The Kinetics and Mechanistic Study of Ru(III) Catalysed Oxidation of Paracetamol by $KBrO_3$ in Alkaline Medium

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Abstract

The oxidation kinetics of the said compound was studied iodometrically at 313K and the reaction stoichiometry was determined. Oxidation product was identified by spectroscopic techniques. The order of the reaction was studied with respect to each reactant by varying concentration of each, keeping other experimental conditions constant. The effect of variation of other constituents on the rate of reaction was also studied under same experimental condition. The effects of dielectric constant and ionic strength were also investigated, on the reaction rate .Thermodynamics parameters were computed by performing the kinetic run at various temperatures. The reaction kinetics was studied and a suitable mechanism consistent with kinetic results was stabilised and rate law was derived.

Keywords: Kinetics, mechanism, oxidation, Potassium bromate, rate law.

Introduction

Potassium bromate is a versatile oxidizing agent in both acidic and basic media**.** It generally undergoes electron exchange reaction resulting in the formation of Quinoxime. A number of oxidants like N-bromosuccinamide[(1)], Chloramine-T[(2)] and Sodium periodate[(3)] have been used for oxidation of drugs and other compounds but a detailed study revealed that still there is a little information about Ru(III) catalysed oxidation[(4-5)] of drugs with $KBrO_3$ as an oxidant therefore ,we have done a careful study of oxidation of paracetamol by Potassium bromate in basic medium, Well known drugs (Paracetamol) finds extensive applications in pharmaceutical industries. It is a non - steroidalanalgesic, anti-inflammatary and antipyretic agent [(6-7)]. It is used in acute conditions such as Headache, Arthralgia, Myalgia and other cases requiring mild analgesia. It is therefore of interest to investigate the kinetics of its reaction with oxidizing agents. The development of a simple, economical and accurate analytical method for the determination of active ingredients of paracetamol would be useful for many commercial applications and also in investigating the stability of paracetamol in pharmaceutical preparations for quality control [(8-9)].

Experimental

Pharmaceutically pure drug paracetamol complying with purity standard was obtained. Its solution was prepared by dissolving the appropriate amount of sample in double distilled water. The required amount of paracetamol was taken from the stock solution. The stock solution

of potassium bromate ($KBrO_3$) was prepared in double distilled water and its concentration was checked iodometrically [10]. The solution of $KBrO_3$ was kept in block coated flask to avoid photochemical decomposition. All other reagents Ru(III), NaOH, $Hg(OAc)_2$ were of A.R grade[11]. All solutions were prepared in double distilled water. All other reaction vessels were also coated black to avoid any photochemical decompositions. The progress of the reaction was monitored by iodometric estimation of unconsumed oxidant present in the known aliquots of the reaction mixture withdrawn at regular intervals of time. Some kinetics runs were carried out at 313 K [12]. The temperature variation was also done.

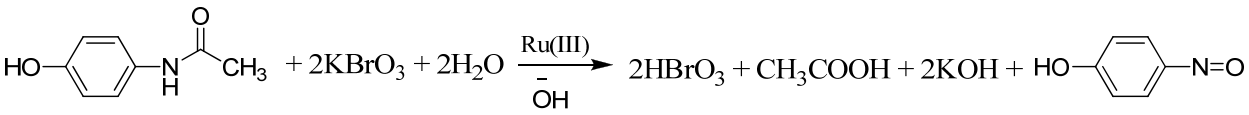
Method

A thermostatic water bath was used to maintain the desired temperature. Aliquots (5ml) of the reaction mixture was pipetted out at regular intervals of time and was poured into a conical flask containing 5ml of 4% KI solution and 5ml of dilute sulphuric acid with a few drops of starch solution as an indicator .The liberated iodine was titrated against standard hypo (sodium thiosulphate) solution[13]. The rate was obtained from the slope of concentration against time graph in the initial stages of the reaction by plane mirror method [14-15].

The stoichiometry of the reaction was determined by equilibrating the reaction mixture containing various ratios of $KBrO_3$and Paracetamolat afixed temperature for 48hrs.The oxidant product was confirmed by UV and IR spectroscopic techniques [16-17].

Stoichiometry Andproduct Analysis:

The reaction mixtures containing a known excess of [$KBrO_3$] over [Paracetamol] were kept in the presence of NaOH and Ruthenium at 25^0C for 48hrs.



The reaction products were extracted with ether. From ether layer the oxidation product was identified as Quinone oxime.

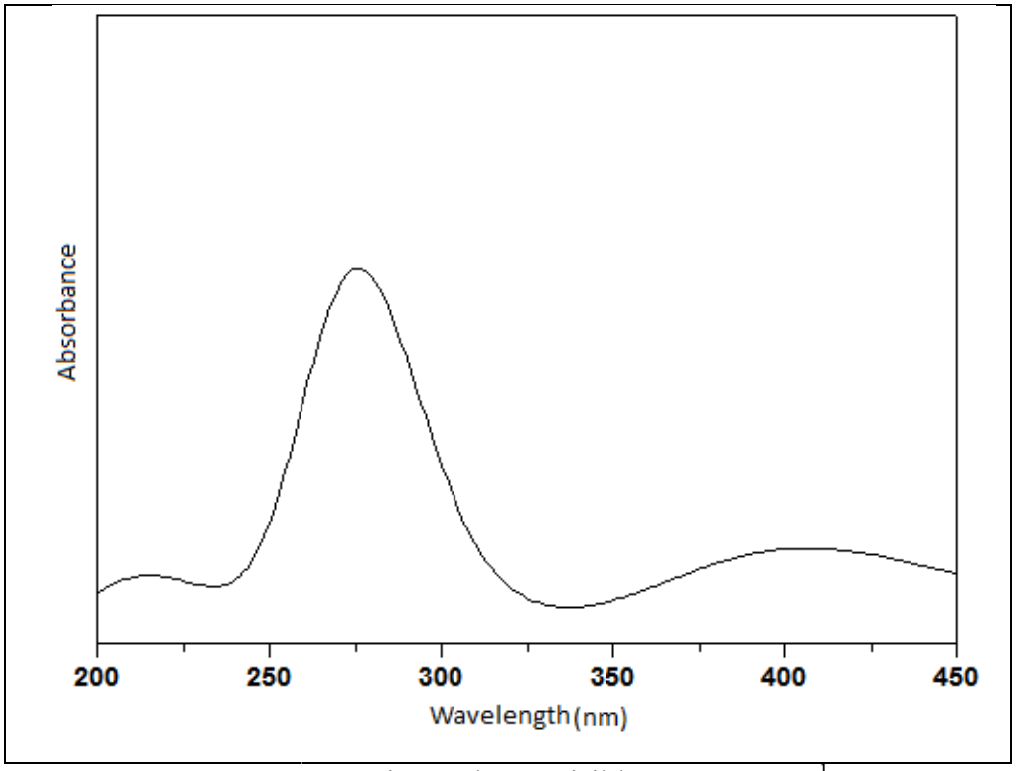
Spectroscopic Measurement

U.V Spectroscopy:

The electronic spectra were measured on a UV-VIS spectrophotometer in the range of 200-450 nm in methanol solutions. The reaction mixture of oxidant and compound in presence of HCI shows the peak observed at 276nm.

FTIR Spectroscopy:

The reaction products were extracted with ether.From the ether layer the oxidation product was identified as quinone oxime.The nature of quinone oxime was confirmed by FTIR(1700 cm^{-1} due to C=O stretching,1580 cm^{-1} due to C=N stretching of oxime, 3200 cm^{-1} due to OH stretching frequency[18-20].



Figurr 1 Experimental UV-Visible spectrum cm^{-1}

Kinetic Results And Discussion:

A suitable mechanism has been derived on the basis of experiments results obtained and from that rate law has been derived as- $-\frac{dc}{dt}[KBrO_3]$, [Ru(III)]

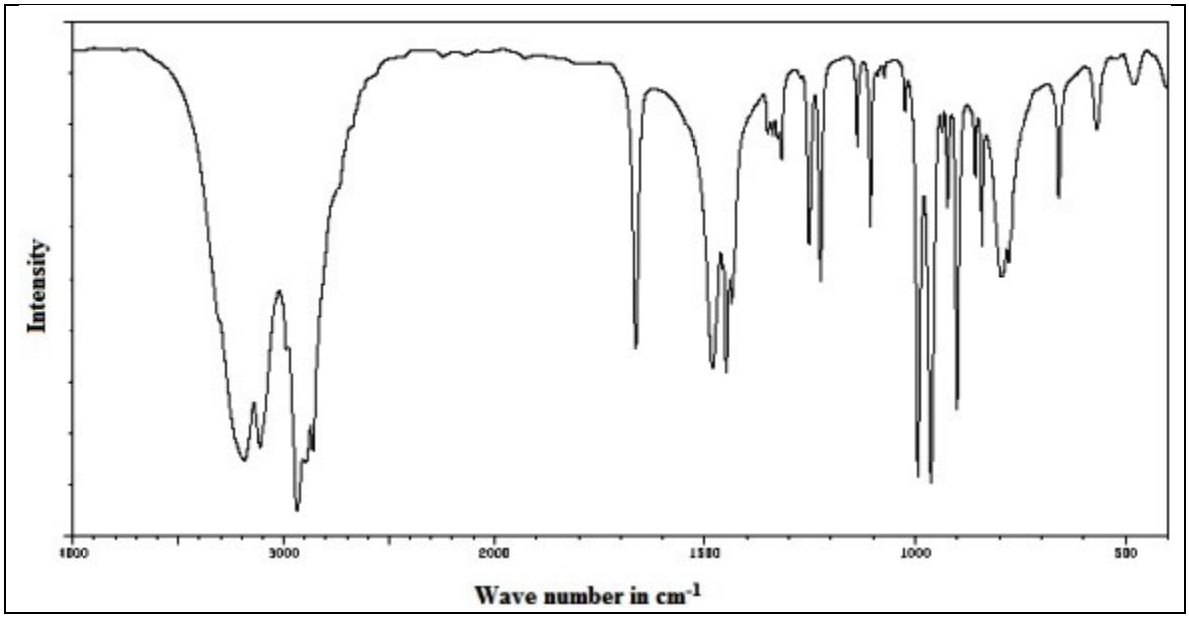


Figure 2 Experimental FTIR spectrum of 4-(hydroxyimino) cyclohexa-2,5-dienone

The oxidation of paracetamol by potassium bromate in presence of Ru(III) as catalyst was studied at the constant temperature at 313K.The first order rate constant remained nearly the same at different concentrations of paracetamol showing zero order dependence. Variation in the perchloric acid concentration did not bring about any significant changes in K values, establishing that the reaction is zero order in H^+. The reaction was marked influenced by increases in Ru(III) concentration, and a linear relationship between $KBrO_3$ and Ru(III) was observed .

Mechanism:

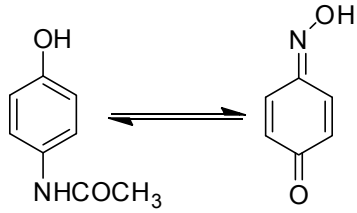
On the basis of the above discussion for the Ru(III) catalysed oxidation of paracetamol by $KBrO_3$ in basic medium. The following reaction steps are suggested.

$$[RuCl_6]^{3-} + H_2O \rightleftharpoons [RuCl_5(H_2O)]^{2-} + Cl^-$$

$$KBrO_3 \rightleftharpoons K^+ + BrO_3^- \quad —(1)$$

$$BrO_3^- \rightleftharpoons HBrO_3 \quad —(2)$$

$$\underset{[R]}{HBrO_3} + [RuCl_5(H_2O)]^{2-} \underset{K_{-1}}{\overset{K_1}{\rightleftharpoons}} \underset{[Q]}{[RuCl_5(H_2O)HBrO_3]^{2-}} \quad —(3)$$

$$\underset{[Q]}{[RuCl_5(H_2O)HBrO_3]^{2-}} + \underset{[P]}{\text{  }} + [BrO_3^-] + [RuCl_5(H_2O)]^{2-} \quad —(4)$$

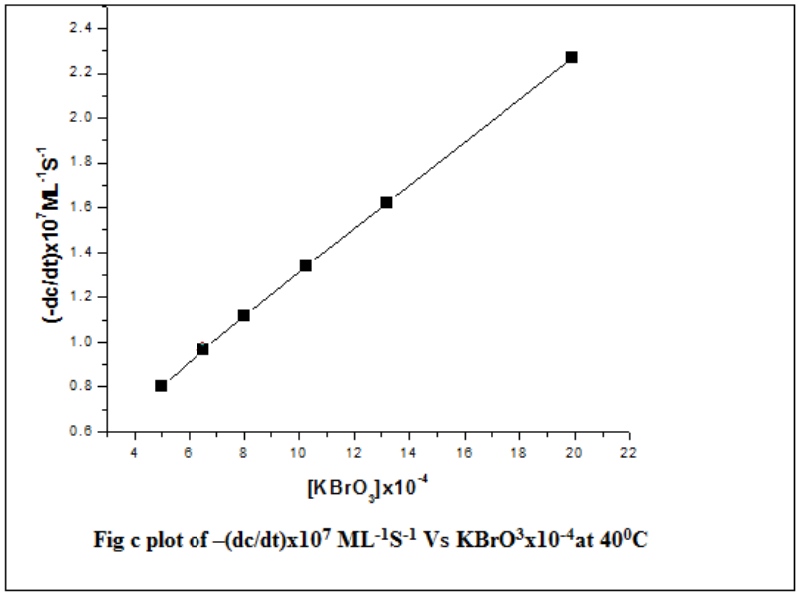


Fig c plot of –(dc/dt)x10^7 ML^{-1}S^{-1} Vs KBrO^{3}x10^{-4}at 40^{0}C

Figure 3

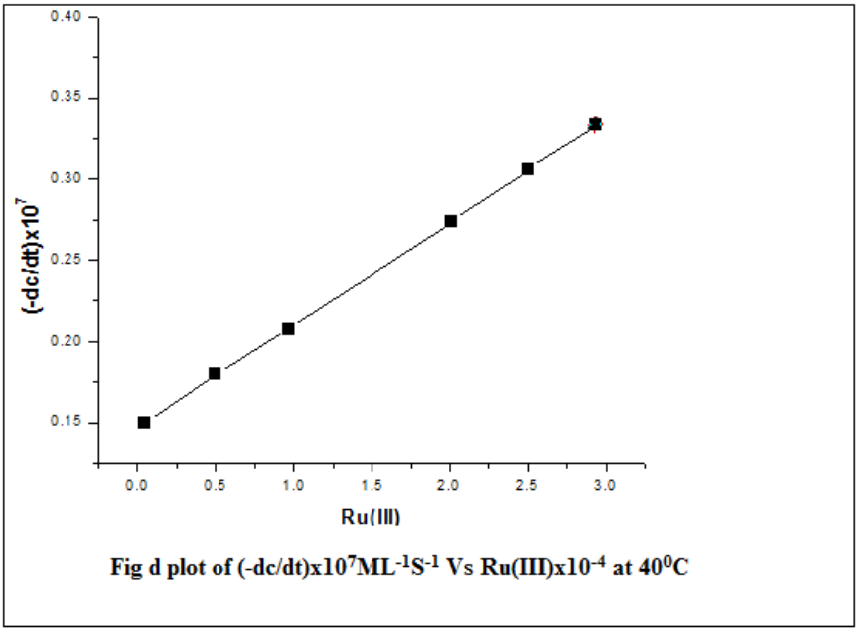


Fig d plot of (-dc/dt)x$10^7$$ML^{-1}S^{-1}$ Vs Ru(III)x10^{-4} at 40^0C

Figure 4

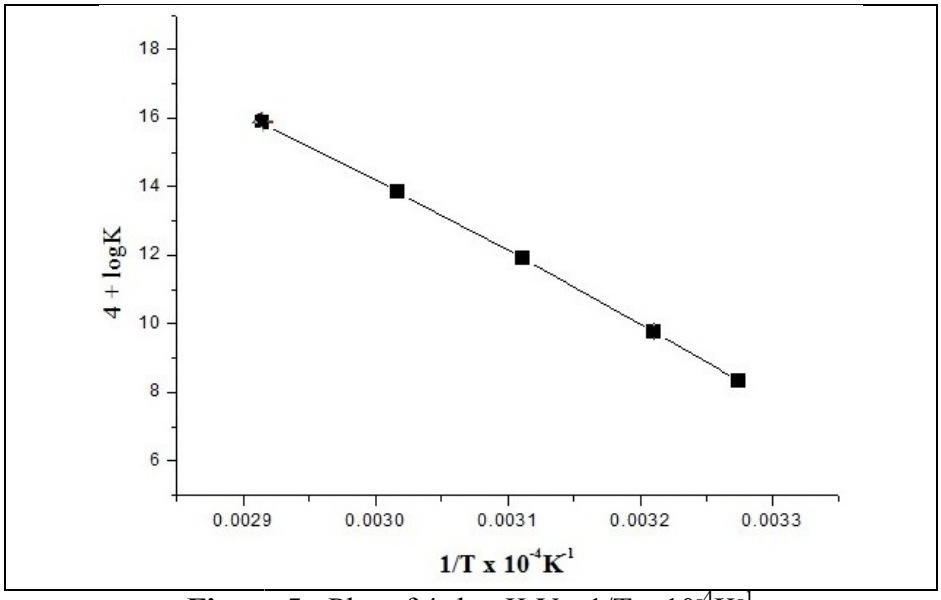


Figure 5 : Plot of 4+log K Vs 1/T x $10^{-4}K^{-1}$

Step (4) is slow and this is rate determining step. The rate of reaction is term of consumption of concentration of [BrO_3^-] ions may be written as equation (i)

$$\frac{d[BrO_3^{-1}]}{dt} = K_2[Q][P] \qquad \text{……..(i)}$$

$$\frac{d[Q]}{dt} = K_1\,[HBrO_3]\,[R] - K_{-1}[Q] - K_2[Q]\,[P]$$

$$[Q] = \frac{K_1[HBrO_3][R]}{K_{-1} + K_2[P]} \quad \text{..... (ii)}$$

$$\frac{d[BrO_3^{-1}]}{dt} = \frac{K_2K_1[HBrO_3][R][P]}{K_{-1} + K_2[P]} \text{..... (iii)}$$

Concentration of Ru(III)Chloride i.e. $[Ru(III)]_T$

$[Ru(III)]_T = [R] + [Q]$ .....(iv)

Put the value from eq(ii)

$$[Ru(III)]_T = [R] + \frac{K_1[HBrO_3][R]}{K_{-1} + K_2[P]}$$

$$[Ru(III)]_T = [R]\left(\frac{K_1 + K_2[P] + K_1[HBrO_3]}{K_{-1} + K_2[P]}\right)$$

$$[R] = [Ru(III)]_T\left(\frac{K_{-1} + K_2[P]}{K_{-1} + K_2[P] + K_1[HBrO_3]}\right) \quad \text{.....(v)}$$

Putting the value of R from eq (v) to eq (III) we get

$$\frac{d[BrO_3^{-1}]}{dt} = \frac{K_2K_1[HBrO_3][Ru(III)]_T + K_{-1} + K_2[P]}{K_{-1} + K_2[P]\{K_{-1} + K_1[HBrO_3] + K_2[P]\}}$$

$$\frac{d[BrO_3^{-1}]}{dt} = \frac{K_2K_1[HBrO_3][Ru(III)]_T[P]}{K_{-1} + K_1[HBrO_3]K_2[P]} \quad \text{.....(vi)}$$

On assuming $K_2[P] >> K_{-1} + K_1[HBrO_3]$ and neglecting this second term in the below side written equation (vi)-

$$\frac{d[BrO_3^{-1}]}{dt} = \frac{K_2K_1[HBrO_3][Ru(III)]_T[P]}{K_2[P]} = K_1[HBrO_3][Ru(III)]_T \text{.....(vii)}$$

The rate law (vii) is in agreement with all observed kinetics.

Table-1 Effect of variation of [Paracetamol], $KBrO_3$ and Ru(III) on reaction rate at 40^0C

$[KBrO_3]$ x10^3mol dm^3	[sub] x10^3mol dm^3	Ru(III) x10^3mol dm^3	$-(dc/dt)x10^7$ mol dm^3
5.0	1.0	1.96	0.8
6.7	1.0	1.96	1.1
8.0	1.0	1.96	1.2
10.0	1.0	1.96	1.4
13.3	1.0	1.96	1.7
20.0	1.0	1.96	2.1
1.0	1.25	1.96	0.11
1.0	2.9	1.96	0.11
1.0	3.5	1.96	0.12
1.0	4.5	1.96	0.13
1.0	6.25	1.96	0.13
1.0	10.0	1.96	0.13
1.0	1.0	0.05	0.15
1.0	1.0	0.50	0.18
1.0	1.0	1.0	0.20
1.0	1.0	2.0	0.27
1.0	1.0	2.5	0.31
1.0	1.0	3.0	0.41

Table-2 Effect of variation of [NaOH], KCl and $[Hg(OAc)_2]$ at 313K.

[NaOH] x10^3M	[KCl] x10^3M	$Hg(OAc)_2$ x10^3M	-(dc/dt)x‡10^6M
10.0	1.0	1.0	0.13
5.0	1.0	1.0	0.12
3.33	1.0	1.0	0.11
2.5	1.0	1.0	0.12
2.0	1.0	1.0	0.13
1.66	1.0	1.0	0.11
1.0	5.0	1.0	0.13
1.0	3.3	1.0	0.13
1.0	2.5	1.0	0.14
1.0	2.0	1.0	0.12
1.0	1.66	1.0	0.11
1.0	1.25	1.0	0.12
1.0	1.0	0.80	0.70
1.0	1.0	1.25	0.70
1.0	1.0	1.67	0.72
1.0	1.0	2.00	0.68
1.0	1.0	2.50	0.73
1.0	1.0	3.33	0.70

Table-3 Effect of temperature variation on the reaction rate

T^0C	$(-dc/dt) \times 10^7$
30	1.5
35	2.4
40	3.0
45	3.6
50	4.0

Table-4 Values of Activation parameters on the reaction rate

Substrate	Parameter
Ea($KJmol^{-1}$)	58.0
Log A	3.3
$\Delta S(K^{-1}Jmol^{-1})$	12.94
$\Delta H^*(K^{-1}Jmol^{-1})$	17.89
$\Delta G(K^{-1}Jmol^{-1})$	330.2

Conclusion

The reaction between $KBrO_3$ and paracetamol has been carried out alkaline medium. Quinoxime been identified as the reaction product in alkaline medium. The order of reaction with respect to each reactant was computed in respective medium and compared. There is formation of most reactive activated complex $[RuCI_5(H_2O)]$ between reactive species of Ru(III) chloride and reactive species of $KBrO_3$.Mercuric acetate as one of the reactants plays the role of inhibitor in addition to its role as CI- scavenger. From the Arrhenius plots the thermodynamics parameters have been computed and a mechanism has been proposed which was in conformity with the observed rate law.

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Conflict of Interest

None of the authors of the above manuscript has declared any conflict of interest which may arise from being named as an author in the manuscript.

Reference

[1] Srivastava, L. chaudhary, K.singh,International J. of Research in physical chemistry 2 (2012)6-10.
[2] Singh Ajay, Negi Reena, Jain Bhavana, Katre Yokraj, Surya P. Sharma, Virandr Catalysis Letters-1/2 (2009) 285-291.
[3] U. Kaushwaha, A. singh, A. kumar, A.K. singh, F, khan Journal of chemical and Pharmaceutical Research 4 (2012) 3144-3353.
[4] Hiremath CV, Kiran TS, Nandibewoor ST. J Mol Catalysis A Chem., 248 (2006) 163.
[5] Aftab Aslam, Anish Khan,Abdulla Ansar, Naved Azum, Malik Abdul Journal of Taiwan Institute of Chemical Engineers, 2014; 45/1: 127-133.

[6] A. srivastava and S. L. Bansal, International Journal of chemical and physical sciences 4 (2015) 39-48.
[7] A. srivastava and N. Agrawal, World Journal of Pharmaceutical Research 4 (2015) 1729-1738.
[8] S. O. Adejo, R. A. Wuana, S. G. Yiase, and M. M. Ekwenchi, Int'l J. of Chemistry, 18(2) (2008) 63-70.
[9] P.O. Baralles, R.P. Weigand, and A. M. Dias, Analytical *Sci. J.*, 18 (2002) 1241-1246.
[10] S. Srivastava , P. Singh ,Oxidation Communication 27 (2004)813-814.
[11] N. Kambo, S. K.Uppadhhaya, Trasition Metal Chemistry 25 (2000)461-464.
[12] R.A. Singh, K. Singh, S.K.Singh, Journal chem. pharma Research 2 (2010)684-690.
[13] N. K. soni, R.Sailani, C.L. Khandelwal,P.P. Sharma, Trasition metal chemistry 39 (2014) 41-45.
[14] Y. L.kumar, R. V. Nadh,P.S.radha, K.Murti,Russian Journal of physical chemistry A 90 (2015) 300-307.
[15] A.Srivastava, N.InternationalJournal of Applied Research 10 (2015)380-384.
[16] J. altmanns, S. palkovitis, R. Palkovits, applied catalysis A, 456(2013) 168-173.
[17] S. Srivastava and P.Srivastava, Peigia Research Library1(1) (2010)13-19
[18] A.aslam, P.Khan, A. Khan, Abdullah M.asiri, A. K. singh,Int. J. Electrochemistry.Sci.,10 (2015) 759-774.
[19] R. Mehrotra, kinetics and Mechanics of oxidation of isopropanal by chloramines T Asian journal of chemistry ,4(3) (1992) 438-443
[20] S. L. Suruki, M. sugiyama, Y. Mihara, K. hashiguchi and K.Yokozeki, Biosci, Biotechnal, Biochem. 66 (2002) 2614-2620.