) Deamination and Decarboxylation: A Kinetic and Mechanistic Study, *Industrial & Engineering Chemistry Research,* 2006, 45 (24), 8029–8035. (DOI: 10.1021/ie060612d)

[13] A. M. Angadi, & S. Tuwar, Oxidation of Fursemide by Diperiodatocuprate (III) in Aqueous Alkaline Medium—a Kinetic Study, *Journal of Solution Chemistry*, 2010, 39, 165-177. (DOI: 10.1007/s10953-009-9492-2)

[14] A] J. I. Gowda, R. M. Hansabaratti, Nandini A. Paattanash, & S. T. Nandibewoor, Oxidation of glycine by Diperiodatocuprate (III) in aqueous alkaline medium, *Indian Journal of Chemistry*, 2013, 52, 200-206.

[14] B] Z. Ahmad, M. Asghar, S. Ali, N. Munawar, A. Nabi, & M. Yaqoob, Flow Injection Determination of Asparagine and Histidine Using Diperiodatocuperate Based on Spectrophotometric Inhibition Detection in Amino Acid Supplements, *Indo Am. J. P. Sci*., 2017; 4(11). ISSN: 2349-7750. (DOI: 10.5281/zenodo.1048813)

[15] S. A. Chimatadar, T. Basavaraj, and S. T. Nandibewoor, A study of the kinetics and mechanism of oxidation of L-tryptophan by diperiodatonickelate (IV) in aqueous alkaline medium, *Russ. J. Phys. Chem*, 2007, 81, 1046–1053. (DOI: 10.1134/S0036024407070072)

[16] M. W. Lister. The stability of some complexes of trivalent copper*, Canadian Journal of Chemistry*, 1953; 31(7):638-652. (DOI: 10.1139/v53-087)

[17] S. Nadimpalli, J. Padmavathy, & K. K. M. Yusuff, Determination of the nature of the diperiodatocuprate (III) species I aqueous alkaline medium through a kinetic and mechanistic study on the oxidation of iodide ions*, Transition Metal Chemistry*, 2001, 26 (3): 315-321. (DOI: 10.1023/A:1007116932047)

[18] B. Chowdhury, M. H. Mondal, M. K. Barman, and B. Saha, A study on the synthesis of alkaline Copper (III) periodate (DPC) complex with an overview of its redox behavior in aqueous micellar media, *Research on Chemical Intermediates (Springer*), 2018. (DOI: 10.1007/S11164-018-3643-2)

[19] C. B. Smith, & M. Finland, Carbenicillin: Activity in vitro and absorption and excretion in normal young men, *Applied Microbiology*, 1968, 16, 1753-1760, American Society for Microbiology.

[20] K. Butler, A. R. English, V. A. Ray, & A. E. Timereck, Carbenicillin: Chemistry and mode of action*, The Journal of Infectious Diseases,* 1970, *122, (issue supplement 1), S1-S8.* (DOI: 10.1093/infdis/122.Supplement_1.S1)

[21] A. R. English, J. A. Retsema, V. A. Ray, & J. E. Lynch, Carbenicillin Indanyl Sodium, An Orally Active Derivative Of Carbenicillin, *Antimicrobial Agents And Chemotherapy*, 1972, 1(3), 185-191. American Society for Microbiology.

[22] J. T. da Silva, & S. Fukai, The impact of carbenicillin, cefotaxime, and vancomycin on chrysanthemum and tobacco TCL morphogenesis and Agrobacterium growth, *J. Appl. Hort*., 2001, 3. (DOI: 10.37855/jah.2001.v03i01.01)

[23] K. Marta, F. Rafal, & F. Magdalena, Hydrolysis of Penicillin G and Carbenicillin in Pure Water - As Studied by HPLC/ESI-MS, *Mass Spectrometry Letters*, 201910, 4, 108-111. (DOI: 10.5478/MSL.2019.10.4.108)

[24] T. C. Eickhoff, In vitro effects of carbenicillin combined with gentamycin or polymyxin B against Pseudomonas aeruginosa, *Appl Microbiol*, 1969, 18 (3), 469-473. PMID: 4313764; PMCID: PMC378006

[25] M. I. Marks, R. Prentice, R. Swarson, E. K. Cotton, & T. C. Eickhoff, Carbenicillin and gentamicin: Pharmacologic studies in patients with cystic fibrosis and pseudomonas pulmonary infections, *The Journal of Paediatrics,* 1971, 79, 5, 822-828, 1971. (DOI: 10.1016/S0022-3476(71)80401-8)

[26] H. A. Holt, J. M. Broughall, M. McCarthy, and D. S. Reeves, Interactions between Aminoglycoside Antibiotics and Carbenicillin or Ticarcillin, *Infection*, 1976, 4 (2), 107–109. (DOI: 10.1007/BF01638726)

[27] B. Lynn, Administration of carbenicillin and ticarcillin-pharmaceutical aspects, *European Journal of Cancer* (1965), 1973, 9 (6), 425-433. (DOI: 10.1016/0014-2964 (73)90107-2)

[28] N. Rosdahl, & V. F. Thomsen, Activity of carbenicillin against gram negative rods compared with that of penicillin, ampicillin, and cephalosporins, *Chemotherapy*, 1970, 15, 137-147. (DOI: 10.1159/000220677)

[29] Y. R. Sahu, & P. Mishra, Kinetics and Mechanism of Oxidation of Carbenicillin by Copper (III) Periodate Complex in Aqueous Alkaline Medium, *Journal of Chemistry (Hindawi*), 2020, Article ID 4060984, 13 pages. (DOI: 10.1155 2020 4060984)

[30] G. P. Panigrahi & P. K. Misro, Kinetics and mechanism of oxidation of osmium (VIII) catalyzed oxidation of unsaturated acids by sodium periodates, *Indian Journal of Chemistry*, 1977, 15A,1066–1069.

[31] P. K. Jaiswal, & K. L. Yadava, Determination of sugars and organic acids with periodato complex of Cu (III), *Indian Journal of Chemistry*, 1973, 11, 837-838.

[32] G. P. Panigrahi, & A. C. Pathy, Kinetics and mechanism of oxidation of potassium thiocyanate by the Potassium Bis(tellurato)cuprate (III), *Indian Journal of Chemistry*, 1986, 25A, 354-357.

[33] K. C. Ingham, On the application of Job's method of continuous variation to the stoichiometry of protein-ligand complexes, *Analytical Biochemistry*, 1975, 68 (2), 660–663. (DOI: 10.1016/0003-2697 (75)90666-1)

[34] A] L. Michaelis, & M. Menten, Die kinetik der invertinwirkung, *Biochemistry Zeitung,* 1913, 79, 333-369.

[34] B] B. Srinivasan, A Guide to the Michaelis-Menten equation: Steady state and beyond, *The FEBS Journal*. 289, 20, 6086–6098. (DOI: 10.1111/febs.16124)