Available online at **www.joac.info**

ISSN: 2278-1862

Journal of Applicable Chemistry

2021, 10 (1): 22-34

(International Peer Reviewed Journal)

A thermodynamic and Comparative Study of Pharmaceutical Drug (Paracetamol) by Ir(III) and Pd(II) Catalyzed Oxidation in Acidic Medium ($HClO_4$): Kinetic Model

Reena Patel[1], Shailesh Kumar[1], Arvind Kumar Pandey[2] and Sheila Srivastava[3]*

1 Department of Applied Chemistry B.B.A.U. Lucknow, U.P., **INDIA**

2. Department of Chemistry University of Allahabad, U.P., **INDIA**

3. Department of Chemistry Feroze Gandhi College, Raebareli, U.P., **INDIA**

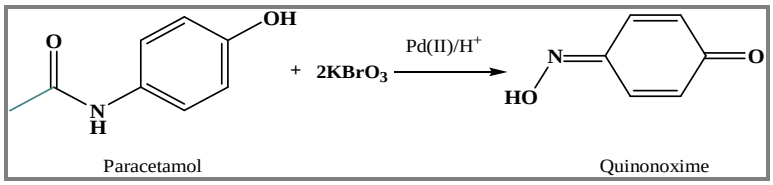
Email: she_ila72@yahoo.com

Accepted on 5th January, 2021

ABSTRACT

A comparative study of Pharmaceutical drug (Paracetamol) by Ir(III) and Pd(II) catalysed oxidation in acidic medium ($HClO_4$] at 35℃ to 45℃. The reaction is carried out in the presence of mercuric acetate as a scavenger for bromide ion. 1-carboxy cyclohexane l-acetic acid was obtained as the oxidation product and identified chromatographically. The rate law followed a first order and zero order dependence with respect to $KBrO_3$ and potassium chloride respectively. The reaction followed first order with respect to Ir(III) and Pd(II) chloride. Negligible effect of [$Hg(OAc)_2$] and ionic strength of the medium was observed. The rate of reaction decreased with increasing [H^+] was observed for the oxidation of paracetamol. Rate of reaction exhibits fractional positive order kinetics with respect to Paracetamol. The values of rate constants observed at different temperatures (30 to 45℃) were utilized to calculate the activation parameters. Quinoneoxime and acetic acid have been identified as main oxidation products of the reactions. Feasible mechanism is proposed which are be composed with the kinetics, Stoichiometry and product of the reaction. The rate law has been derived from obtained kinetic data.

Graphical Abstract



Keywords: Kinetics, Ir(III) chloride, Pd(II) chloride oxidation, Paracetamol, Potassium bromate, Acidic medium.

INTRODUCTION

The transition metal catalysed reactions are important for the chemical industry from both practical and economic point of view. Transition metal ions are found to be good catalysts and their complexes

are also able to catalyse a wide variety of reactions like hydrogenation, oxidation and polymerization. The applications of transition metal catalyst such as Ru(III) [**1, 2**], Rh(III) [**3, 4**], Cu(II) [**5, 6**], and Pd(II) [**7, 8**] in kinetic studies of redox reaction involving organic substrate are reported in literature. It was found that these catalysts work efficiently in both acidic and alkaline media. The use of Ir(III) chloride as a non-toxic and homogeneous catalyst has been reported [**9-11**]. The reaction path depends not only upon the nature of the oxidant and the nature of the substrates but also upon the ways in which reactive species of transition metal ion forms complex with the reactant molecules before changing into final products under experimental conditions. Oxidant such as NBS [**13, 14**], NBA [**14, 15**], periodate [**16, 17**], and iodate [**18, 19**], have been successfully utilized in kinetic and mechanistic investigations of various organic substrate. Amongst various inorganic oxidants, iodate has been used as an oxidant in the uncatalyzed oxidation of oxalic acid [**20**], acetophenone [**21**], and benzaldehyde [**22**]. Singh *et al* [**23-26**] have introduced various reports in the literature regarding the oxidation of reducing sugars involving Ir(III) as homogeneous catalyst. Potassium bromate is known to be a powerful oxidizing agent with redox potential 1.44 volts and has been used widely in the oxidation of several organic substrates [**27**]. Potassium bromate is used for oxidation of uncatalyzed reactions by several workers [**28, 29**]. Uncatalyzed reactions of aldoses and aldosamines [**30**], carbohydrates [**31**] compound oxidation by potassium bromate have also been reported. Ir(III) catalysed cyclic alcohols [**32**], cyclic ketones [**33**] oxidation by potassium bromate has also been reported. Comparatively Ir(III) catalysed oxidation has been dealt than other catalyst and scant attention has been paid with potassium bromate as an oxidant. The kinetics of paracetamol (PAM) oxidation has been studied both spectrophotometrically and iodometrically. Spectrophotometric determination of paracetamol in drug formulation has been a subject of several investigators [**34-42**]. It is antipyretic and analgesic compound of high therapeutic value [**43, 44**]. It is also used as an intermediate for pharmaceutical (as a precursor in penicillin) and azo dye [**45-47**]. Oxidation reactions are important in the synthesis of organic compounds, create new functional groups or modify existing functional groups in a molecule [**48, 49**]. Various advanced oxidation processes such as electrochemical [**50-52**] ozonation and H_2O_2/UV oxidation [**53-56**] have been employed to remove aqueous paracetamol. Several authors have performed studies using Pd(II) because of the commercial importance of reactions catalysed by Pd(II). The kinetics for the oxidation of ethylene by aqueous Pd (II) is an example [**57, 58**]. In this study the effect of chloride ion on the reaction rate was studied in order to establish the active species of the catalyst. Generally the mechanism of catalysis depends on the nature of the substrate, the oxidant, and other experimental conditions [**59, 60**]. In most of the catalytic studies for organic transformations, the nature of active form of Pd(II) remain obscure. The kinetic methods of analysis are highly sensitive, selective, simple, accurate, and less expensive. The present study examines, in detail the kinetic and mechanistic aspects of the Ir(III) catalysed oxidation of paracetamol by $KBrO_3$ in acidic media with the following objective. In this paper it has been tried to consolidate the various work done on the well-known drug that finds extensive application in pharmaceutical industries in the last few decades. In most of the catalytic studies for organic transformations, the nature of active form of Pd(II) remain obscure. The kinetic methods of analysis are highly sensitive, selective, simple, accurate, and less expensive. In recent years, several kinetic Paracetamol (4-hydroxyacetanilide or acetmidophenol) is a well-known drug that is having extensive application in pharmaceutical industries. The present study examines, in detail the kinetic and mechanistic aspects of the Ir(III)/ Pd(II) catalysed oxidation of paracetamol by $KBrO_3$ in acidic media.

MATERIALS AND METHODS

Materials: Aqueous solution of Paracetamol (CDH), potassium bromate (S.D. Fine A.R.) and mercuric acetate (E. Merck) were prepared by dissolving the weighed amount of sample in triple distilled water. Perchloric acid (60% E. Merck) was used as a source of hydrogen ions. Iridium (III) chloride and palladium chloride (Johnson Matthey) was prepared by dissolving the sample in hydrochloric acid of known strength. All other reagents of analytical grade were available. Sodium perchlorate (E. Merck) was used to maintain the ionic strength of the medium. The reaction stills were blackened from outside to prevent photochemical effect.

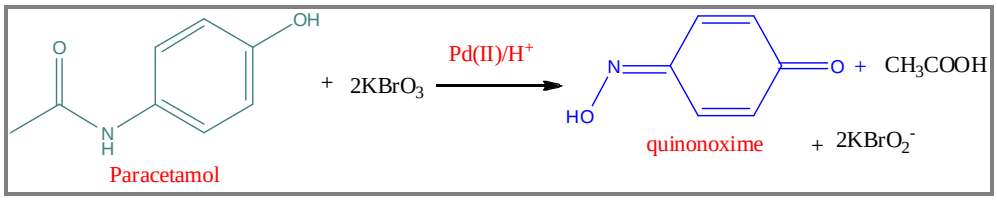
Table1. Effect of variation of oxidant, substrate, catalyst at 35°C

[Oxidant] x 10^3M (Potassium bromated)	[Substrate]x 10^2M (Paracetamol)	[Pd(II) / Ir(III)] x 10^5M	(-dc/dt)x10^7ML^{-1}s^{-1}	
			Pd(II)	Ir(III)
0.80	1.00	11.2	1.92	4.30
1.00	1.00	11.2	2.60	5.20
1.25	1.00	11.2	2.82	6.45
1.69	1.00	11.2	3.81	8.65
2.50	1.00	11.2	5.32	12.80
5.00	1.00	11.2	10.60	25.50
1.00	0.40	11.2	1.32	3.80
1.00	0.50	11.2	1.60	4.30
1.00	0.66	11.2	2.10	4.62
1.00	1.00	11.2	2.60	5.20
1.00	2.00	11.2	4.25	6.65
1.00	4.00	11.2	6.20	8.25
1.00	1.00	5.60	1.33	2.56
1.00	1.00	11.2	2.60	5.20
1.00	1.00	16.8	4.60	10.30
1.00	1.00	22.4	5.18	15.32
1.00	1.00	33.6	8.35	20.40
1.00	1.00	44.8	**10.21**	25.90

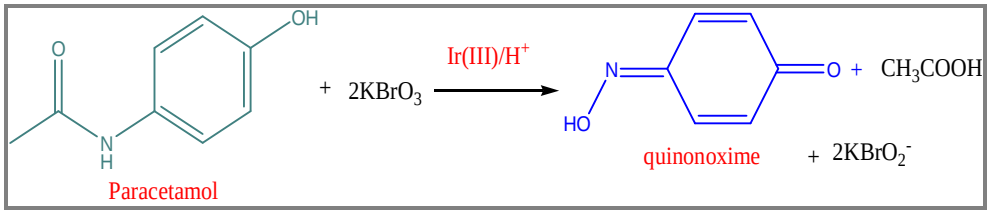
Solution Condition: $[HClO_4]$ = 1.00 X 10 $^{-3}$ M, [KCl] = 1.00 X 10 $^{-3}$ M, $[Hg(OAC)_2]$ = 1.25 X 10 $^{-3}$ M.

Kinetic Procedure: A thermostated water bath was used to maintain the desired temperature within ± 0.1°C. Calculated amount of the reactants i.e. paracetamol, perchloric acid, mercuric acetate, Ir (III)/Pd(II) chloride, KCl and water, except potassium bromate were taken in a reaction vessel which was kept in a thermostatic water bath. After allowing sufficient time to attain the temperature of the experiment, requisite amount of potassium bromate solution, also thermostated at the same temperature was rapidly pipetted out and run into the reaction vessel. The total volume of reaction mixture was 50 mL in each case. Aliquots (5 mL) of the reaction mixture were pipetted out at regular intervals of time and poured in to a conical flask containing 5 mL of 4 % KI solution and 5 mL of dilute sulfuric acid. The liberated bromine equivalent to consumed oxidant was estimated with standard sodium thiosulphate solution using starch as an indicator. The rate of reaction (-dc/dt) was determined from the slope of the tangent drawn at a fixed $[BrO_3^-]$ in each kinetic run. The order of reaction in each reactant was measured with the help of log plot of (-dc/dt) versus concentration of the reactants.

Determination of stoichiometry and product analysis of Pd(II) chloride for the oxidation of paracetamol



Determination of stoichiometry and product analysis of Ir(III) chloride for the oxidation of paracetamol



Different sets of the reaction mixture containing Paracetamol, Ir(III)/Pd(II) chloride, and $HClO_4$ with excess $KBrO_3$ were equilibrated for 72 h at 303 K. Estimation of unconsumed $KBrO_3$ in each set revealed that for the oxidation of 1 mole of Paracetamol, 2 moles of $KBrO_3$ were consumed. Accordingly, the stoichiometry equation may be expressed as the reaction products were extracted with ether after completion of the reaction (monitored by TLC). Evaporation of the ether layer was followed by column chromatography on silica gel using a gradient elution (from dichloromethane to chloroform). After the initial separation, the products were further purified by recrystallization. Acetic acid and quinine oxime were identified as oxidation products of Paracetamol and $2KBrO_2$ was the reduction product of $KBrO_3$. The quinone oxime was identified by its IR spectrum (1652 cm^{-1}, C=O stretching; 1615 cm-1, C=N stretching of oxime; 3332 cm^{-1}, O-H stretching). Identification was further confirmed by its melting point of 131°C (literature mp 132°C).

Table 2. Effect of variation of perchloric acid ($HClO_4$), potassium chloride(KCl), mercuric acetate [$Hg(Ac)_2$] and sodium per chlorate at 35°C

$[HClO_4]$ x10^3M	[KCl] x 10^3M	$[Hg(OAc)_2]$x 10^3M	$NaClO_4$ x 10^3M	(-dc/dt) x $10^7 ML^{-1}s^{-1}$	
				Pd(II)	Ir(III)
0.83	1.00	1.00	1.00	3.12	5.60
1.00	1.00	1.00	1.00	2.60	5.20
1.25	1.00	1.00	1.00	2.41	4.60
1.67	1.00	1.00	1.00	2.00	4.25
2.50	1.00	1.00	1.00	1.22	3.60
5.00	1.00	1.00	1.00	0.82	2.95
1.00	0.83	1.00	1.00	2.23	4.90
1.00	1.00	1.00	1.00	2.60	5.20
1.00	1.25	1.00	1.00	2.00	4.52
1.00	1.67	1.00	1.00	2.81	5.45
1.00	2.50	1.00	1.00	2.52	5.12
1.00	5.00	1.00	1.00	2.42	4.72
1.00	1.00	0.83	1.00	2.21	4.52
1.00	1.00	1.00	1.00	2.60	4.93
1.00	1.00	1.25	1.00	2.60	5.20
1.00	1.00	1.67	1.00	3.00	4.62
1.00	1.00	2.50	1.00	2.42	5.55
1.00	1.00	5.00	1.00	2.51	5.32
1.00	1.00	1.00	0.83	2.00	5.00
1.00	1.00	1.00	1.00	2.60	4.63
1.00	1.00	1.00	1.25	2.00	5.20
1.00	1.00	1.00	1.67	2.22	5.10
1.00	1.00	1.00	2.50	2.10	5.63
1.00	1.00	1.00	5.00	2.00	5.11

Solution Condition: [Oxidant ($KBrO_3$)] = 1.00 X 10^{-3}M, [Paracetamol (PA)] = 1.00 X 10^{-2} M, [Ir (III)and Pd(II) Chloride] = 11.2 X 10^{-5} M.

RESULTS AND DISCUSSION

The kinetic results were collected at several initial concentrations of reactants (Table 3). The initial rate (-dc/dt) in each kinetic run was calculated by the slope of tangent drawn at fixed time for the variation of [$KBrO_3$] while in the variation of other [reactants], tangents drawn at fixed [$KBrO_3$] which was written as [$KBrO_3^*$]. The first order rate constant K_1 was calculated as, K_1= -(dc/dt)[$KBrO_3^*$].

Each kinetic run was studied for two half-lives of the reaction. The observed rates of reaction were reproducible with in ± 5% in replicate kinetic run. The order of reaction in each reactant was determined with the help of log-log plot of (-dc/dt) vs. Concentration of reactant. First order rate constant k_1 i.e. (-dc/dt/$KBrO_3^*$) were calculated from the plots of unconsumed potassium bromate vs. time. The comparative plots of log(-dc/dt) versus log (oxidant) were linear indicating first order dependence on $KBrO_3$ (Figure 1). Insignificant effect on the rate was observed on increasing the concentration of [Cl^-] indicating zero order in [KCl], i.e. potassium chloride (Table 2). The rate of reaction increases as the

concentration of Iridium (III) chloride and Pd(II) chloride is increased, It was observed that values of (-dc/dt) were doubled when the concentration of iridium(III)/Pd(II) was made two times, showing first order dependence on $IrCl_3/PdCl_2$ indicating first order of catalyst i.e. Ir(III) chloride and Pd(II) chloride

Table 3. Activation parameters for Pd(II) / Ir(III) chloride catalyzed oxidation of paracetamol by $KBrO_3$ at 35°C

Parameter	Temperature (T°C)	Paracetamol(-dc/dt)x 10^7	
		Pd(II)	Ir(III)
$k_1 \times 10^4 s^{-1}$	30	1.55	3.70
$k_1 \times 10^4 s^{-1}$	35	2.60	5.20
$k_1 \times 10^4 s^{-1}$	40	3.18	7.35
$k_1 \times 10^4 s^{-1}$	45	5.18	10.12
log A	--	10.80	9.51
ΔE_a^* (k J mol^{-1})	35	60.98	55.25
ΔG^* (k J mol^{-1})	35	74.63	76.12
ΔH^* (k J mol^{-1})	35	71.45	55.52
ΔS^* ($JK^{-1}mol^{-1}$)	35	-10.03	-66.82

(Table 1) and comparative graph (Figure 3). Kinetic result obtained on varying concentrations of substrate indicates fractional positive order of paracetamol, which implies that rate of reaction increases when the concentration of [PA] is increased with both catalyst (Table 1) and (Figure 2) .With increasing the concentration of $[H^+]$, the value of reaction rate decreases for both catalyst (Table 2) and (Figure 4). This shows negative effect of the reaction rate with respect to $[H^+]$ on the rate of oxidation of paracetamol. The rate measurements were taken at 30-45°C and specific rate constants were used to draw a comparative graph plot of log k vs. 1/T which was linear (Figure 5).

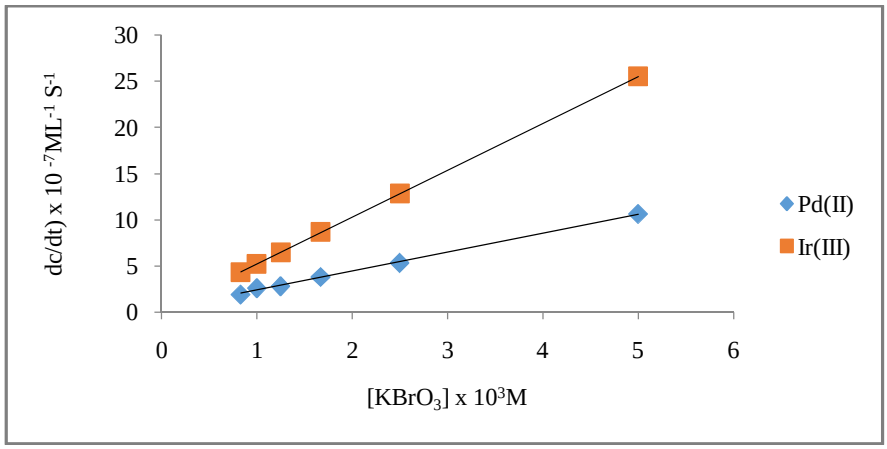


Figure 1. A comparative graph between rate of reaction (-dc/dt) vs $[KBrO_3]$ for the oxidation of paracetamol at 35°C. $[HClO_4]$ = 1.00 x 10^{-3} M, [KCl] = 1.00 x 10^{-3} M, $[Hg(OAc)_2]$ = 1.25 x 10^{-3} M, Paracetamol [PAM] = 1.00 x 10^{-2} M, Pd(II)/Ir(III) Chloride = 11.2 x 10^{-5} M

Role of Entropy of activation and other activation parameters: The value of energy of Activation (ΔEa) Arrhenius factor (A), entropy of activation (ΔS*) and free energy of activation (ΔG*) were calculated from rate measurement at 30°, 35°, 40°, 45°C and these values have been recorded in table 3. Moderate ΔH* and ΔS* values are favourable for electron transfer reaction. The value of ΔH* was due to energy of solution changes in the transition state. The high positive values of change in free energy of activation (ΔG*) indicates highly solvated transition state, while fairly high negative values of change in entropy of activation(ΔS*) suggest the formation of an activated complex with reduction in the degree of freedom of molecule. The observed modest enthalpy of activation and a higher rate constant for the slow step indicates that the oxidation presumably occurs via an inner-sphere mechanism. This conclusion is supported by earlier observations. The high positive values of change

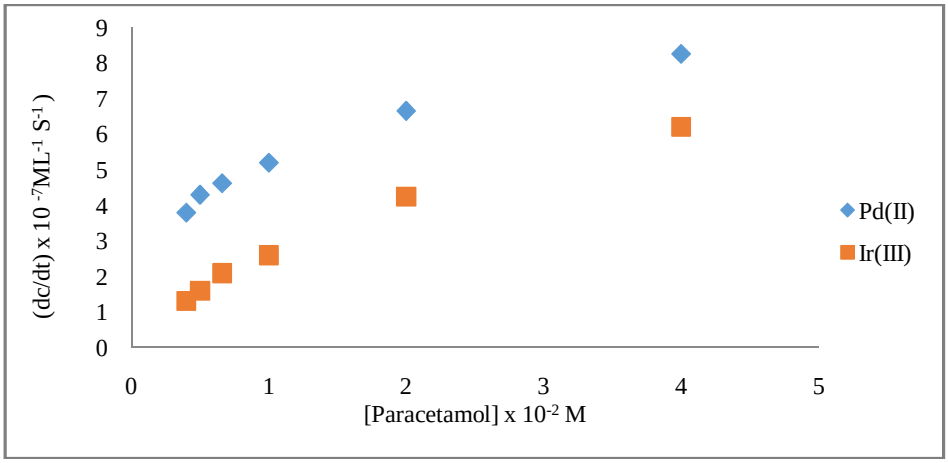


Figure 2. A comparative graph between rate of reaction (-dc/dt) vs [Paracetamol] for the oxidation of paracetamol at 35^{0}C. [$HClO_4$] = 1.00 x 10 $^{-3}$M, [KCl] = 1.00 x 10 $^{-3}$ M, [$Hg(OAc)_2$] = 1.25 x 10 $^{-3}$ M, Paracetamol [Ir(III) / Pd(II)] = 11.20 x 10 $^{-5}$ M, [$KBrO_3$] = 1.00 x 10^{-3} M.

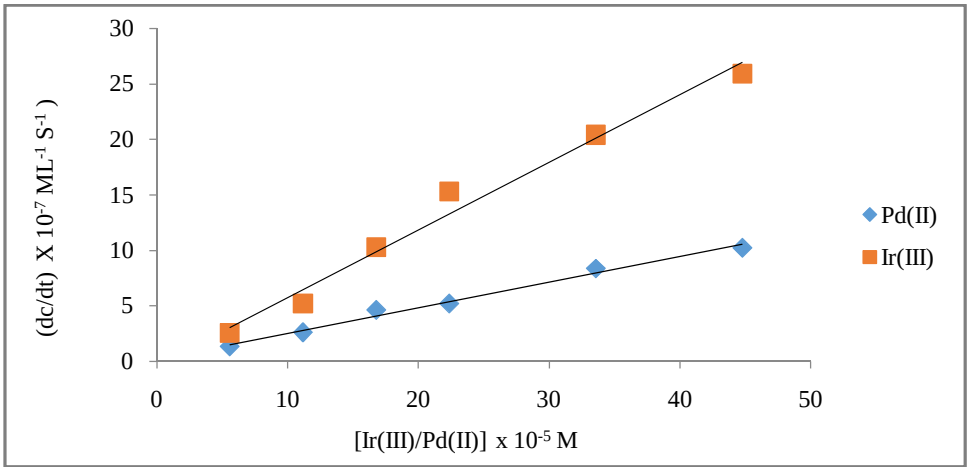


Figure 3. A comparative graph between rate of reaction (-dc/dt) vs [Pd(II)] and [Ir(III)] chloride for the oxidation of paracetamol at 35^{0}C. [$HClO_4$] = 1.00 x 10 $^{-3}$M, [KCl] = 1.00 x 10 $^{-3}$ M, [$Hg(OAc)_2$] = 1.25 x 10 $^{-3}$ M, Paracetamol [PAM] = 1.00 x 10 $^{-2}$ M, [$KBrO_3$] = 1.00 x 10^{-3} M.

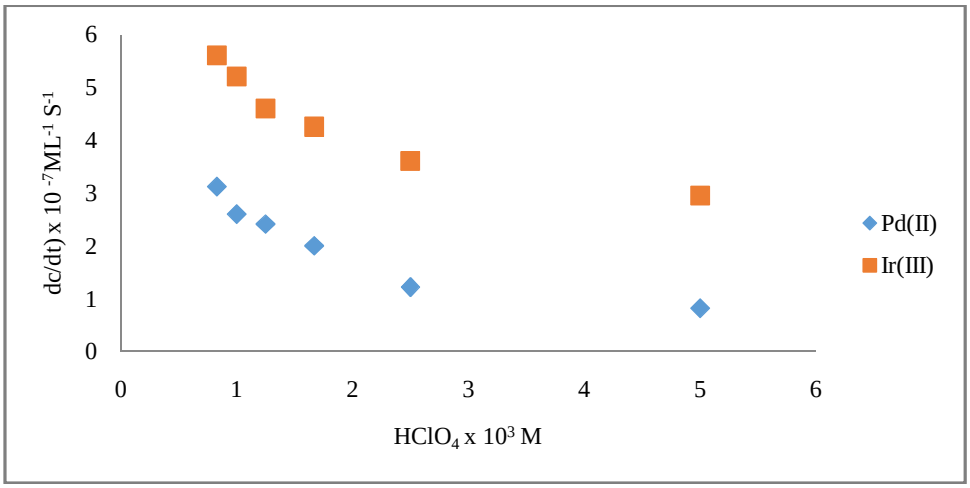


Figure 4. A comparative graph between rate of reaction (-dc/dt) vs [$HClO_4$] for the oxidation of paracetamol at 35^{0}C. [Ir(III)/ [Pd(II)] = 11.20 x 10^{-5}M, [KCl] = 1.00 x 10 $^{-3}$ M, [$Hg(OAc)_2$] = 1.25 x 10 $^{-3}$ M, Paracetamol [PAM] = 1.00 x 10 $^{-2}$ M, [$KBrO_3$] = 1.00 x 10^{-3} M.

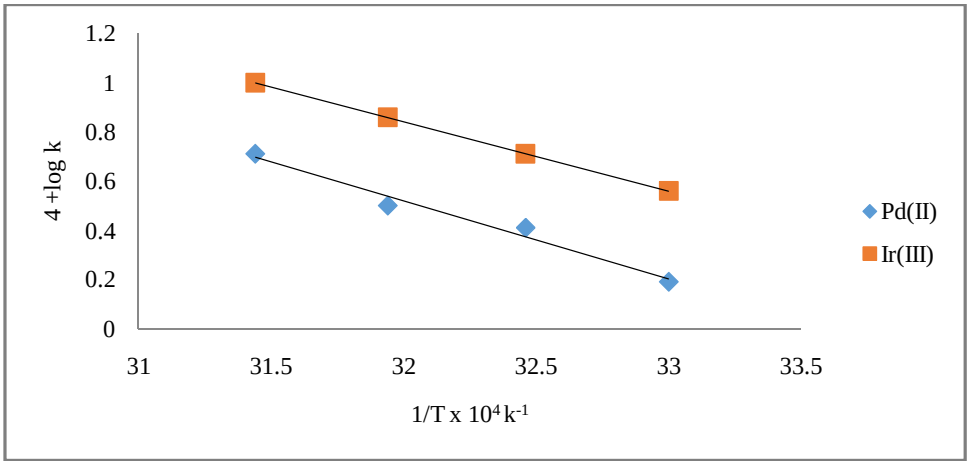
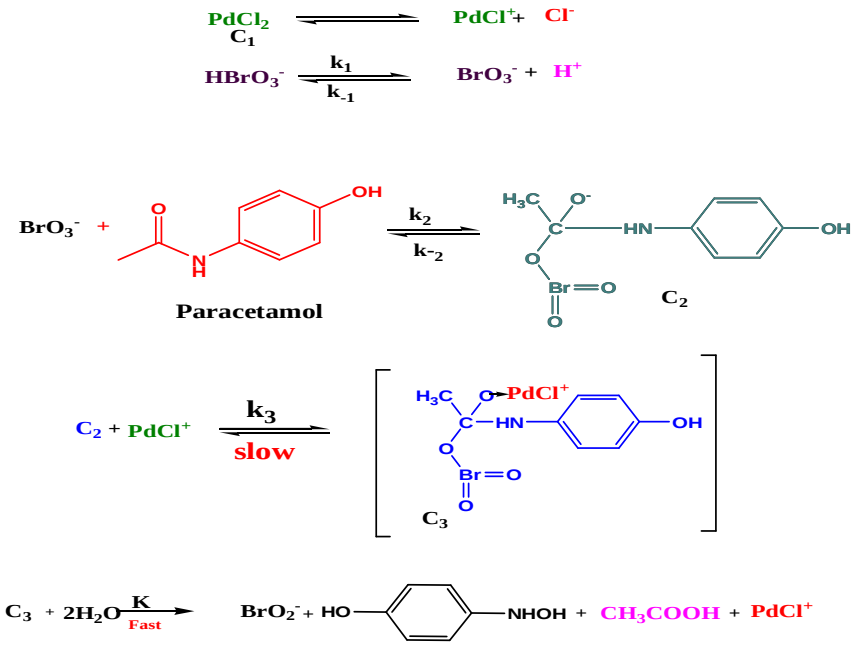


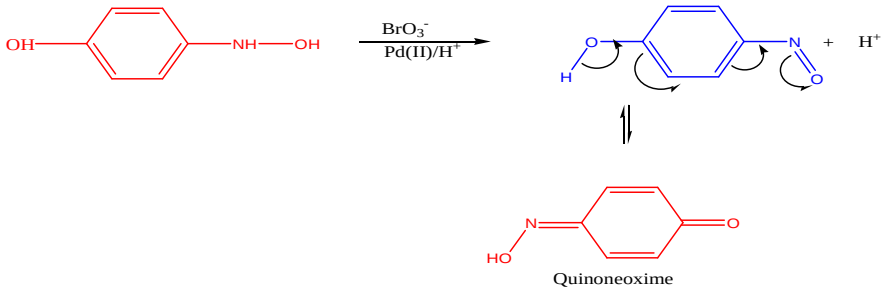
Figure 5. A comparative arrhenius plot of the oxidation of paracetamol on the reaction rate at 35^0C [Pd(II)/ [Ir(III)] Chloride] = 11.2 x 10^{-5} M, [KCl] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M [Oxidant ($KBrO_3$)] = 1.00 x 10^{-3} M, [Paracetamol] = 1.00 x 10^{-2} M, [$HClO_4$] = 1.00 X 10^{-3} M.

in free energy of activation (ΔG*) indicates highly solvated transition state, while fairly high negative values of change in entropy of activation(ΔS*) suggest the formation of an activated complex with reduction in the degree of freedom of molecule [61]. The activation parameters evaluated for the catalysed and uncatalyzed reaction explain the catalytic effect on the reaction. Entropy of activation plays an important role in the case of reaction between ions or between an ion and a neutral molecule or a neutral molecule forming ions. When reaction takes place between two ions of opposite charges, their union will results in a lowering of net charge, and due to this some frozen solvent molecules will released with increase of entropy but on the other hand when reaction takes place between two similarly charged species, the transition state will be more highly charged ion and due to this, more solvent molecules will be required for separate the ions, leading to decrease the entropy.

Mechanism and derivation of rate law: The reaction mechanism involves interaction of $KBrO_3$ with the reactive species of the catalyst to form a complex. The BrO_3^- species has been reported to act as an oxidising agent in acidic as well as in alkaline medium. Pd (II) and Ir(III) chloride has been reported to give a number of possible chloro species dependent on pH of the solution.

Mechanism 1:





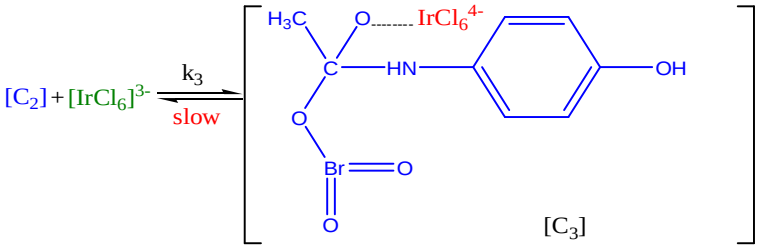
Mechanism 2: It has been already discussed that $[IrCl_6]^{3-}$ is the reactive species of iridium chloride in acidic medium. In view of the reactive species of Ir(III) chloride and $KBrO_3$ and other kinetic features with respect to [Substrate], $[H^+]$, [Hg(II)], $[Cl^-]$ and ionic strength of the medium, the following mechanism steps are proposed. In acidic solution of $KBrO_3$, quick formation of $HBrO_3$ has been reported. Negligible effect of mercuric acetate excludes the possibility of its involvement either as a catalyst or as an oxidant because it does not help the reaction proceed without potassium bromate. Hence the function of mercuric acetate is to act as a scavenger for any $[Br^-]$ ion formed in the reaction. It helps to eliminate the parallel oxidation by Br_2 which would have been formed as a result of interaction between Br^- and bromate ion. Potassium bromate has been used as an oxidant for a variety of compounds in acidic media (Srivastava, S., (1999). sometimes in the presence of a catalyst. In alkaline and acidic medium, potassium bromate is ionised.

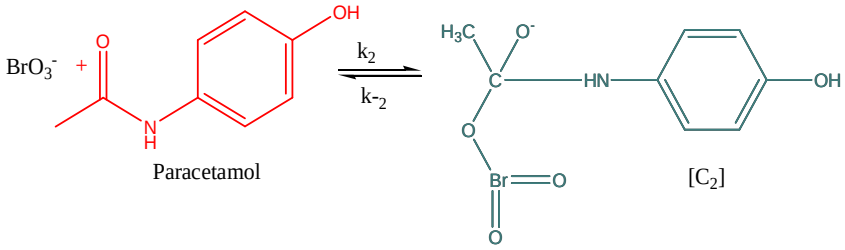
$$KBrO_3 \longrightarrow K^+ + BrO_3^-$$

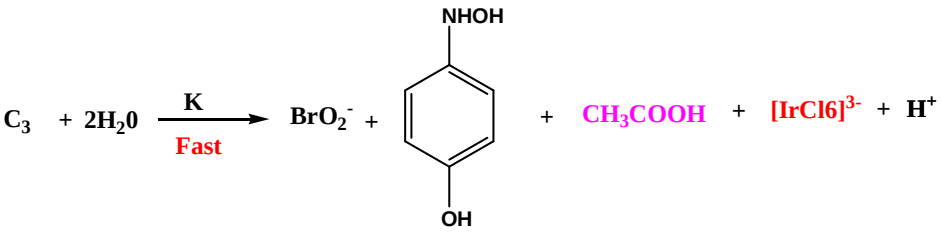
$$[IrCl_5(H_2O)]^{2-} + Cl^- \rightleftharpoons [IrCl_6]^{3-} + H_2O$$

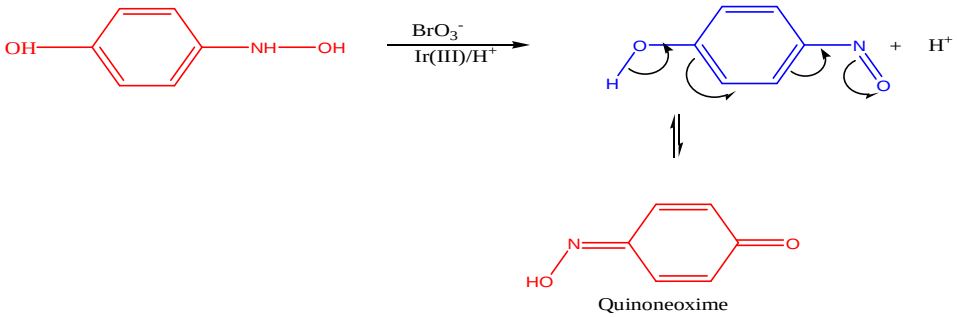
$[C_1]$

$$HBrO_3 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} BrO_3^- + H^+$$









Considering the fact that 1 mole of paracetamol is oxidized by 2 mole of bromate for both catalyst Pd(II) and Ir(III) chloride and applying the steady state treatment, with reasonable approximation, the rate law may be written as equation.

$$\text{rate(R)} = \frac{-\text{d}\,[BrO_3]^-}{dt} = 2\text{k}[C_3] \quad \ldots (1)$$

On the basis of scheme above step (1) to (4) equation 2-5 can be obtained in the following forms respectively as-

$$R = \frac{2k\,K_1K_2K_3[Pd(II)]/\,[Ir(III)]\,[PA][HBrO_3]}{[H]^+} \quad \ldots (2)$$

At any time in the reaction the total concentration of $HBrO_3$ that is $[HBrO_3]_T$ can be expressed as-

$$[HBrO_3]_T = [HBrO_3] + [C_1] + [C_2] + [C_3] \quad \ldots (3)$$

Substitution of the variable of $[C_1]$ $[C_2]$ and $[C_3]$ in equation [3]. Equation [4] is obtained.

$$[HBrO_3] = \frac{[HBrO_3]_T}{[H]^+ + K_1 + K_1K_2[PA] + K_1K_2k_3[Pd(II)]/\,[Ir(III)][PA]} \quad \ldots (4)$$

Substituting the value of $[HBrO_3]$ in equation [2] we obtained the expression equation [5].

$$R = \frac{2k\,K_1K_2K_3[Pd(II)]/[Ir(III)[PA][HBrO_3]_T}{[H]^+ + K_1 + K_1K_2[PA] + K_1K_2K_3[Pd(II)]/[Ir(III)][PA]} \quad \ldots (5)$$

APPLICATION

The present study examines, in detail the kinetic and mechanistic aspects of the Ir(III) catalyzed oxidation of paracetamol by $KBrO_3$ in acidic media with the following objective. In this paper it has been tried to consolidate the various work done on the well-known drug that finds extensive application in pharmaceutical industries in the last few decades. In most of the catalytic studies for organic transformations, the nature of active form of Pd(II) remain obscure. The kinetic methods of analysis are highly sensitive, selective, simple, accurate, and less expensive. In recent years, several kinetic Paracetamol (4-hydroxyacetanilide or acetmidophenol) is a well-known drug that is having extensive application in pharmaceutical industries.

CONCLUSION

The present study examines, in detail the kinetic and mechanistic aspects of the Ir(III) / Pd(II) catalysed oxidation of paracetamol by $KBrO_3$ in acidic media with find the ascertain reactive species

of the catalyst and the oxidant. The deduce rate law consistent with the kinetic results. And identify the oxidation products as well as estimate activation parameters. In additional elucidate the plausible reaction mechanism based on the observed reaction rate law and stoichiometry.

ACKNOWLEDGEMENT

The authors grateful thank to UGC Delhi for provide the financial support and also thank to Department of Chemistry Feroze Gandhi College, Raebareli, UP, India for provide the infrastructure.

REFERENCES

[1]. A. K. Singh, S. Srivastava, R. Srivastava, P. Singh, Studies in kinetics and mechanism of oxidation of d-glucose and d-fructose by alkaline solution of potassium iodate in the presence of Ru(III) as homogeneous catalyst, *J.Mol Catal A: Chem*, 2007, 278, 1(2), 72-81.

[2]. R. V. Hosahalli, K. S. Byadagi, S. Nandibewoor, S. A. Chimatadar, Kinetics and mechanism of ruthenium (III) catalysed oxidation of chloramphenicol-An antibiotic drug by diperiodatocuprate (III) in aqueous alkaline medium, *Kinet Catal*, **2012**, 53(1), 65–74.

[3]. A. K. Singh, R. Srivastava, S. Srivastava, J. Srivastava, S. Rahmani, B. Singh, N-Bromosuccinimide oxidation of maltose and d-galactose using chloro-complex of Rh(III) in its nano-concentration range as homogeneous catalyst: A kinetic and mechanistic study, J *Mol Catal A: Chem*, **2009**, 310, 64-74.

[4]. Singh, Ashok Kumar, Kinetics of oxidation of d (+) melibiose and cellobiose by N-bromoacetamide using a rhodium (III) chloride catalyst, *Transition Metal Chemistry*, 2010, 35(3), 349-355.

[5]. Jian-Mei Li, Xiang-Guang Meng, Chang-Wei Hu, Juan Du, Xian-Cheng Zeng, Oxidation of 4-chlorophenol catalysed by Cu(II) complexes under mild conditions: Kinetics and mechanism, *J. Mol. Catal. A*, **2009**, 299 (1-2), 102-107.

[6]. Veeresh C. Seregar, Chanabasayya V. Hiremath,Sharanappa T. Nandibewoor, Palladium(II) Catalysed Oxidation of L-proline by Heptavalent Manganese in Aqueous Alkaline Medium: A Free Radical Intervention and Decarboxylation, **2006**, 31, 4,541–548.

[7]. B. I. Koli, S. T. Nandibewoor, Kinetics and mechanism of palladium (II) catalysed oxidation of dimethyl sulfoxide by alkaline periodate, *Indian J Chem IJC*, **2009**, 8A(7), 958-963.

[8]. A. K. Singh, S. Yadav, R. Srivastava, J. Srivastava, S. Rahmani, Kinetic and mechanistic investigation of Pd(II)-catalysed and Hg(II)-co-catalysed oxidation of d(+)melibiose by N-bromoacetamide in acidic medium, **2010**, 695(19–20), 2213-2219.

[9]. XIA Yun-Sheng;ZHULiang-Fang;LIGui-Ying;HU Chang-Wei , Direct Oxido-amination of Benzene to Aniline over Nickel-Vanadium Catalysts, *Acta Phys. Chim. Sin.*, **2005**, 21, 1337-1342.

[10]. A. K. Singh, S. Rahmani, B. Singh, R. K. Singh, Singh , Kinetic and Mechanistic Studies of Rh(III)-Catalysed Oxidation of D-Xylose and Sorbose by N-Bromoacetamide in Perchloric Acid Medium, *J. Iran. Chem. Soc.*, **2011**, 8, 622-635.

[11]. A. K. Singh, S. Rahmani, B. Singh, R. K. Singh, Singh ,Mechanism of Ir(III)-catalyzed and Hg(II)-co-catalyzed oxidation of reducing sugars by N-bromoacetamide in acidic medium, *J Phys Org. Chem.*, 17(3), 249-156. Year missed

[12]. W-S., Zhai, Y-Q., Liu, H-M., Lu H-Y., Song. W.Y., Kinetic and mechanism of Ir(III) catalysed oxidation of ethylene glycol by cerium(IV) in sulfuric acid media, *Indian Journal of Chemistry* **2008**, 47 A 1194-1198.

[13]. Kinetic and mechanistic studies of the iridium, (III) catalyzed oxidation of sulphanilic acid by diperiodatocuprate(III) in aqueous alkaline medium, *Reaction Kinetics and Catalysis Letters*, **2008**, 94, 2, 359-366.

[14]. C. N. R. Rao, G. U. Kulkarni, P. J. Thomas, P. Edwards, PSize-dependent chemistry: properties of nanocrystals, *Chemistry–A European Journal*, **2002**, 8(1), 28-35.

[15]. K. N. Mohana, K, R, Ramya ,Ruthenium (III)-catalysed oxidative cleavage of thiamine hydrochloride with N-bromosuccinimide in presence of hydrochloric acid medium: A kinetic and mechanistic approach, **2009**, 302(1–2), 80-85.
[16]. A. Singh, R.Swamini Bala, Jaya Srivastava, Ranju Pradhan, Rupam Yadav, S. Rahmani , Kinetic studies of Rh(III)-catalysed oxidation of pentoxifylline by potassium iodate in alkaline medium, *IJChemTech Research*, **2017**, 10(9), 416-425.
[17]. R. D. Kaushik, M. Kaur, R. Malik, A, Kumar, Studies on manganese (II) catalyzed oxidation of N-methyl aniline by periodate ion, *Int J Chem Sci.*, **2010**, 8, 1379-1388.
[18]. Gupta, Nivedita, Dengue in India, *Indian Journal of Medical Research*, 2012, 136(3), 373-390.
[19]. Singh, Bharat, Singh, Aniruddh Kumar, Singh, Anamika, Mechanistic studies of aquachlororhodium(III) catalysis in potassium iodate oxidation of 1,2-propanediol in acidic medium: A kinetic approach, *IJC-A*, **2011**, 50A(05) 650-657.
[20]. Alice Chanakira, , Edward Chikwana, David H Peyton, Reuben H Simonyi, Oxyhalogen-sulfur chemistry-Kinetics and mechanism of the oxidation of cysteamine by acidic iodate and iodine, *Canadian Journal of Chemistry*, **2006**, 84(1): 49-57
[21]. Ramana P. V. Rao, R. V. Appa, Kinetics and mechanism of oxidation of oxalic acid by iodate in aqueous sulphuric acid medium, *JC-A* 30A, **1991**, 11, 971-97.
[22]. P. Manikyamba, P. R. Rao, E. V. Sundaram., Kinetics and Substituent Effect in the Oxidation of Acetophenones by Acid Iodate in Aqueous Methanol Medium, *Journal of the Indian Chemical Society*, **1983**, 60(7), 652-655.
[23]. Singh, Ashok Kumar, Kinetics and mechanism of the Ir (III)-catalysed oxidation of xylose and maltose by potassium iodate in aqueous alkaline medium, *Carbohydrate research*, **2007**, 342(8) 1078-1090.
[24]. Hashimoto, Shuichi, Mechanism of fluorescence quenching of pyrene with purines in polar media: formation of the pyrene triplet state via exciplex formation, *The Journal of Physical Chemistry*, **1993**, 97(15), 3662-3667.
[25]. A. Brahmaiah, P. Manikyamba, RU (III) Catalyzed Oxidation of Alpha-Hydroxy Acids By Iodate-A Kinetic-Study, *Indian Journal of Chemistry Section A-Inorganic Bio-Inorganic Physical Theoretical & Analytical Chemistry*, **1995**, 34(11), 900-903.
[26]. G. K. Muthakia, Kinetics and Mechanism of Indigo Carmine-Acidic Iodate Reaction. An Indicator Reaction for Catalytic Determination of Ru(II1) Ion, *International Journal of Chemical Kinetics*, **1989**, 21, 519-533
[27]. P. S. Radhakrishnamurti, K. S. Tripathy, Kinetis of OX (Viii) and RU (Iii) Catalyzed Oxidations of Styrene and Stilbene by Acid Iodate." *Ijc Section A-Inor Bio-InorPhy The and Anal Chem.*, **1986**, 25(8), 762-763.
[28]. N. Mathiyalagan, R. Sridharan, Kinetics and mechanism of oxidation of aromatic aldehydes by N-chlorosuccinimide in aqueous acetic acid, *Indian J Chem., A*, **2005**, 44(10), 2044-2047.
[29]. C. Sanjeev Reddy, P. Sunitha Manjari, Kinetics and mechanism of acid bromate oxidation of substituted 4-oxoacids, *Indian J. Chem.*, **2010**, 49A, 418–424.
[30]. B.Akermerk.S.Hasson,Trainman,VgbregAndreas,HeumannJan-ErlingBackvall,Palladium-catalyzed allylic acetylation: an exploratory study of the influence of added acids, *Journal of Organometallic Chemistry*, **1989**, 369(3), 433-444
[31]. Linear free energy relationships near isokinetic temperature. Oxidation of organic sulphides with nicotinium dichromate." *CroaticaChemica Acta*, **2001**, 74(1), 51-59.
[32]. Sheila Srivastava, Rajendra kumar Sharma, Sarika Singh:Kinetics and mechanism of iridium (III) catalyzed oxidation of some cyclic alcohols by potassium bromate in acidic medium. *India Chem. Soc*, **2006**, 83, 282-287
[33]. A. Kumar, Comparative Study of Kinetics of Catalyzed Oxidation of D (+)galactose and lactose by Ruthenium (III) in Alkaline Medium, **2013**, 29(2), 815-821
[34]. Wallace, J. E. Determination of ephedrine and certain related compounds by ultraviolet spectrophotometry, *Analytical chemistry*,**1967**, 39(4), 531-533
[35]. F. M. Plakogiannis, A. M. Saad, Spectrophotometric determination of acetaminophen and dichloralantipyrine in capsules. Journal of pharmaceutical science, **1975**, 64, 1547-1549.

[36]. K. K. Verma, A. K. Gulati, S. Palod, P. Tyagi, Spectrophotometric determination of paracetamol in drug formulations with 2- iodylbenzoate, *The Analyst*, **1984**, 109, 735-737.
[37]. S. M. Sultan, I. Z. Alzamil, A. M. Aziz Alrahman, S. A Altamrah, Y. Asha, Use of cerium (IV) sulphate in pharmaceutical preparations. *The Analyst*, **1986**, 111, 919-921.
[38]. F. A. Mohamed, M. A. Abdallah, S. M. Shammat, Selective Spectrophotometric determination of p-aminophenol and acetaminophen, *Talanta,***1997**, 44, 61-68
[39]. J. F. Van Staden, M. Tsanwani, Dtermination of paracetamol in pharmaceutical formulations using a sequential injection system, Talanta, **2002**, 58, 1095-1101.
[40]. M. Oliva, R. A. Olsina, A.N. Masi, Selective spectrofluorometric method for paracetamol determination through coumarinic compound formation, *Talanta,* **2005**, 66, 229-235.
[41]. M. K. Srivastava, S. Ahmad, D. Singh, I. C. Shukla, Titrimetric determination of dipyrone and paracetamol with potassium hexacyanoferrate (III) in an acidic medium, *The Analyst,***1985**, 110, 735-737.
[42]. Gorle, Ashish Prakash. A way to increase effectiveness of paracetamol drug through transdorsal patch. *International research journal of pharmacy,* **2016**, 7, 30-34.
[43]. A. K. Singh, Negi, Reena. Yokraj Katre, S. P. Singh, V. K. Sharma Mechanistic study of novel oxidation of paracetamol by chloramine-T using micro-amount of chloro-complex of Ir (III) as a homogeneous catalyst, *J. Mol. Catal.* A, **2009**, 302, 36–42.
[44]. Singh, A. K. Negi, Reena. Yokraj Katre, S. P. Singh, V. K. Sharma, Kinetics and mechanism of Ru (III)-catalyzed oxidation of paracetamol by chloramine-T in aqueous acidic medium. *Catal. Lett.*, **2009**, 132, 285–291.
[45]. Yang, Liming. E Yu., Liya, Madhumita B. Ray, Photocatalytic Oxidation of Paracetamol: Dominant Reactants, Intermediates, and Reaction Mechanisms, *Environ. Sci. Technol*, **2009**, 43, 460–465.
[46]. Mulla, R. M. Gurubasavaraj, S. P. Nandibewoor, Kinetics of ruthenium (III)-catalysed oxidation of paracetamol by diperiodatonickelate (IV) in aqueous alkaline medium (stopped flow technique), *Appl. Catal A,* **2006**, 314, 208–215.
[47]. T. S. Kiran, C. V. Hiremath, S. T. Nandibewoor, Kinetic, mechanistic and spectral investigations of ruthenium (III)/osmium (VIII) catalysed oxidation of paracetamol by alkaline diperiodatoargentate (III) (stopped flow technique), *Appl. Catal A*, **2006**, 305, 79–89.
[48]. T. S. Kiran, C. V. Hiremath, D. C. Nandibewoor, Oxidation of N-(4-hydroxyphenyl) acetaminophen (paracetamol) drug by diperiodatocuperate(III) in aqueous alkaline medium by stopped flow technique, Z.*Phys Chem*, **2007**, 221, 501–517.
[49]. M. Hudlicky, Oxidations in Organic Chemistry; ACS Monograph 186; *American Chemical Society: Washington, DC* , **1990**, 838.
[50]. G. A. Russel, E. G. Janzen, A. G. Bemis, E. J. Geels, A. J. Moye, S. Mak, E. T. Strom, Oxidation of Hydrocarbons in Basic Solution in Selective Oxidation Processes; Fields, E. K., Ed.; *American Chemical Society; Washington, DC,* **1965**, 51,112-172.
[51]. Brillas, E. Sire's, I. Arias, C. Cabot, P. L. Centellas, F Rodriguez, R. M. Garrido, J.A. Mineralization of paracetamol in aqueous medium by anodic oxidation with a boron-doped diamond electrode. *Chemosphere,* **2005**, 58, 399–406.
[52]. Sir es, I. Garrido, J. A. Rodr_iguez, R. M. Cabot, P. L. Centellas, F. Arias, C. Brillas, E. Electrochemical degradation of paracetamol from water by catalytic action of Fe2þ, Cu2þ, and UVA light on electro generated hydrogen peroxide, *J. Electrochem. Soc.* **2006**, 153, 1–9.
[53]. Waterston, K. Wang, J. W. J. Bejan, D. Bunce, N. J. Electrochemical waste water treatment: Electro oxidation of acetaminophen, *J. Appl. Electrochem.* **2006**, 36, 227–232.
[54]. Vogna, D. Marotta, R. Napolitano, A. d'Ischia, M. Advanced oxidation chemistry of paracetamol. UV/H2O2 -induced hydroxylation/degradation pathways and 15N-aided inventory of nitrogenous breakdown products, *J. Org. Chem,* **2002**, 67, 6143–6151.
[55]. R. Andreozzi, V. Caprio, R. Marotta, D. Vogna, Paracetamol oxidation from aqueous solutions by means of ozonation and H2O2/Subsystem, *Water Res,* **2003**, 37, 993–1004.

[56]. Skoumal, M. Cabot, Centellas, P. L. F. Arias, C. Rodr_iguez, R. M. Garrido, J. A. Brillas, E. Mineralization of paracetamol by ozonation catalyzed with Fe2þ, Cu2þ and UVA light, *Appl. Catal. B*, **2006**, 66, 228–240.
[57]. Yang, L. M. Yu, L. E. Ray, M. B. Degradation of paracetamol in water using advanced oxidation processes, *Water Res.*, **2008**, 42, 3480–3488.
[58]. Jagadeesh, R. V. Puttaswamy. Ru (III), Os(VIII), Pd(II), and Pt(IV) catalysed oxidation of glycyl glycine by sodium N-chloro ptoluenesulfonamide: Comparative mechanistic aspects and kinetic modelling, *J. Phys. Org. Chem.*, **2008**, 21, 844–858.
[59]. J. Tsuji, Synthetic applications of the palladium-catalyzed oxidation of olefins to ketones, *Synthesis*, **1984**, 05, 369-384.
[60]. Singh, Ashish, S. P. Singh, A. K. Singh, Mechanistic study of palladium(II) catalysed oxidation of crotonic acid by periodate in aqueous perchloric acid medium, *J. Mol. Catal. A*, **2007**, 266: 226–232.
[61]. A. K. Singh, Jain, Bhawana. Negi, Reena. Katre, Yokraj, S. P Singh, Oxidation of valine by N-bromophthalimide in presence of chlorocomplex of Pd(II) as homogenous catalyst: A kinetic and mechanistic study, *Open Catal. J.*, 2**009**, 2, 12–20.
[62]. A. S. Onkar, P. N. Naik, S. D. Gunagi, S. T. Nandibewoor, A. S. Chimatadar, Kinetics and mechanism of oxidation of tyrosine by vanadium (V) in aqueous hydrochloric and ethanoic acid medium, *Ind. J. Chem.*, **2012**, 51A, 1574-1579.