Pd(II) and Ir(III) catalyzed oxidation of Pharmaceutical drugs (Gabapentin and Paracetamol) by Potassium bromate in acidic medium: A Comparative study

THESIS

SUBMITTED TO

BABASAHEB BHIMRAO AMBEDKAR UNIVERSITY
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2019

Dedicated to
My Beloved Parents

CERTIFICATE

This is to certify that the thesis titled **“Pd(II) and Ir(III) catalyzed oxidation of Pharmaceutical drugs (Gabapentin and Paracetamol) by Potassium bromate in acidic medium: A Comparative study”** submitted by Ms. **Reena Patel** is an original research work and has not been previously submitted in part or full for the award of any other degree or diploma to this or any other university.

The thesis submitted to Babasaheb Bhimrao Ambedkar University Lucknow satisfies all the requirements as stipulated in the Doctor of Philosophy (Ph.D.) regulations-1999 as amended in 2008/2010/2013 and it is fit for submission and evaluation for the award the of the degree of Doctor of Philosophy of the University.

Co-Supervisor **Supervisor**

Date: **Head of the Department**

DECLARATION

I hereby declare that the thesis **“Pd(II) and Ir(III) catalyzed oxidation of Pharmaceutical drugs (Gabapentin and Paracetamol) by Potassium bromate in acidic medium: A Comparative study”** submitted for the degree of Doctor of Philosophy (Ph.D), is the record of work carried out by me under the supervision of **Dr. Shailesh Kumar, Assistant Professor, Department of Applied Chemistry, School For Physical Sciences,** Babasaheb Bhimrao Ambedkar University (A Central University), Lucknow, India and co-supervision of **Dr. Sheila Srivastava, Associate Professor** and **Head, Department of Chemistry, Feroze Gandhi College Raebareli, India** and I further confirm that the work has not been published anywhere else for the award of any degree, diploma, fellowship etc. either in this or any other University or other institution of higher learning. I further declare that the material obtained from other sources has been duly acknowledged in the thesis. I also declare that the thesis is essentially free from all kinds of plagiarism.

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PREFACE

The present thesis, based on the kinetics of pharmaceutical drugs is expected to attract the attention of scientists of international and national status. Commonly the study of oxidation of pharmaceutical drugs has great importance in medical sciences. Some drugs are used as an additive because of their humectants properties.

In this thesis it has been tried to consolidate the various work done on the well-known drugs that find extensive application in pharmaceutical industries.

Paracetamol is antipyretic and analgesic drug with high therapeutic value. It is also used as an intermediate for pharmaceutical (as precursor in penicillin) and azo dye. Gabapentin drug, ([1-amino methyl cyclohexyl] acetic acid), is a neuroleptic drug. The study of kinetics of oxidation of Gabapentin and Paracetamol is an area of active experimentation because of their biological significance and selectivity towards oxidant i.e. oxidation products differ with different oxidants.

Currently analgesics and non-steroidal anti-inflammatory drugs are classified as one of the most emerging group of xenobiotics and have been detected in various natural matrices. A wide range of pharmaceuticals and their metabolites or resideres are continuously introduced into various environments mainly from hospital and municipal waste water, consumer use or disposal and discharges from pharmaceutical production. Among them paracetamol, ibuprofen and gabapentin widely used to treat moderate pain and seizures are the most popular. Since long term adverse effects of these xenobiotics and their biological and pharmacokinetic activity are better understood, degradation of such contaminants has become a major concern. Moreover, till date, conventional waste water treatment plants are not fully adapted to remove this kind of micropollutants either by chemical or microbial degradation. So the present study makes on attempt to provide some chemical pathway for degradation of such pharmaceutical drugs presents as micropollutants in drinking water.

Thanking you
Reena Patel
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ABSTRACT

The role of catalyst was widely recognized in modern chemical industry and therefore been subjected to quantitative and qualitative studies. The studies in the oxidation of organic compounds involving an effective and suitable homogenous catalyst have been given little incentive to work out their kinetics and mechanism. With the development of theory of reaction rates, it was demonstrated that the role of a catalyst is to lower down the energy of activation of a reaction and it was described that the lowering of the activation energy occurs, through the direct interaction of the catalyst with the substrates. The role of catalyst was widely recognized in chemical industries. The present investigation explores and describes factors involved in kinetic study of oxidation reactions via taking examples of transition metal catalyst i.e. Ir(III) and Pd(II) catalyzed reactions of pharmaceutical drugs oxidation by using $KBrO_3$ as an oxidant. The goals of the study have been:-

- To investigate the impact of catalyst palladium(II) chloride and Iridium(III) chloride), substrate and $Hg(OAc)_2$ on the rate of reaction rate and also to elucidate the reaction order with respect to each of them in proposed medium.
- To propound the impact of $[H^+]$, $[Cl^-]$, ionic strength and define its effect on the reaction rate.
- To define the role of temperature on the reaction rate.
- To calculate the thermodynamic activation parameters e.g. ΔE^*, ΔG^*, ΔS^* and ΔH^* for investigated reactions.
- To derive the rate law from proposed mechanistic steps in conformity to the experimental results.

Therefore the main goal of proposed work is to elucidate the oxidation path of drugs by $KBrO_3$ in redox system and elaborate the catalytic efficiency of transition metal ions. Proposed work defines the oxidation of some biochemically and biologically important pharmaceutical drugs which are helpful to understand the complicated biochemical process occurring in living systems. The aim of the present study is to propose the most probable reaction path for the oxidation of pharmaceutical drugs and emphasize on biological importance of paracetamol and gabapentin using chloro-complex of Ir(III)/ Pd(II) as homogenous catalyst in acidic medium.

GLOSSARY OF SYMBOLS AND ABBREVIATIONS

[Ir(III)] = Concentration of Iridium(III) chloride.

[Pd(II)] = Concentration of palladium(II) Chloride

[$KBrO_3$] = Concentration of potassium bromate.

[Substrate] = Concentration of Substrates.

[$HClO_4$] = Concentration of Perchloric Acid.

[KCl] = Concentration of Potassium Chloride.

[$Hg(OAc)_2$] = Concentration of Mercuric Acetate.

[PA] = Concentration of Paracetamol.

[GB] = Concentration of Gabapentin.

μ = Ionic Strength.

D_2O = Heavy Water.

ΔT = Change in Temperature.

ΔE or E_a = Energy of Activation.

A = Arrhenius Factor

ΔS^* = Entropy of Activation.

ΔH^* = Enthalpy of Activation.

ΔG^* = Free Energy Change of Activation.

R = Gas Constant

CONTENTS

INTRODUCTION

Chemical kinetics(1) is the systematic detailed study of the rate of chemical reactions and the factors which control and influence their progress and course. The ultimate object is to ascertain the behaviour of molecules and ions during the course of chemical reaction and to draw definite conclusion about their detailed mechanism i.e. the specific course which it follows. Chemical kinetics deals with the study of the reaction rate and its mechanism. The thermodynamic parameters of any chemical reaction include Gibbs or Helmholtz energy and its relevant equilibrium constant. At equilibrium these parameters are adequate to forecast the suitable product, but have modest application in determining the timescale over which the reactions take place. Consequently thermodynamics may utter that a reaction is spontaneous, but does it happen in 10^{-15} s. The answer to this question lies in the province of chemical kinetics. Chemistry, as Porter(2) rightly points out is “part of statics and part of dynamics” and treated kinetics as later birth and difficult child. Wilhelmy(3) during his first kinetic measurements, in 1850 measured the rate of inversion of sucrose and investigated the influence of concentration of sucrose at that moment. In 1862, Berthelot and Gills(4), in 1865-67, Harcourt and Esson(5) concluded analogous result.

Experimental chemical kinetics consist of new innovative techniques to study the chemical reaction which defines the measurement and analysis of chemical reaction dynamics. Along with experimental study some theoretical work has also been performed to justify the reaction mechanisms and the underlying physics that govern the rates of chemical transformations. The concordance between experiment and theoretical chemical kinetics has been provided for spectacular advances in this field. Finally, the significance of chemical kinetics is authentified by its utilization in nearly every field of chemistry. In areas such as enzyme catalysis, materials processing and atmospheric chemistry, chemical kinetics is undoubtedly a crucial aspect of physical chemistry(6).

In kinetics, the reactions are classified into two groups:

(a) Homogeneous reactions which come about in one phase.

(b) Heterogeneous reactions where the transformation occurs on the surface of a catalyst or the walls of a container.

Temperature dependence of reaction rates

Temperature has insightful impact on the reaction rate. The consequence of temperature change on the reaction rates can be intimitated in two ways-

1. Temperature coefficient of kinetics of reaction.
2. Arrhenius equation of reaction rates.

1. Temperature coefficient of reaction rates -

The experiments demonstrate that rate of reaction for a homogeneous thermal reaction is doubled or tripled at every ten degree ascent in temperature. To exemplify the temperature dependence of the rate of a chemical reaction, the temperature coefficient of reaction rate or chemical reaction was quantified.

Temperature co-efficient is denoted by 'γ'. It is defined as the fraction of rate constant of a chemical reaction at two temperatures differing by 10ºC. For example the two temperatures may be taken as 25ºC and 35ºC. Hence, temperature coefficient of reaction rate is expressed as

$$\gamma = \frac{k_{35}}{k_{25}}$$

where k_{35} = Velocity constant of the reaction at 35ºC

k_{25} = Velocity constant of same reaction at 25 ºC.

In general, the temperature coefficient is expressed as

$$\gamma = \frac{k(t+10)}{k_t}$$

Where k_t = Velocity constant of the reaction at t ºC

$k_{(t+10)}$ = Velocity constant of the same reaction at (t+10) ºC

2. Arrhenius Equation:

The influence of temperature on rate of a chemical reaction is very appropriate in nature and has a less experimental value. This lead Arrhenius to put forward his own equation, known as Arrhenius equation$^{(7)}$, to articulate the impact of temperature on velocity of a reaction.

$$k = A.e^{-E/RT}$$

It is the integrated form of the Arrhenius equation.

where A = Constant called frequency factor.

E = Energy of activation. It has the dimension of energy.

k = Velocity constant of the reaction at temp. T.

Taking log of both sides, we get

$$\ln k = \ln A - \frac{E}{RT}$$

$$2.303 \log k = 2.303 \log A - \frac{E}{RT}$$

$$\log k = \log A - \frac{E}{2.303RT} \qquad ....(1)$$

The expression (1) represents a straight line, i.e., plot of log k vs. 1/T as shown in Figure(1.1)

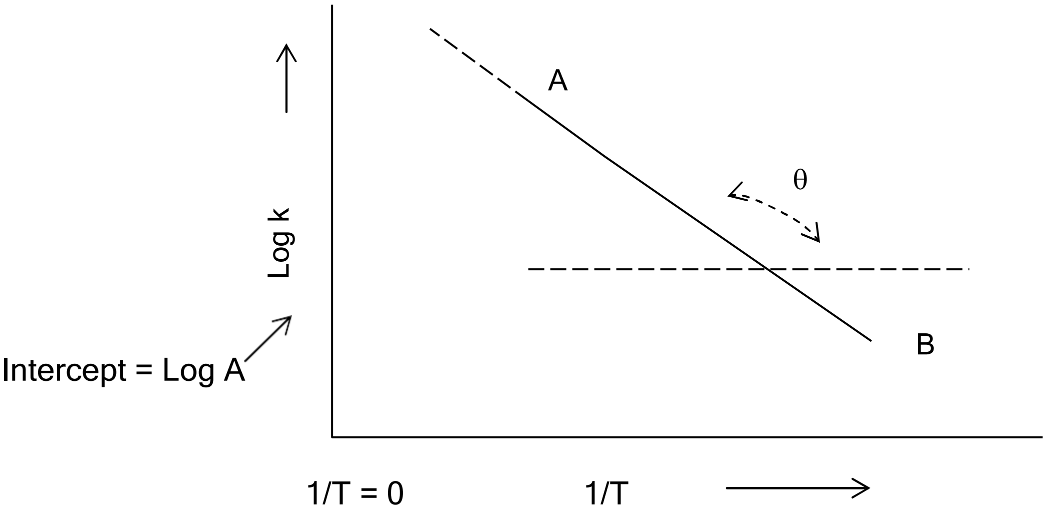

Fig.1.1 Logarithm of rate constant (log k) of reaction versus inverse temperature (1/T)

⇒ In Arrhenius equation $k = A\ e^{-Ea/RT}$, when the absolute temperature of reaction becomes infinity, the rate constant of reaction becomes equal to A, the pre exponential factor.

$$\boxed{k = A}$$

⇒ When energy of activation E_a of a reaction is zero, the reaction rate becomes self-governing with respect to temperature.

Mostly kinetic investigations are performed to demonstrate insight into the mechanism by which chemical transformations occur. Investigation may be exclusively concerned to set up the series of steps by which the reactants are transformed into products. While if reaction mechanism is acknowledged, study of kinetics of reaction may be engaged to elucidate the details of the interaction among the reactant molecules. This aims towards the fact that the experimental data, given in equations has concordance with theoretical aspects of reaction kinetics. The evidence of the authenticity of reaction mechanism is obtained by the product recognition, use of isotopic tracers(8), detection of short lived intermediates, variation of ionic strength(9), catalyst and change of solvent(10) etc. Chemical kinetics deals with measurement of rate of reactions proceeding under given conditions of temperature, pressure and concentration. The study of this subject has been highly useful in determining the factors which work out conditions for getting maximum yield of several industrial products. It is natural that the majority of kinetic investigations should have been concerned with reaction whose rates influence rate of reactions as well as in understanding mechanisms of a number of chemical reactions. The experimental data have led to the development of the modern theories related to chemical reactivity of molecules. During recent years, partly as a result of the development of new electronic techniques, a good deal of efforts have been devoted to the study of reactions that are difficult to study by conventional methods. Examples are reactions occurring at very high hydrostatic pressures or temperatures and reaction occurring at very high velocity.

Kinetics has an answer to many difficult analytical problems(10-12). Kinetics also help in mixture analysis(13), enzyme analysis and use of enzyme in the determination of rate dependence on substrate concentration by the direct use of kinetic data(14). Kinetic studies are also very useful in polymer chemistry and for determining the greater stability conditions for better yields of desired polymer(15-16)

Earlier in 1836. J. J. Berzelius(17) introduced a new term catalyst for the substance which have tendency to activate the chemical reactions. According to him these substances have a special catalytic force upon the reactants. After that in 1902, W. Ostwald named these substances as catalytic agents which enhance the rate of chemical reactions without altering the chemical equilibrium. Later on this definition was found to be valid only for reversible reactions and not for autocatalysis.

The role of catalyst was widely recognized in modern chemical industry and therefore been subjected to quantitative and qualitative studies. A survey of the literature on homogenous catalytic processes indicate that the studies in the oxidation of organic compounds involving an effective and suitable homogenous catalyst have been given little incentive to work out their kinetics and mechanism. With the development of theory of reaction rates, it was demonstrated that the role of a catalyst is to lower down the energy of activation of a reaction and it was described that the lowering of the activation energy occurs, through the direct interaction of the catalyst with the substrates. The role of catalyst was widely recognized in chemical industries.

The introduction of present thesis is comprised of four parts.

Part (A) - deals with palladium (II) chloride and Iridium (III) chloride as catalyst.

Part (B) - deals with potassium bromate as an oxidant in acidic medium.

Part (C) - deals with pharmaceutical drugs i.e. paracetamol and gabapentin as reductant in acidic medium.

Part (D) - Present study and its objectives.

Accordingly the results are given and the proposed mechanism discussed in last chapter.

[PART : A]

1.1: Iridium (III) chloride as a Catalyst:

Transition metal ions have a vast application as homogeneous and heterogeneous catalysts in the oxidation of organic and inorganic compounds whether the medium is acidic or alkaline medium. The kinetics of redox reactions involving transition metal ions like Osmium(VIII), Ruthenium(III), Ruthenium(VIII) and palladous ions etc. as homogeneous catalyst has been widely investigated(18-22) but from kinetic aspect the role of Ir(III) chloride as catalyst(23-24) has been least investigated.

1.1.1. Iridium (III) chloride as a catalyst in acidic/alkaline medium:

The kinetic and mechanistic study of Ir(III) catalyzed oxidation of Tellurium(IV) by Manganese(III) in sulfuric acid was proposed by S.N. Dindi and K.G. Sudarsan. They suggested that the oxidation of Tellurium(IV) by Manganese(III) is kinetically sluggish but the process gets efficiently catalyzed by ruthenium(III) at ultra trace concentration. Besides Ru(III) some other transition metals can also be used for reaction mentioned above and product obtained was totally different from uncatalysed reaction(25) as well as the Ruthenium(III) catalyzed (26) reactions reported earlier.

In 1981 Singh (27) has oxidized some amino acids in alkaline medium using Iridium(III) chloride catalyst by hexacynoferrate(III) in which reaction follows first order kinetics with respect to amino acids and for $[OH^-]$ ion but as the concentration increases it tends towards zero order. They have also reported reactive species of Ir(III) chloride in aqueous alkaline medium. Kinetics and mechanism of Ir(III) catalysis in N-bromoacetamide oxidation of some acids in perchloric acid medium was investigated by Madhu Saxena, R. Gupta, A. Singh, B. Singh and A.K. Singh (28). They observed first order kinetics with respect to oxidant (NBA) and zero order for $[H^+]$ while both Ir(III) and $Hg(OAc)_2$ have first order dependence on reaction. Change in concentration of $[H^+]$ and $[Cl^-]$, show negative effect on the reaction velocity. Addition of acetamide has negative effect on the reaction velocity. They concluded that the reactive species of [NBA] is HOBr and the reactive species of Ir(III) chloride in acidic medium is $[IrCl_5.H_2O]^{2-}$.

Work has also been done in the field of kinetics of oxidation of valeric acid by Ir(III) as homogeneous catalyst(29). Singh et.al(30) studied Iridium(III) catalysis of N-bromo succinimide oxidation of reducing sugars in acidic medium. They reported first order for N-bromo succinimide and zero order for substrate. The reaction exhibited first order in Ir(III) at lower [Ir(III)], but tended towards zeroth order at higher [Ir(III)]. Inverse fractional order has been observed in [H^+], [Cl^-] and [succinimide]. Variation in ionic strength and [$Hg(OAc)_2$] (used as Br^- ion scavenger) have negligible impact on the oxidation rate. They reported HOBr and $[IrCl_5.H_2O]^{2-}$ as reactive species of NBS and Ir(III) chloride respectively.

The kinetics of Ir(III) catalysed oxidation of ethylene glycol(EG) and methyl glycol (MG) by N-bromosuccinimide in $HClO_4$ in presence of $Hg(OAc)_2$ as a scavenger for

Br^- has been studied by Bharat Singh, Manju Singh, Preeti Bhatnagar and Ashutosh Kumar**.** Oxidation of some hydroxy acids by [NBA] in the presence of perchloric acid and Ir(III) chloride have been studied by Madhu Saxena et at.(31)

1.1.2 Preparation of Iridium chloride catalyst:-

Anhydrous iridium trichloride varies in colour according to its state of division, the fine powder being olive green, colour changing as the material gets coarser to brown and then blackish blue which depends on the fineness of original metallic powder, and also on temperature to which the chloride has been heated. The hydrated Ir(III) chloride ($IrCl_3.$ $3H_2O$) is made by heating the oxychloride in hydrogen chloride gas (32). Another hydrate $IrCl_3.5H_2O$ has also been reported.

The oxychloride $IrCl_2(OH)$(32) aq. is prepared by action of hydrogen chloride on iridium tetra hydroxide $Ir(OH)_4$. At room temperature the product is the trihydrate $IrCl_2$ $(OH).3H_2O$, a dark green hygroscopic solid having water solubility. But at 2100 ºC, if it is heated in a stream of hydrogen chloride it changes into similar monohydrate, which gives a dark green solution in water. The mechanism of redox reactions in presence of certain transition metal ions like Osmium(VIII), Ruthenium (III), Ruthenium(VIII) and palladous ions has been widely investigated.(33-36).

1.2 Palladium chloride as a catalyst.

A number of catalysts have been used to study various reactions of industrial as well as academic importance. A few of them are Os(VIII), Ir(III)(37-39), Cr(III)(40), Mn(II)(41), Cu(II)(42-44), Ru(III)(45-47) and so on. Amongst these Os(VIII) is considered to be a very effective catalyst for the degradation of organic compounds (48-51).

Pd(II) chloride(52-58) is also an effective catalyst whether the condition is acidic or alkaline in presence of suitable oxidizing agents. Therefore the role of Pd(II) chloride as effective catalyst for proposed work is on the basis of following facts.

⇒Cu (II) is also suitable catalyst in its higher concentration. Since it is also an oxidant and liberates iodine, it's application may cause some complications in iodometric titration.

⇒ Ag(I) may have greater complexity in iodometric estimation because of its precipitation as halides.

⇒ Osmium tetra oxide is a little toxic so it should be avoided.

⇒ Osmium tetra oxide may also cause further activation in oxidation of proposed reaction.

Pd(II) chloride is comparatively cheaper and has least toxic character. In addition it does not initiate further oxidation of products under controlled condition. Another advantage of this catalyst lies in the fact that it is used in concentration as low as 1.0 x 10^{-6} M in solution and gives efficient results.

In last few years platinum metals like Pd(II), Ru(III), Ir(III), Rh(III) have wide range of applications as catalyst mainly because these elements have strong catalytic influence in many reactions such as oxidation, reduction, hydrogenation and alkylation of organic substrate(59-65)

1.2.1: Pd(II) chloride as a catalyst in acidic medium:

Recently, Pd(II) catalyzed oxidation of D-arabinose, D-xylose and D-galactose by N-bromosuccinimide in acidic solution have been studied by Ashok Kumar Singh et al(66). They have observed that reaction shows first order kinetics in each pentose and hexose at low concentrations, which tend to zero order at high concentrations. First order kinetics with respect to NBS and Pd(II) and inverse fractional order, i.e., decreasing effect of [H^+] and [Cl^-], were observed, whereas ionic strength, $Hg(OAc)_2$ succinimide did not influence the oxidation rate.

Ashish et al carried out mechanistic study of palladium(II) catalyzed oxidation of crotonic acid by periodate in acidic medium(67). They have observed that the linear dependence of the reaction rate at lower [IO_4^-] and [Pd(II)] tends towards zero order at their higher concentrations. The reaction exhibited zero order in [CA]. Negligible effect of change in [H^+], ionic strength of medium and varying [Cl^-] on the rate of reaction is observed. Somanalli K. et. al studied Palladium(II) catalyzed oxidation of α-hydroxy acids with Sodium N-chlorobenzene Sulfonamide in perchloric acid solution(68) and found that kinetics of oxidation of glycolic acid (GA), lactic acid (LA) and 2-hydroxybutanoic acid (BA) with Chloramine-B (CAB) catalyzed by Pd(II) in $HClO_4$ solution shows first-order dependence each on [CAB], [Hydroxy acid] and [Pd(II)] and a fractional order with respect to [H^+]. Variation of ionic strength and dielectric permittivity of the medium have no effect on the rate.

Puttaswamy, Anu Sukhdev and J.P. Shubha studied palladium(II) catalyzed oxidation of tranexamic acid by bromamine-B in alkaline medium and uncatalyzed reaction in acidic medium(69) and found that in acidic medium, the reaction exhibits a first-order dependence of rate on $[BAB]_0$ and less than unity order dependence on $[TA]_0$. The reaction rate shows inverse less than unity order dependence with respect to [H^+]. In alkaline medium, the reaction shows first order dependence on both $[BAB]_0$ and [Pd(II)] and zero-order with respect to $[TA]_0$. The order with respect to [OH^-] is less than unity.

There are several other palladium(II) catalyzed reactions(70-75) in acidic medium in which palladium acts as an effective catalyst to catalyze the reactions. Ajaya Kumar Singh, Reena Negi, Yokraj Katre, Surya Prakash Singh have studied “Mechanistic study of oxidation of acetaminophen by chloramine-T using micro-amount of chloro-complex of Ir(III) as catalyst in acidic medium”(76). The reaction traverses first-order kinetics with respect to [chloramine-T], [paracetamol] and [Cl^-] in their lower concentration range and show a tendency towards zero-order at their higher concentrations. First-order kinetics with respect to [Ir(III)] was observed for the oxidation of acetaminophen. The reaction rate is supressed with enhancing [H^+] and p-toluene sulphonamide [PTS] for the oxidation of paracetamol. The variation of ionic strength of the medium did not have any impact on the rate of the reaction. The rate constant of reaction enhanced with decrease in the dielectric constant of the medium. Ajaya kumar Singh , Reena Negi , Bhawana Jain, Yokraj Katre , Surya P. Singh , Virender K. Sharma, have studied “Kinetics and mechanistic study of Ru(III)-catalyzed oxidation of paracetamol by chloramine-T”(77). The experimental result shows a first order dependence on acetaminophen at lower concentration but it becomes zero order as its concentration increases. The reactions follow a first order rate dependence with respect to oxidant [CAT] and [Ru(III)]. The reaction showed negative fractional-order dependence on the rate for $[H^+]$ and p-toluenesulphonamide. Variation in $[Cl^-]$ and ionic strength of the medium had no significant impact on reaction rate. The dielectric constant of the medium had negative impact on reaction rate as observed in the oxidation of paracetamol.

1.2.2: Palladium chloride as a catalyst in alkaline medium:

Ajaya Kumar Singh, Reena Negi, Bhawana Jain,Yokraj Katre, Surya Prakash Singh, and Virender K. Sharma have studied “Oxidation of paracetamol by CAT in presence of Pd(II) as catalyst”(78). The determined stoichiometric ratio was 1:2 ([PA]:[CAT]) and quinone oxime was identified as the oxidized product of PA. However, the kinetic patterns in both media were different. In the acidic medium, the rate law was $-d[CAT]/dt = k[CAT][PA]^{0.9}[Pd(II)]^{0.8}[H^+]^{-0.4}$ and the rate law was $-d[CAT]/dt = k[CAT][PA]^{0.9}[Pd(II)]\ [PTS]^{-0.4}\ [NaOH]^{-1}$ in the alkaline medium. P-Toluenesulphonamide (PTS) is the reduced product of CAT. By further survey of literature it was found that Palladium also acts as effective catalyst in alkaline medium. Iftikhar Ahmad, C. Muhammad Ashrat studied the kinetics and mechanism of palladium(II) chloride catalyzed oxidation of allyl alcohol by potassium hexacyanoferrate(III)(79) and found that the reaction was first order with respect to allyl alcohol and palladium(II) chloride, inverse second order with respect to $[Cl^-]$ and zero order with respect to potassium hexacyanoferrate(III). The rate is found to increase linearly with hydroxyl ion concentration.

B.I. Kohli & S.T. Nandibewoor studied the kinetics and mechanism of palladium(II) catalyzed oxidation of dimethyl sulfoxide by alkaline periodate(80) and found that the reaction exhibited first order dependence with respect to $[IO_4^-]$, an apparent less than unit order in [DMSO], $[OH^-]$ and [palladium(II)] under the experimental conditions. U. Kazmaier studied the applications of non-stabilized enolates as nucleophiles in palladium catalyzed allylic alkylation(81) and found them to be important reactions in organic synthesis.

Gauri A. Hiremath, Prakash L. Timmanagaudar, Sharanappa T. Nandibewoor studied oxidation of allyl alcohol by alkaline periodate in the presence of micro amounts of palladium(II)(82) and found that active species of the catalyst was $PdCl^+$ and alkaline species of periodate was $[H_2IO_6]^{3-}$.Veeresh C. Seregar, Chanabasayya V. Hiremath and Sharanappa T. Nandibewoor studied palladium(II) catalyzed oxidation of L-proline by heptavalent manganese in aqueous alkaline medium: a free radical intervention and decarboxylation(83) and found that the reaction was first order with respect to $[MnO_4^-]$ and [Pd(II)], an apparent less than unit order in [alkali] and zero order in [L-proline] under the experimental conditions. There are several other palladium(II) catalyzed reactions(84-88) in basic medium in which palladium acts as an effective catalyst to catalyze the reactions.

1.2.3: Preparation and properties of Palladium chloride catalyst:-

- Palladium (Pd) has electronic configuration of [Kr] $4d^{10}$ and has zero, II and IV oxidation states.
- Pd is a grey white or brownish powder.
- Palladium chloride $[PdCl_2]$ used in present investigation had molecular weight 177.31.
- Palladium(II) chloride is prepared by dissolving palladium metal in aqua regia or hydrochloric acid in presence of chlorine. Alternatively it may be prepared by heating palladium sponge with chlorine gas at 500^0C.
- $[PdCl_2]$ exists in two forms (89). In both forms the palladium centers adopt the square planer co-ordination geometry that is characteristic of Pd(II). The β-form of $PdCl_2$ is molecular, consisting of an octahedral cluster of six Pd- atoms. Each of the twelve edges of this octahedral is spanned by Cl^-.
- α-$PdCl_2$ has flat chain polymeric structure.

[PART– B]

1.3 Potassium bromate as an oxidant in uncatalyzed and catalyzed reactions:-

1.3.1 Oxidising action of potassium bromate in alkaline medium.

As an oxidant $KBrO_3$ is chosen for present work because of its powerful oxidizing property with redox potential$^{(90)}$ 1.44 volt in acidic media, and 0.61 volts in alkaline medium. The potentials reveal that Br_2 in basic medium can disproportionate spontaneously to BrO^- and Br^-. However, in acidic solution Br_2 does not disproportionate but infact it accumulates by an auto-catalytic reaction. Therefore in presence of acidic and excess bromide ions, bromate can exclusively act as a bromide generator and the resultant bromine can either oxidize or brominate the organic compound under study depending on its nature.$^{(92)}$ Potassium bromate has found application in preparative organic chemistry as an oxidizing agent, and also to estimate various organic and inorganic compounds. Some kinetic investigations involving $KBrO_3$ as an oxidant with various compounds in both acidic and basic media have been carried out. However, kinetic results involving $KBrO_3$ as an oxidant in the presence of Ir(III) and Pd(II) catalysts in acidic medium have been little investigated. The main oxidative mode of $KBrO_3$ with pharmaceutical drugs in redox system, explore catalytic potentials of transition metal catalyst i.e. Ir(III) and Pd(II) with $KBrO_3$ as an oxidant in the aforesaid reactions. The present study comprises of oxidation of pharmaceutical drugs i.e. Paracetamol and Gabapentin so that some useful information may be revealed from proposed work to elucidate the complications of biochemical modification in metabolic process. Various powerful oxidizing agents like potassium permanganate, potassium dichromate and chromic acid have been widely used. Work has been done on oxidation by NBS (N-bromosuccinimide) both uncatalyzed$^{(91-96)}$ and catalyzed$^{(97-100)}$ Similarly several papers have been devoted to the kinetics and mechanism of uncatalyzed oxidation of few alcohols$^{(101)}$, ketones$^{(102-105)}$ and dimethyl sulphoxide$^{(106)}$ by NBA. Catalyzed oxidation by NBA$^{(107)}$ has also been reported. $KBrO_3$ has been extensively applied in oxidation of alcohols, ketones,$^{(108)}$ aniline,$^{(109)}$ phenols,$^{(110)}$ aldehydes,$^{(111-112)}$ tartaric acid,$^{(113)}$ some labile substrate,$^{(114)}$ nitrites,$^{(115)}$ pyrogallic acid,$^{(116)}$ amino acids,$^{(117)}$ diols,$^{(118)}$ unsaturated carboxylic acids$^{(119)}$ and n-substituted phenyl methyl sulphides(120) with ruthenium(III) chloride as catalyst.

Potassium bromate has been extensively used for oxidation of homogeneous uncatalysed reactions(121-126). Uncatalyzed reactions of aldoses and aldosamines(127), carbohydrates(128) and α,β-unsaturated compound(129) oxidation by potassium bromate have also been reported. Vanadium catalyzed methylene green(130), 1-napthylred(131), selective cerium catalyzed alkyl benzene(132), Ru(VI) catalyzed diethylene glycol(133), cyclopentanol,(134) Ru(III) catalyzed glycols(135-136), D-sorbitol(137), proline(138), auto catalytic oxidation of haemin(139), Ir(III) catalyzed cyclic alcohols(140), cyclic ketones(141) oxidation by potassium bromate has also been reported. Comparatively Ir(III) catalyzed oxidation has been least reported in comparision to other catalysts. Potassium bromate has been used as an efficient oxidant for the oxidation of crotonic acid(142), allyl alcohols(143) and other compounds(144-148), with ruthenium, Iridium and other catalysts. However, scant studies are available for Ir(III) and Pd(II) catalyzed oxidation by acidic and alkaline bromate.

[PART – C]

1.4 Pharmaceutical drugs:

1.4.1 Oxidation of analgesic drug (paracetamol) in acidic and alkaline medium:

The mechanistic study of paracetamol has been studied by several investigators(149-157). In proposed work we tried to consolidate the application of the drug in pharmaceutical industries on the basis of work done previously because PA is an antipyretic and analgesic drug with high therapeutic value(158-159). It also acts as an intermediate for pharmaceutical (as a precursor in penicillin) and azo dye(160-163). Oxidation reactions play a vital role in the synthesis of new organic compounds, create new functional groups or modify existing functional groups in a molecule (164-165). Various advanced oxidation processes such as electrochemical(166-168), ozonation and H_2O_2 / UV oxidation (169-172) have been employed to eliminate aqueous paracetamol. The degradation of paracetamol drug by oxidant like organic haloamines, metal ion oxidants, metal complex, use of catalyst, variation of media, product effect has importance to elucidate the mechanism of paracetamol oxidation in biological systems and also justify the reactive species of the oxidant in acidic as well as basic medium.

1.4.2 Oxidation of neuroleptic drug (Gabapentin) in acidic and alkaline medium.

Gabapentin (GBP), 2-[1(aminomethyl) cyclohexyl] acetic acid, is a neuroleptic drug. It has great biological significance and selectivity towards the oxidant. Gabapentin has wide range of application as anti-convulsant agent that is used for the treatment of epileptic seizures(173-176). It has also has shown to be a potential drug for treatment of neurogenic pain (177-178) aminobutyric acid, but potent subsequently has no interaction with any of the enzymes on the GBP metabolic pathway(179). Furthermore, GBP has also been applicable for the treatment of some mood disorders, anxiety and tardive dyskinesia (a neurological syndrome caused by the long term use the neuroleptic drugs). Currently analgesics and non-steroidal anti-inflammatory drugs are classified as one of the most emerging group of xenobiotics and have been detected in various natural matrices. A wide range of pharmaceuticals and their metabolites or resideres are continuously introduced into various environments mainly from hospital and municipal waste water, consumer use or disposal and discharges from pharmaceutical production.

Among them paracetamol, ibuprofen and gabapentin widely used to treat moderate pain and seizures are the most popular. Since long term adverse effects of these xenobiotics and their biological and pharmacokinetic activity are better understood, degradation of such contaminants has become a major concern. Moreover, till date, conventional waste water treatment plants are not fully adapted to remove this kind of micropollutants either by chemical or microbial degradation. So the present study makes on attempt to provide some chemical pathway for degradation of such pharmaceutical drugs presents as micropollutants in drinking water.(180-187)

[PART – D]

1.5 Present study and its objectives.

The main intent and goal of the proposed investigation may be summarized as follows:-

⇒To elucidate the effect of oxidant (Potassium bromate) variation on the rate of reaction in acidic medium.

⇒To investigate the impact of catalyst palladium(II) chloride and Iridium(III) chloride, substrate and $Hg(OAc)_2$ on the rate of reaction rate and also elucidate the order with respect to each of them in proposed medium.

⇒ To propose the impact of $[H^+]$, $[Cl^-]$ and ionic strength and also to define its effect on the reaction rate.

⇒ To define the role of temperature on the reaction rate.

⇒ To calculate the thermodynamic activation parameters which are ΔE^*, ΔG^*, ΔS^* and ΔH^* for investigated reactions.

⇒ To derive rate law and propose mechanistic steps conforming to the rate on the basis of experimental results.

Summary:

Therefore the main goal of proposed work is to elucidate the kinetics and mechanism of oxidation of drugs by $KBrO_3$ in redox system and elaborate the catalytic efficiency of transition metal catalyst Pd(II) and Ir(III) with potassium bromate as an oxidant in aforesaid reactions. Thus this thesis presents a study of the oxidation of some biochemically and biologically important pharmaceutical drugs that may prove to be very useful in understanding the complicated biochemical process occurring in living systems.

[Part- E]

1.6 References

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CHAPTER- 2

EXPERIMENTAL PROCEDURE

SEC. A.

2.0 Preparation of stock solution

Before performing the experiment solutions were prepared as follows-

(1) Potassium bromate

Solution of potassium bromate was made by dissolving 0.334 gm. of sample in 100 ml of distilled water making the strength N/50 which inturn was checked with the help of copper sulphate solution (S.d. fine. Chem. Ltd). The solution thus obtained was kept in dark coated flask to avoid any photochemical degradation.

(2) Substrate (Paracetamol and Gabapentin)

Weighed amount of drugs, paracetamol and gabapentin was dissolved in hot water to achieve their standard solution little prior to initiation of kinetic study. A.R. grade samples of substrate PA and GB were obtained from central drug house private Ltd. New Delhi-110002 (India).

(3) $HClO_4$

Measured suitable volume of perchloric acid (60 % E. merck) was poured into measured volume of double disttled water to get required strength. The solution thus obtained was titrated with standard solution of strong base, NaOH using few drops of phenolphthalein which acted as indicator in all experiments. Perchloric acid was used as a generator of H^+ ion.

(4) Palladium(II) chloride-

1 gram of the palladium(II) chloride (Johnson Matthey) sample was dissolved in 0.018N solution of HCl to make the total volume 1000 ml. This resulted in formation of 9.64×10^{-4} M strength of homogenous catalyst $PdCl_2$.

(5) Iridium(III) chloride-

The solution of Ir(III) (Johnson Matthey) has been prepared by taking one gram of sample and making it upto 1 litre in hydrochloric acid of known strength. Iridium(III) in all the reactions undertaken, has been used as a homogenous catalyst.

(6) Mercury(II) Acetate-

Mercuric acetate (E. Merck) solution has been obtained by dissolving weighed amount of it firstly in glacial acetic acid (AR) and then making up to its required volume with double distilled water but acetic acid strength in $Hg(OAc)_2$ should never exceeded 10% v/v.

(7) Potassium chloride

The standard stock solution of KCl (E. Merck) has been prepared by dissolving fixed amount of sample in double distilled water.

(8) Potassium Iodide

4% solution of potassium iodide (E. Merck) has been prepared fresh every day just before starting the reactions by dissolving its sample in double distilled water.

(9) Acetic acid

Acetic acid solution (99.5%, LR Extrapure, s.d. fine Chem. Ltd.) was used as such.

(10) Sodium Thiosulphate ($Na_2S_2O_3.5H_2O$)

Appropriate weighed amount of sodium thiosulphate (E. Merck) was dissolved in known volume of double distilled water and the same has been standardized against standard copper sulphate (S.d. fine Chem. Ltd.) solution by iodometric titration using potassium iodide, where starch has been used an indicator.

(11) Starch

For making 1% starch (S.d. fine Chem. Ltd) solution specific amount of starch has been dissolved in double distilled water and boiled for few minutes. The solution has been prepared fresh each day and used as indicator in the present investigation.

(12) Sulphuric Acid (H_2SO_4)

H_2SO_4 (2N) solution has been prepared by making up measured volume of its sample in appropriate volume of double distilled water.

SEC. B.

2.1 Methodology

Throughout the course of investigation, for all the reactions the measuring conical flask (Jena glass) used were black coated from outside, so as to prevent any photochemical reactions. Use of double distilled water was ensured throughout the research work to avoid any undesired ion effect. The reagents used were of analytical grade. The real assessment of the reaction has been governed by estimating the amount of potassium bromate consumed during the course of reaction at regular time intervals against standard solution of hypo (Sodium thiosulphate (Hypo) iodometrically.

The reaction mixture is prepared by taking definite amount of all reactants i.e., perchloric acid, palladium(II) chloride/ Iridium(III) chloride, mercuric acetate, sodium perchlorate , substrate and water, except oxidant ($KBrO_3$) in a blackened conical flask and placing it in thermostatic water bath maintained at a constant temperature of 35^0C ($\pm0.01^0C$). Simultaneously fresh solution of oxidant was also kept in a separate black coated conical flask within the same thermostatic water bath at the same temperature. After half an hour when the reaction mixture acquired the temperature of the bath, required amount of oxidant solution was sucked out and poured in the conical flask which was already containing mixture all other reactants (i.e. appropriate amounts of each $HClO_4$, $PdCl_2$ / $IrCl_3$, $Hg(OAc)_2$, $NaClO_4$, substrate. (paracetamol or gabapentin and water) to initiate the reaction. The total volume of the reaction mixture after addition of oxidant has been maintained as 50 ml for each set of reactions. As soon as half of the oxidant solution has passed out from the pipette into reaction mixture, the stop watch was started to record time and immediately 5 ml. of reaction mixture is sucked out and quickly transferred to a conical flask already containing 5 ml. of KI (4%) solution and 10 ml. of (2N) H_2SO_4 solution and few drops of starch which acts as indicator.

The advancement of the reaction was tracked by estimation of unconsumed amount of $KBrO_3$ iodometrically. The remaining unconsumed amount of $KBrO_3$ interacts with KI and liberates an equivalent amount of iodine from KI solution, which was calibrated with standard solution of hypo, using starch as an indicator, which gives blue colour at the end point. This provided duplicable results with marked precision. Added mercuric acetate did not intervene in the reaction. It acts only as a scavenger(1) for any bromide ion created during the onward movement of the reaction . It eradicates completely oxidation by Br_2, the formation of which might have been initiated by the interaction of Bromate with Br^-. Thus, mercuric acetate makes certain that the oxidation observed has been purely through potassium bromate.

Various sets of experiments have been initiated upon altering the concentrations of diffrent constituents viz. substrate, mercuric acetate, perchloric acid, oxidant ($KBrO_3$), etc., at specific temperature and the changes in various experiments were assessed.

On the basis of the above variations the rate of reaction and order of reaction with respect to different constituents have been studied and mechanistic steps for the reaction were proposed taking into consideration the above results. The activation parameters (ΔH^*, ΔE_a, ΔG^* etc.) were calculated by performing the investigation in the temperature range 30-45^{0}C.

Summary:

In this chapter preparation of standard stock solutions to be utilized in the experiments i.e. $KBrO_3$, $HClO_4$, $PdCl_2$, $IrCl_3$, $Hg(OAc)_2$, $NaClO_4$, paracetamol, Gabapentin. Starch and H_2SO_4, KI, CH_3COOH, and $Na_2S_2O_3.5H_2O$ has been discussed. Ostwald isolation method and the steps to be undertaken for performing the experiment have been elaborated in order to determine the impact of various constituents on the rate of reaction, which inturn would assist in derivation of rate law.

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CHAPTER -3

DETERMINATION OF ORDER OF REACTION WITH RESPECT TO REACTANTS IN Pd(II) CATALYZED OXIDATION OF PHARMACEUTICAL DRUGS BY POTASSIUM BROMATE IN ACIDIC MEDIUM

3.1 Determination of order of reaction with respect to oxidant in Pd(II) catalyzed oxidation of pharmaceutical drugs by potassium bromate in acidic medium.

In this section, an attempt has been made to study the dependence of reaction rate on potassium bromate concentration i.e. [$KBrO_3$]. An experimental study of rate of reaction can be made by estimating the concentration(c) of the reactant as function of time (t) which will give the reaction rate i.e. dc/dt) at that instant of time. The relation between reaction rate and reactant concentrations will give rate equation for general reaction, as illustrated below:

$$\underset{\text{(Reactants)}}{A + B + C} \longrightarrow \text{Product}$$

The rate equation for the above reaction can be written as:

$$\text{Rate} = k[C_A]^{n_1}[C_B]^{n_2}[C_C]^{n_3} \ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

where k is the rate constant for the reaction and n_1, n_2 and n_3 indicate order with respect to the reactants A, B and C respectively. The total order (n) of the above reaction can be obtained as:-

$$n = n_1 + n_2 + n_3 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

In the present section for determination of order of reaction with respect to various reactants, we have followed isolation method in which the experiments have been carried out by taking all the reactants except one in fixed quantities, so that the concentration of other reactants remain constant throughout the investigation. Considering potassium bromate, pharmaceutical drugs, Pd(II) chloride, perchloric acid and potassium chloride as main reactants, the rate equation can be written in the following way:-

$$\text{Rate} = dc/dt = k\,[KBrO_3]^{n_1}\,[\text{Pharmaceutical drugs}]^{n_2}\,[Pd(II)]^{n_3}\,[H^+]^{n_4}\,[Cl^-]^{n_5} \ldots (3)$$

In proposed investigation, the order of reaction with respect to each reactant taking part in the reaction has been elucidated with the help of Ostwald isolation method, graphical and differential method.

In Ostwald isolation method, the reaction whose order is to be evaluated is taken in least concentration in comparison to other reactants. Therefore we are able to determine the order for that particular reactant which was taken in least amount.

For the elucidation of order of reaction with respect to potassium bromate (n_1), concentration of potassium bromate is changed while keeping the concentration of other reactants as constant, therefore the velocity of the reaction will mainly be determined by change in concentration of potassium bromate. Now rate equation will take the form:-

$$Rate = k_1 \, [KBrO_3]^{n_1} \quad \ldots\ldots\ldots\ldots\ldots(4)$$

where $k_1 = k[Pharmaceutical\ drugs]^{n_2} [Pd(II)]^{n_3} [H^+]^{n_4} [Cl^-]^{n_5}$

Rate of reaction is assessed in terms of decrease in the concentration of potassium bromate and may be written as:-

$$\frac{-d[KBrO_3]}{dt} = k_1 \, [KBrO_3]^1$$

If n=1

or

$$\frac{-d[KBrO_3]/\mathrm{dt}}{[KBrO_3]} = k_1 \ldots\ldots(5)$$

where k_1 is the first order rate constant. Equation (5) shows that a plot between $d[KBrO_3]/dt$ and $[KBrO_3]$ will give a straight line passing through the origin.

3.1.A: Reaction order for Potassium bromate in oxidation of gabapentin by acidic bromate in presence of $PdCl_2$ as catalyst.

Reaction order for potassium bromate in [Pd(II)] catalyzed oxidation of Gabapentin has been determined by performing various experiments at 35ºC and constant concentration of other reactants. Results obtained for various kinetic runs are presented in Table 3.1A(a) Concentration of potassium bromate was varied from 0.83 x 10^{-3} M to 5.00 x 10^{-3} M at constant concentration of all other reactants. Rate of reaction (-dc/dt) in each run was determined by slope of tangent at fixed time (5 min.)

A close perusal of Table 3.1A(a) indicates that the rate of reaction is almost linearly related to the concentration of potassium bromate i.e., with increase in concentration of potassium bromate, rate of reaction enhances in same proportion. Hence first order kinetics with respect to potassium bromate is confirmed. A plot of (-dc/dt) Vs. [$KBrO_3$] gives a straight line passing through the origin [Fig. 3.1A (a)]. 5th row in Table 3.1A(a) shows almost constant values of k_1 throughout the variation of [$KBrO_3$] which also supports the first order kinetics with respect to [$KBrO_3$]. First order kinetics is further confirmed by least square method from table 3.1 A(b) [Fig. 3.1A,(b)].

Table: 3.1A (a)

[GB] = 1.00×10^{-2} M   [KCl] = 1.00×10^{-3} M
[Pd(II)] = 11.20×10^{-5} M   [Hg(OAc)$_2$] = 1.25×10^{-3} M
[HClO$_4$] = 1.00×10^{-3} M   Temperature = 35^0C

[KBrO$_3$] → / 10^{-3} M	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	8.33	10.00	12.50	16.70	25.00	50.00
5	8.08	9.60	11.82	15.40	21.75	42.50
10	7.83	9.00	11.14	14.20	19.25	36.00
15	6.91	8.20	10.50	13.50	18.00	31.84
20	6.66	8.00	9.87	12.88	16.94	29.22
25	6.24	7.45	9.25	11.58	16.00	27.55
35	5.91	7.00	8.50	10.86	15.10	26.00
45	5.33	6.55	7.75	9.94	14.25	24.98
60	5.00	6.00	6.80	8.98	13.02	23.80
(-dc/dt) → / 10^{-7} Ms^{-1}	1.03	1.27	2.00	2.15	3.20	6.30
$k_1 = \frac{(-dc/dt)}{[KBrO_3]}$ → / 10^{-4} s^{-1}	1.24	1.27	1.60	1.28	1.28	1.26

.

C* = Volume of hypo used (N/400) in ml.

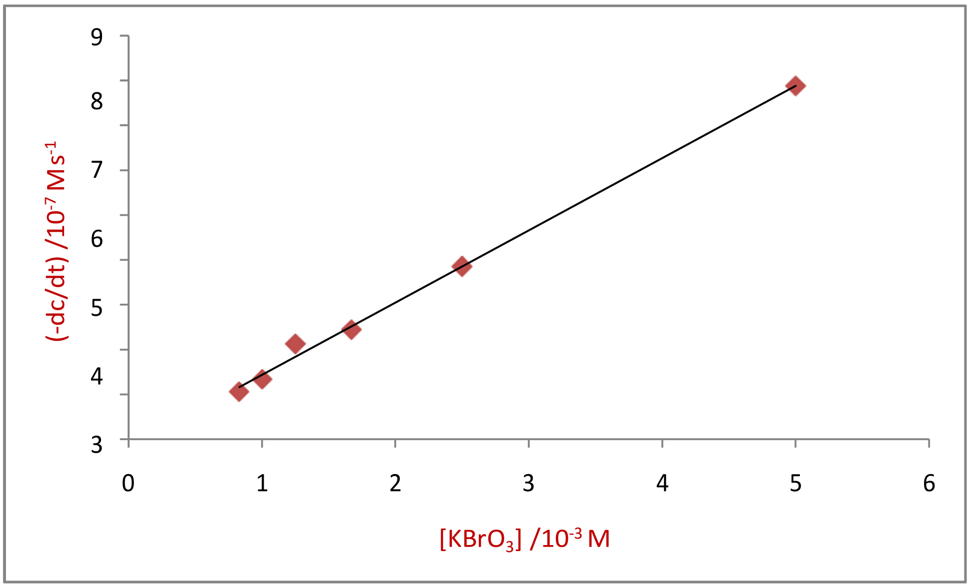

Figure3.1A(a): Plot between rate of reaction (-dc/dt) vs [$KBrO_3$] for the oxidation of gabapentin at 35 ºC. [$HClO_4$] = 1.00 x 10^{-3}M, [KCl] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [GB] = 1.00 x 10^{-2} M, [Pd(II)] =11.20 x 10^{-5} M

Table: 3.1A(b)

$[KBrO_3]$ / 10^{-3} (M)	(-dc/dt) (Y)	x (conc. – n)	x^2	xy	(a + bx)
0.83	1.03	-1.21	1.46	-1.24	1.15
1.00	1.27	-1.04	1.08	-1.32	1.36
1.25	2.00	-0.79	0.62	-1.58	1.67
1.67	2.15	-0.37	0.13	-0.79	2.19
2.50	3.20	0.46	0.21	1.47	3.22
5.00	6.30	2.96	8.76	18.64	6.32
12.25/6 n = 2.04	$\Sigma y = 15.95$	$\Sigma x = 0.00$	$\Sigma x^2 = 12.26$	$\Sigma xy = 15.18$	

$\Sigma y = Na + b\Sigma x$

$15.95 = 6a + 0$

$a = 15.95/6$

$= 2.65$

$\Sigma xy = a\,\Sigma x + b\Sigma x^2$

$15.18 = 0 + b \times 12.26$

$b = 15.18/12.26$

$= 1.24$

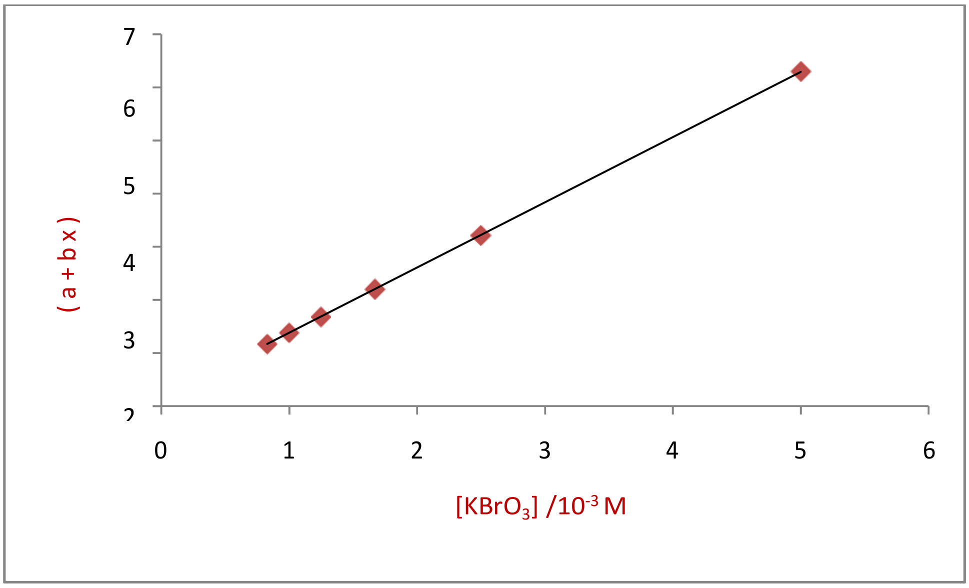

Figure3.1A(b): Plot between rate of reaction (a+bx) vs $[KBrO_3]$ for the oxidation of gabapentin at 35°C. $[HClO_4]$ = 1.00 x 10^{-3} M, [KCl] = 1.00 x 10^{-3} M, $[Hg(OAc)_2]$ =1.25 X 10^{-3}, [GB] =1.00 x 10^{-2} M, [Pd(II)]=11.20 x 10^{-5}M

3.1B: Determination of order of reaction with respect to oxidant in palladium (II) catalyzed oxidation of paracetamol by potassium bromate in acidic medium.

To determine the order of reaction with respect to potassium bromate in the oxidation of paracetamol in acidic medium, a number of experiments were performed at constant temperature of 35 ºC.

The concentration of potassium bromate was varied from 0.83 x 10^{-3} M to 5.00 x 10^{-3}M. The results obtained are presented in Table 3.1B(a) It is clear from the Table 3.1B(a) that the reaction follows first order kinetics. In each kinetic run upon increasing the concentration of potassium bromate the (-dc/dt) values also increase linearly. This result is further verified by plotting a graph between (-dc/dt) values and [$KBrO_3$] as shown in Fig. 3.1B(a). A straight line passing through the origin is obtained. This has also been confirmed by “least square method” [Table 3.1B(b) and Fig.3.1B (b)].

Table: 3.1B(a)

[PA]	= 1.00×10^{-2} M	[KCl]	= 1.00×10^{-3} M
[Pd(II)]	= 11.20×10^{-5} M	[Hg(OAc)$_2$]	= 1.25×10^{-3} M
[HClO$_4$]	= 1.00×10^{-3} M	Temperature	= 35^0C.

[KBrO$_3$] → / 10^{-3} M	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	8.33	10.00	12.50	16.70	25.00	50.00
5	7.91	9.25	11.37	15.03	22.00	44.50
10	7.48	8.78	10.75	14.19	20.75	40.00
15	7.00	8.22	10.00	13.36	19.40	36.00
20	6.66	7.30	9.37	12.52	18.25	33.95
25	6.33	6.70	8.75	11.62	17.50	30.50
35	6.16	6.25	8.00	10.85	15.00	27.50
45	4.99	5.25	7.50	10.00	13.75	25.00
60	4.58	4.50	6.37	8.35	11.00	22.50
(-dc/dt) → / 10^{-7} Ms^{-1}	1.92	2.60	2.52	3.81	5.32	10.60
$k_1 = \frac{(-dc/dt)}{[KBrO_3]}$ → / 10^{-4}s^{-1}	2.31	2.60	2.01	2.28	2.12	2.12

C* = Volume of hypo used (N/400) in ml

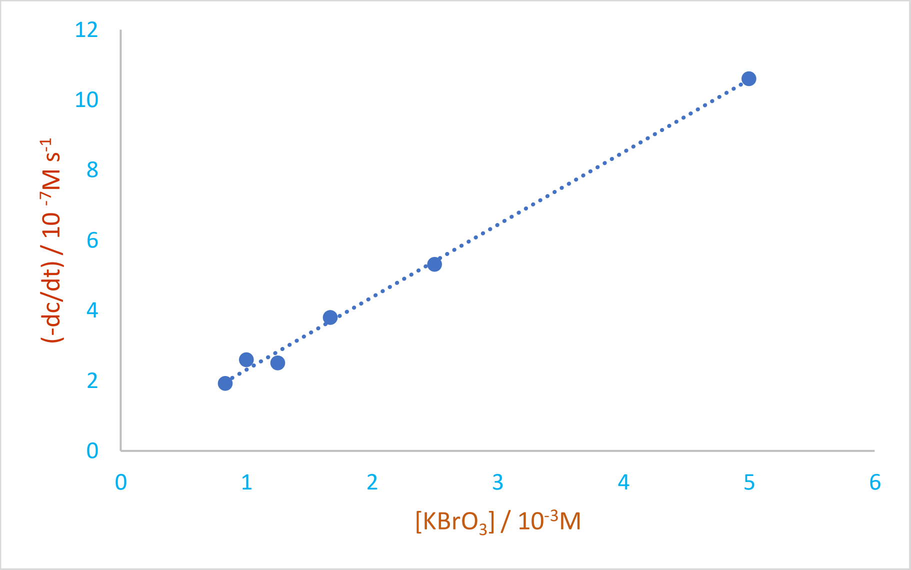

Figure3.1B(a): Plot between rate of reaction (-dc/dt) vs [$KBrO_3$] for the oxidation of paracetamol at 35^0C. [$HClO_4$] = 1.00 x 10^{-3}M, [KCl] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3}, [PA] = 1.00 x 10^{-2} M, [Pd(II)]=11.20 x 10^{-5} M

Table: 3.1B(b)

[$KBrO_3$] / 10^{-3} (M)	(-dc/dt) (Y)	x (conc. – n)	x^2	xy	(a + bx)
0.83	1.92	-1.21	1.46	-2.32	2.03
1.00	2.60	-1.04	1.08	-2.70	2.38
1.25	2.82	-0.79	0.62	-2.22	2.89
1.67	3.81	-0.37	0.13	-1.40	3.75
2.50	5.32	0.46	0.21	2.44	5.45
5.00	10.60	2.96	8.76	31.37	10.58
12.25/6 n = 2.04	Σy = 27.07	Σx = 0.00	Σx^2 = 12.26	Σxy = 25.17	

$$\Sigma y = Na + b\Sigma x$$

$$27.07 = 6 \text{ x } a + 0$$

$$a = 27.07/6$$

$$a = 4.51$$

$$\Sigma xy = a.\Sigma x + b\Sigma x^2$$

$$25.17 = 0 + b \text{ x } 12.26$$

$$b = 25.17/12.26$$

$$b = 2.05$$

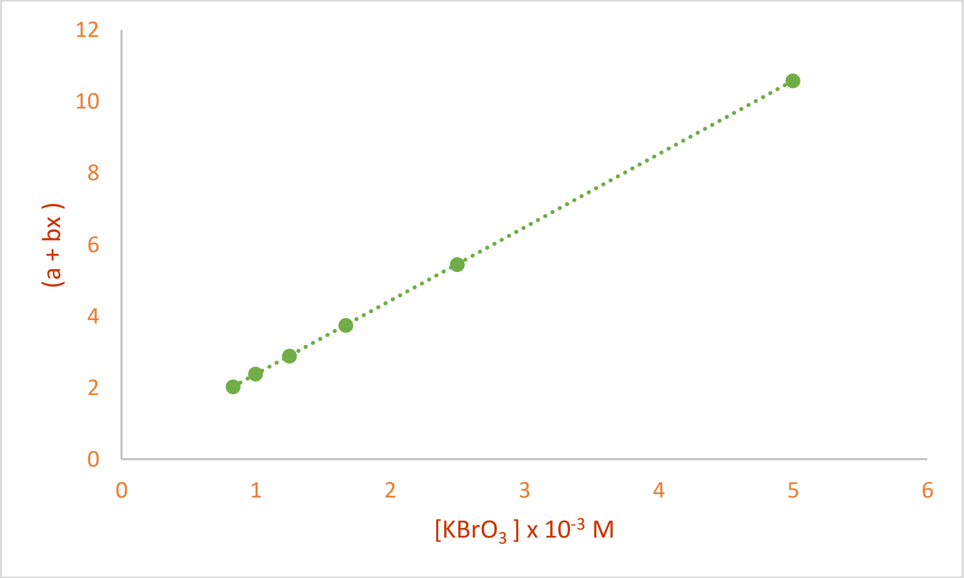

Figure-3.1B(b): Plot between rate of reaction (a+bx) vs [$KBrO_3$] for the oxidation of paracetamol at 35^0C. [$HClO_4$] = 1.00 x 10^{-3}M, [KCl] = 1.00 x 10^{-3}M, [$Hg(OAc)_2$] = 1.25 x 10^{-3}M, [PA] = 1.00 x 10^{-2} M, Pd(II) = 11.20 x 10^{-5} M

3.2: Reaction order for Palladium(II) chloride in oxidation of pharmaceutical drugs by acidic bromate in presence of $PdCl_2$ as catalyst.

The rate equation for Pd(II) catalyzed oxidation of pharmaceutical drugs by potassium bromate can be expressed as:-

$$\text{Rate} = -d\frac{[KBrO_3]}{dt} == k\,[KBrO_3]^{n_1}\,[Comp]^{n_2}\,[Pd(II)]^{n_3}\,[H^+]^{n_4}\,[Cl^-]^{n_5}$$

First order kinetics is observed with respect to potassium bromate i.e. $n_1 = 1$. In the variation of Pd(II) chloride concentration if other reactants are kept constant then equation reduces to

$$Rate = k_1\,[Pd(II)]^{n_3}$$

$$\text{where } k_1 = k\,[KBrO_3]^1[Comp]^{n_2}[H^+]^{n_4}[Cl^-]^{n_5}$$

values of k_1 have been calculated for each kinetic run to predict the order of reaction with respect to Pd(II) chloride.

3.2 A: Determination of order of reaction with respect to catalyst in palladium (II) catalyzed oxidation of gabapentin by potassium bromate in acidic medium.

In order to determine the effect of Pd(II) chloride on the rate of reaction, its concentration has been varied from 5.60×10^{-5} M to 44.80×10^{-5} M at constant temperature 35^0C. All the results obtained are presented in Table 3.2A(a) For each run (-dc/dt) values have been calculated from the slopes of tangents drawn at fixed concentrations of all reactants. A close examination of Table 3.2A(a) suggests that with increase in the concentration of catalyst there is an increase in (-dc/dt) values, showing that there is a linear relationship between (-dc/dt) values and [Pd(II)] (Fig. 3.2A (a). This linear relationship clearly indicates that the reaction follows first order kinetics with respect to catalyst concentrations. This has also been confirmed by “least-square method” [Table 3.2A(b) and fig-3.2A(b)].

Table: 3.2A (a)

[GB]	= 1.00×10^{-2} M	[KCl]	= 1.00×10^{-3} M
[$KBrO_3$]	= 1.00×10^{-3} M	[$Hg(OAc)_2$]	= 1.25×10^{-3} M
[$HClO_4$]	= 1.00×10^{-3} M	Temperature	= 35^0C.

[Pd(II)] / 10^{-5} M →	5.60	11.20	16.80	22.40	33.60	44.80
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.81	9.60	9.30	9.00	8.72	8.54
10	9.30	8.95	8.42	8.12	7.85	7.57
15	8.82	8.40	8.00	7.45	7.02	6.64
20	8.45	8.00	7.63	7.00	6.62	6.00
25	7.98	7.45	7.20	6.46	6.00	5.60
35	7.60	7.00	6.63	6.12	5.43	4.68
45	7.25	6.34	6.20	5.57	4.96	3.94
60	6.98	6.05	5.65	5.10	4.50	3.06
(-dc/dt) / 10^{-7} Ms^{-1} →	0.62	1.27	1.82	2.45	3.66	4.95
$k_1 = \frac{dc/dt}{[Pd(II)]}$ / $10^{-3}s^{-1}$ →	1.10	1.13	1.08	1.09	1.09	1.10

C* = Volume of hypo used (N/400) in ml.

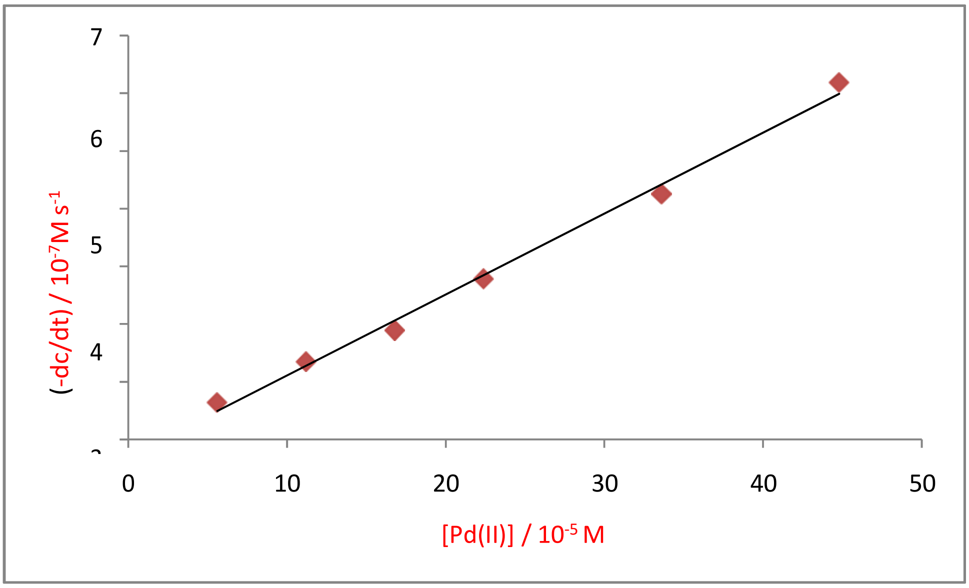

Figure-3.2A(a): Plot between rate of reaction (-dc/dt) vs [Pd(II)] for the oxidation of gabapentin at 35⁰C. [$HClO_4$] = 1.00 x 10^{-3}M, [KCl] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [GB] = 1.00 x 10^{-2} M, [$KBrO_3$] = 1.00 x 10^{-3}

<u>Table: 3.2A(b)</u>

[Pd(II)] / 10^{-5} (M)	(-dc/dt) (Y)	x (conc. – n)	x^2	xy	(a + bx)
5.60	0.62	-16.8	282.24	-10.41	0.61
11.20	1.27	-11.2	125.44	-14.22	1.23
16.80	1.82	-5.6	31.36	-10.19	1.84
22.40	2.45	00	00	00	2.46
33.60	3.66	11.2	125.44	40.99	3.69
44.80	4.95	22.4	501.76	110.88	4.92
134.4/6 n =22.4	Σy = 14.77	Σx = 0.00	Σx^2 = 1,066.24	Σxy = 117.05	

$\Sigma y = Na + b\Sigma x$

$14.77 = 6a + 0$

$a = 14.77/6$

$a = 2.46$

$\Sigma xy = a\Sigma x + b\Sigma x^2$

$117.05 = 0 + b \times 1066.24$

$b = 117.05/1066.24$

$b = 0.11$

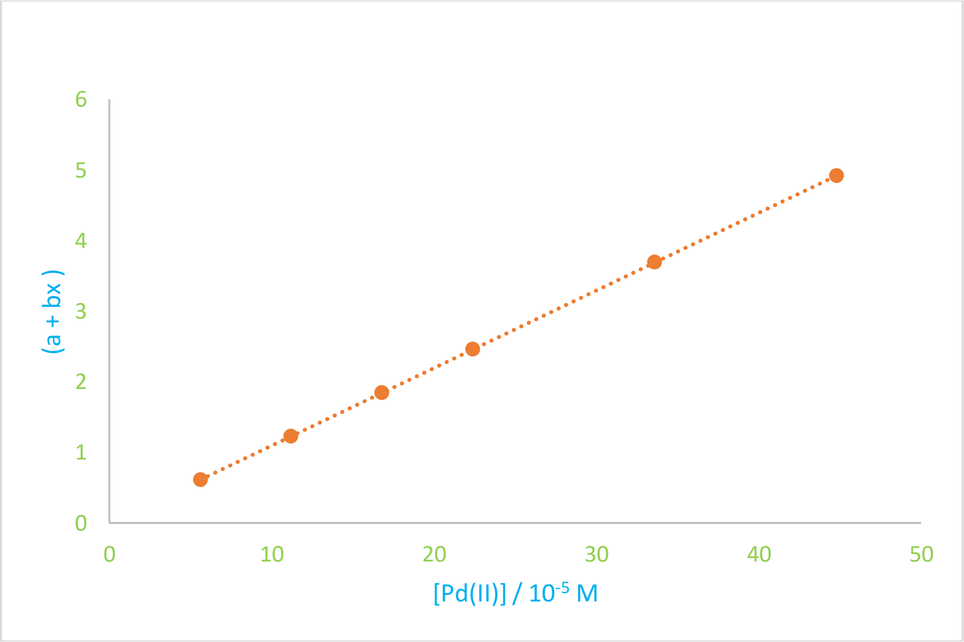

Fig:3.2A (b) Plot between rate of reaction (a+bx) vs [Pd(II)] for the oxidation of gabapentin at 35^{0}C. [HClO$_4$] = 1.00 x 10^{-3} M, [KCl] = 1.00 x 10^{-3} M, [Hg(OAc)$_2$] = 1.25 x 10^{-3}M, [GB]= 1.00 x 10^{-2} M, [KBrO$_3$] = 1.00 x 10^{-3} M

3.2B: Determination and kinetic study of order of reaction with respect to catalyst Pd(II) in Pd(II) catalyzed oxidation of paracetamol by acidic $KBrO_3$.

To determine the order of reaction of Pd(II) chloride on the rate of reaction, its concentration has been varied from 5.60×10^{-5} M to 44.80×10^{-5} M keeping the concentration of all other reactants fixed at constant temperature 35^0C.

All the results obtained are presented in Table 3.2B(a). For each kinetic run (-dc/dt) values have been calculated from the slopes of tangents drawn at constant concentrations of all reactants. The data of Table 3.2B(a). proposed that while enhancing the concentration of catalyst there is an increase in (-dc/dt) values, which represents a linear relationship between (-dc/dt) values and [Pd(II)] (Fig. 3.2B(a). This means that the reaction follows first order kinetics with respect to catalyst. This has further been confirmed by “least-square method” {Table 3.2B(b) and fig-3.2B(b)}.

Table: 3.2B(a)

[PA] = 1.00×10^{-2} M

[$KBrO_3$] = 1.00×10^{-3} M

[$HClO_4$] = 1.00×10^{-3} M

[KCl] = 1.00×10^{-3} M

[$Hg(OAc)_2$] = 1.25×10^{-3} M

Temperature = 35^0C.

[Pd(II)] → / 10^{-5} M	5.60	11.20	16.80	22.40	33.60	44.80
Time (Min.)	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.45	9.25	8.80	8.71	8.60	8.20
10	8.98	8.78	8.22	8.08	7.62	7.34
15	8.50	8.22	7.64	7.30	6.80	6.15
20	8.04	7.30	7.02	6.50	5.92	5.00
25	7.65	6.70	6.57	5.82	5.15	4.35
35	7.20	6.25	5.62	5.00	4.20	3.40
45	6.75	5.25	4.94	4.38	3.58	2.94
60	6.20	4.50	4.05	3.86	2.88	2.30
(-dc/dt) → / 10^{-7} Ms^{-1}	1.33	2.60	5.02	5.18	8.35	10.21
$k_1 = \frac{(-dc/dt)}{[Pd(II)]}$ → / 10^{-3} s^{-1}	2.37	2.32	2.98	2.31	2.45	2.28

C* = Volume of hypo used (N/400) in ml.

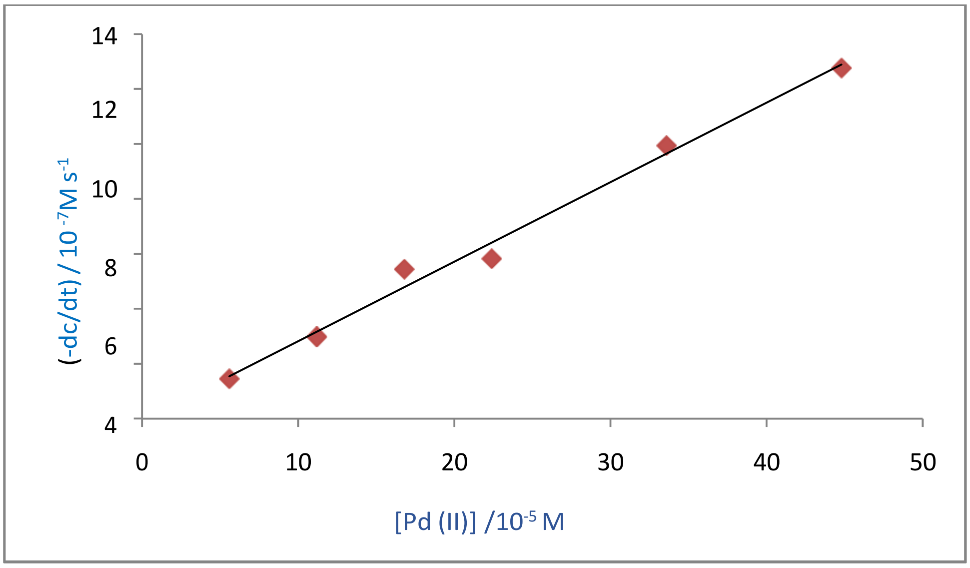

Fig : 3.2B(a): Plot between rate of reaction (-dc/dt) vs [Pd(II)] for the oxidation of paracetamol at 35⁰C. [$HClO_4$] =1.00 x 10^{-3}M, [KCl] =1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [PA] = 1.00 x 10^{-2} M, [$KBrO_3$] =1.00 x 10^{-3} M

Table: 3.2B(b)

[Pd(II)] / 10^{-5} (M)	(-dc/dt) (Y)	x (conc. – n)	x^2	xy	(a + bx)
5.60	1.33	-16.8	282.24	-22.34	1.57
11.20	2.60	-11.2	125.44	-29.12	2.86
16.80	5.02	-5.6	31.36	-28.11	4.15
22.40	5.18	00	00	00	5.44
33.60	8.35	11.2	125.44	93.52	8.02
44.80	10.21	22.4	501.76	228.70	10.59
134.4/6 n =22.4	Σy = 32.69	Σx = 0.00	Σx^2 = 1,066.24	Σxy = 242.65	

$\Sigma y = Na + b\Sigma x$

$32.69 = 6a + 0$

$a = 32.69/6$

$a = 5.44$

$\Sigma xy = a\Sigma x + b\Sigma x^2$

$242.65 = 0 + b \times 1{,}066.24$

$b = 242.65/1066.24$

$b = 0.23$

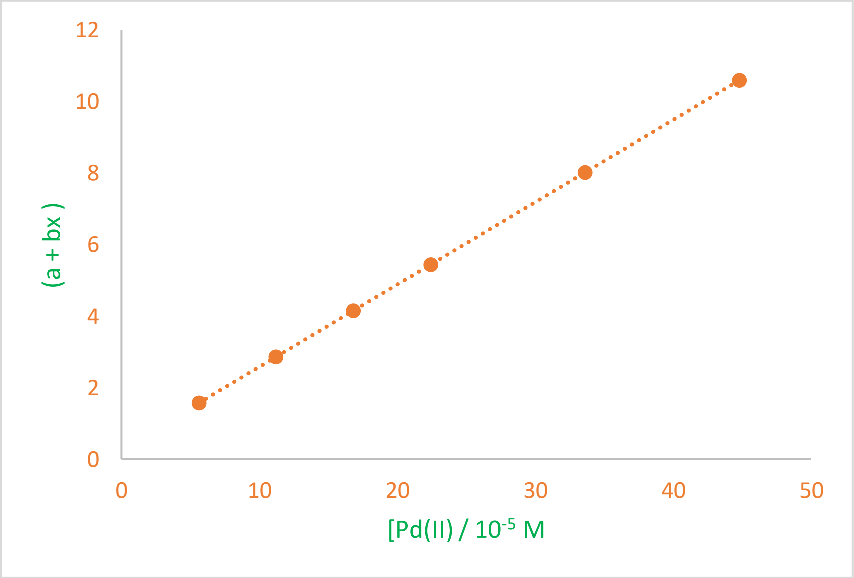

Figure : 3.2B(b) Plot between rate of reaction (a+bx) vs [Pd(II)] for the oxidation of paracetamol at 35^{0}C. [$HClO_4$] =1.00 x 10^{-3}M, [KCl] =1.00 x 10^{-3}M [$Hg(OAc)_2$] = 1.25 x 10^{-3}M, [PA] = 1.00 x 10^{-2} M, [$KBrO_3$] = 1.00 x 10^{-3} M

3.3.A: Determination and kinetic study of order with respect to compound gabapentin in Pd(II) catalyzed oxidation of gabapentin by acidic $KBrO_3$.

To determine the order of reaction with respect to gabapentin when it is oxidized by acidic potassium bromate in presence of Pd(II) chloride as catalyst, concentration of gabapentin has been varied from 0.40 x 10^{-2} M to 4.00 x 10^{-2} M keeping the concentration of all other reactants fixed at constant temperature 35^0C.

All the results obtained are presented in Table 3.3A(a). For each run (-dc/dt) values have been calculated from the slopes of tangents drawn at fixed concentrations of all reactants. A close examination of Table 3.3A(a) suggests that with increase in the concentration of substrate there is no change shown in(-dc/dt) values of gabapentin.

Thus a persusal of table 3.3A(a) reflects that there is no alteration in the rate of reaction when the concentration of substrate is decreased or increased showing zero order kinetics with respect to [GB]. This is also confirmed by plotting a graph between (-dc/dt) versus [GB]. A straight line is obtained parallel to x- axis showing again zero order kinetics with respect to gabapentin.

Table: 3.3A (a)

$[KBrO_3]$ = 1.00×10^{-3} M
$[Pd(II)]$ = 11.20×10^{-5} M
$[HClO_4]$ = 1.00×10^{-3} M

[KCl] = 1.00×10^{-3} M
$[Hg(OAc)_2]$ = 1.25×10^{-3} M
Temperature = 35^0C.

[GB] → / 10^{-2} M	0.40	0.50	0.66	1.00	2.00	4.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.60	9.44	9.35	9.60	9.30	9.58
10	9.23	9.00	8.90	9.00	8.63	8.85
15	8.85	8.53	8.21	8.20	8.12	8.38
20	8.20	7.82	7.80	7.84	7.82	7.80
25	7.84	7.10	7.43	7.35	7.42	7.18
35	7.20	6.68	7.00	6.90	6.80	6.64
45	6.62	6.32	6.44	6.58	6.43	6.38
60	6.00	5.88	6.21	5.94	6.00	5.90
(-dc/dt) → / 10^{-7} Ms^{-1}	1.22	1.10	1.32	1.27	1.13	1.00

C* = Volume of hypo used (N/400) in ml.

3.3B: Reaction order with respect to compound (Paracetamol) in Pd(II) catalyzed oxidation of paracetamol by acidic $KBrO_3$.

To determine the order of reaction for Paracetamol in its Pd(II) catalyzed oxidation by acidic potassium bromate, the concentration of Paracetamol has been varied from 0.40 x 10^{-2} M to 4.00 x 10^{-2} M keeping the concentration of all other reactants fixed at constant temperature 35^0C.

All the results obtained are presented in Table 3.3B(a) For each kinetic run (-dc/dt) values have been calculated from the slopes of tangents drawn at fixed concentrations of all reactants. A close examination of Table 3.3B (a) and fig-3.3B (a) suggests that with increase in the concentration of substrate there is an increase in (-dc/dt) values. This indicates a positive effect with respect to substrate i.e. paracetamol. A plot of log (-dc/dt) vs.log [PA], (fig.3.3B(b), gives a straight line with positive slope of 0.40

Table: 3.3B(a)

[$KBrO_3$] = 1.00 x 10^{-3} M
[KCl] = 1.00 x 10^{-3} M
[Pd(II)] = 11.20 x 10^{-5} M
[$Hg(OAc)_2$] = 1.25 x 10^{-3} M
[$HClO_4$] = 1.00 x 10^{-3} M
Temperature = 35^0C.

[PA] → / 10^{-2} M	0.40	0.50	0.66	1.00	2.00	4.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.65	9.50	9.30	9.25	9.00	8.72
10	9.24	8.85	8.50	8.30	8.12	8.00
15	8.88	8.50	8.20	7.92	7.62	7.20
20	8.50	8.00	7.83	7.42	6.94	6.58
25	8.00	7.75	7.00	6.70	6.21	5.90
35	7.44	7.05	6.21	5.62	5.40	4.98
45	6.90	6.25	5.45	4.60	4.20	4.00
60	6.45	5.50	4.50	4.00	3.40	3.14
(-dc/dt) → / 10^{-7} Ms^{-1}	1.62	1.86	2.10	2.60	3.00	4.12

C* = Volume of hypo used (N/400) in ml.

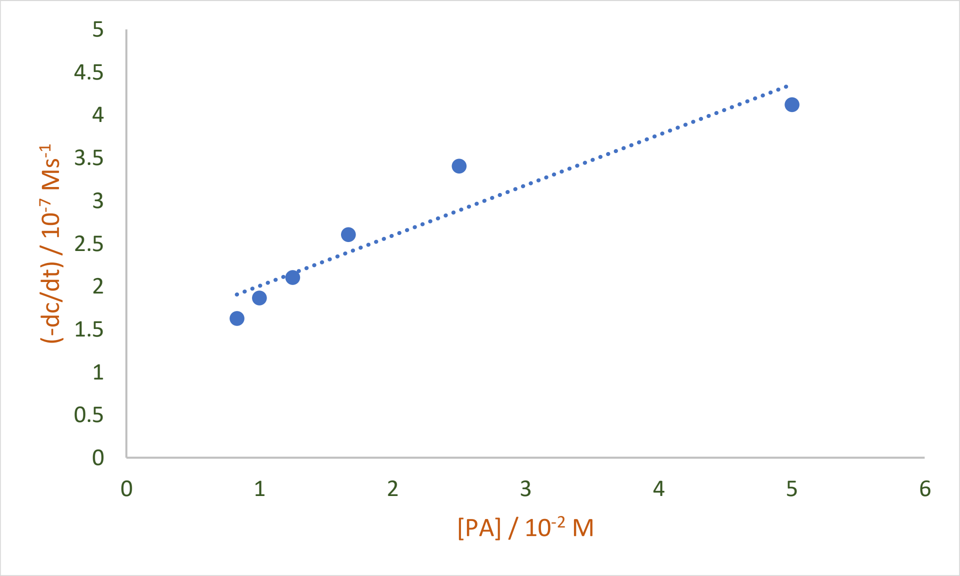

Figure: 3.3B(a): Plot between rate of reaction (-dc/dt) vs [PA] for the oxidation of paracetamol at 35^0C. [$HClO_4$] = 1.00 x 10^{-3}M, [KCl] =1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [$KBrO_3$] = 1.00 x 10^{-3}M, [Pd(II)] = 11.20 x 10^{-5} M

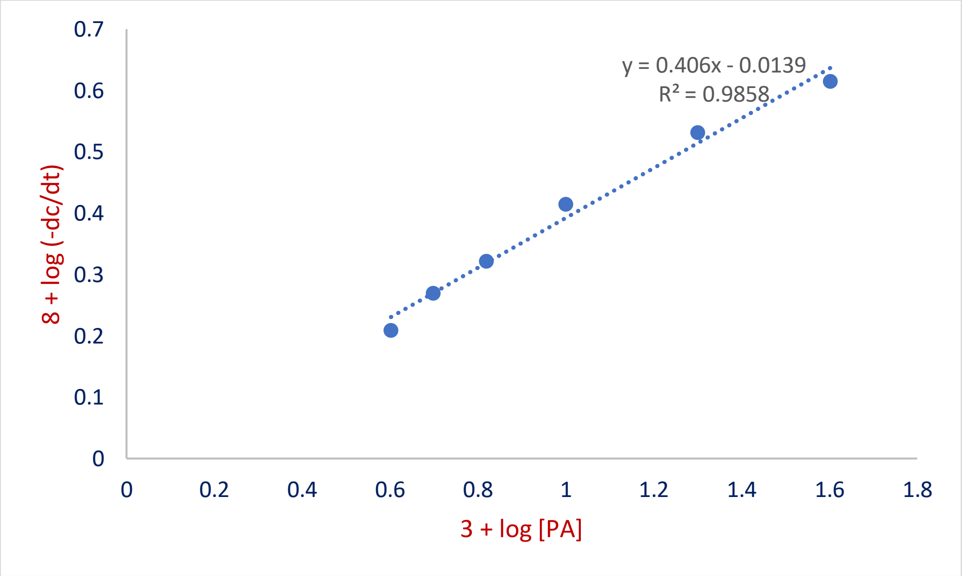

Figure: 3.3B(b): Plot between rate of reaction log(-dc/dt) vs log[PA] for the oxidation of paracetamol at 35^0C. [$HClO_4$] = 1.00 x 10^{-3}M, [KCl] =1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [$KBrO_3$] = 1.00 x 10^{-3}M, [Pd(II)] = 11.20 x 10^{-5} M

3.4: Determination and kinetic study of the effect of chloride ion in Pd(II) catalyzed oxidation of pharmaceutical drugs by acidic $KBrO_3$.

In order to determine the effect of addition of chloride ion on the reaction rate of Pd(II) catalyzed oxidation of pharmaceutical drugs by potassium bromate in acidic medium, different concentrations of KCl were added to the reaction mixture. The concentration of KCl has been varied from 0.83×10^{-3} M to 5.00×10^{-3} M.

3.4A: Impact of change in chloride ion concentration on the rate of Pd(II) catalyzed oxidation of gabapentin by acid bromate.

To investigate the impact of chloride ion in Pd(II) catalyzed oxidation of gabapentin by $KBrO_3$ in acidic medium, the concentration of KCl has been varied from 0.83×10^{-3} M to 5.00×10^{-3} M. The table 3.4A(a) shows that upon increasing the concentration of KCl, rate of reaction also increases. All the results obtained are presented in Table 3.4A(a). For each run (-dc/dt) values have been calculated from the slopes of tangents drawn at fixed concentrations of all other reactants.

The ascending value of (-dc/dt) with increase in concentration of [KCl] indicates a positive effect of KCl on the rate of reaction. A graph plotted between (-dc/dt) and [KCl] values gives a straight line with positive slope, which further confirms that KCl has positive effect on the rate of reaction as shown in Fig 3.4A

Table: 3.4A(a)

[GB] = 1.00×10^{-2} M

[Pd(II)] = 11.20×10^{-5} M

[$HClO_4$] = 1.00×10^{-3} M

[$KBrO_3$] = 1.00×10^{-3} M

[$Hg(OAc)_2$] = 1.25×10^{-3} M

Temperature = 35^0C.

[KCl] / 10^{-3} M →	0.83	1.00	1.25	1.67	2.5	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.82	9.60	9.23	9.00	8.63	8.32
10	9.42	9.00	8.62	8.42	8.12	7.60
15	9.00	8.20	8.12	8.00	7.62	7.12
20	8.56	8.00	7.50	7.23	7.12	6.53
25	8.18	7.45	7.01	6.84	6.46	5.88
35	7.31	7.00	6.43	6.20	6.00	5.20
45	6.84	6.55	6.12	5.74	5.30	4.86
60	6.43	6.00	5.40	5.21	5.00	4.40
(-dc/dt) / 10^{-7} Ms^{-1} →	1.15	1.27	1.35	1.65	2.45	3.92

C* = Volume of hypo used (N/400) in ml.

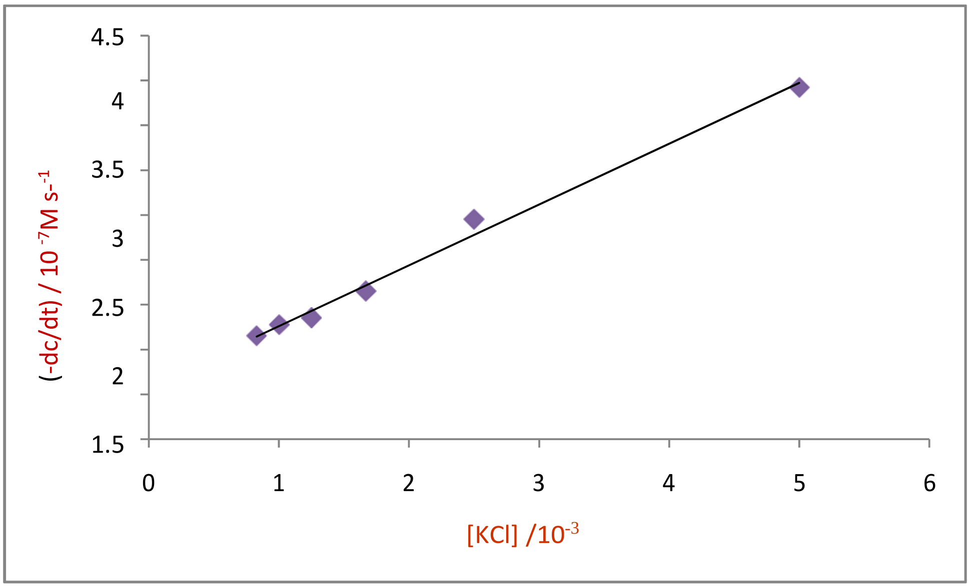

Figure: 3.4A: Plot between rate of reaction (-dc/dt) vs [KCl] for the oxidation of gabapentin at 35^0C. [$HClO_4$] = 1.00 x 10^{-3}M, [$KBrO_3$] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [GB] = 1.00 x 10^{-2} M, [Pd(II)] = 11.20 x 10^{-5} M

3.4B: Kinetic study of the effect of chloride ion in Pd(II) catalyzed oxidation of paracetamol drug by acidic $KBrO_3$.

To determine the impact of chloride ion on Pd(II) catalyzed oxidation of paracetamol by $KBrO_3$ in acidic medium, various concentration of KCl were added to reaction mixture and the result have been obtained and tabulated in table 3.4B(a). The concentration of KCl has been changed from 0.83 x 10^{-3} M to 5.00 x 10^{-3} M. Thus a close perusal of the table concluded that there is no alteration in the rate of reaction when the concentration of KCl is decreased or increased indicating zero order dependence with respect to [KCl] on the reaction rate. This is also confirmed by plotting a graph between (-dc/dt) versus [KCl]. A straight line is obtained parallel to x- axis showing again zero order kinetics with respect to KCl.

Table: 3.4B (a)

[PA]	= 1.00×10^{-2} M	[$KBrO_3$]	= 1.00×10^{-3} M
[Pd(II)]	= 11.20×10^{-5} M	[$Hg(OAc)_2$]	= 1.25×10^{-3} M
[$HClO_4$]	= 1.00×10^{-3} M	Temperature	= 35^0C.

[KCl] → / 10^{-3} M	0.83	1.00	1.25	1.67	2.5	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.22	9.25	9.00	9.30	9.20	9.51
10	8.70	8.78	8.61	8.61	8.55	8.45
15	8.12	8.22	8.00	8.01	7.92	8.00
20	7.80	7.30	7.61	7.82	7.46	7.50
25	7.42	6.70	7.12	7.00	6.98	7.22
35	6.88	6.25	6.50	6.42	6.44	6.88
45	6.24	5.25	6.00	5.98	5.98	6.30
60	5.76	4.50	5.32	5.40	5.35	5.66
(-dc/dt) → / 10^{-7} Ms^{-1}	2.23	2.60	2.00	2.81	2.52	2.42

C* = Volume of hypo used (N/400) in ml.

3.5: Effect of hydrogen ion concentration for Potassium bromate oxidized reaction of pharmaceutical drugs in presence of $PdCl_2$ as catalyst

The impact of hydrogen ion concentration on reaction rate has been studied by varying concentration of perchloric acid. $HClO_4$ acts as a source of hydrogen ion$[H^+]$ in the reaction investigated.

$$\frac{-d[KBrO_3]}{dt} = k[KBrO_3]^{n_1} [\text{Pharmaceutical drug}]^{n_3} [\text{Pd(II)}]^{n_3} [H^+]^{n_4} [Cl^-]^{n_5} \text{……..(i)}$$

In above equation (i), the values of n_1, n_2 and n_3 have already been found out to be one, zero & one respectively, in previous sections of this chapter. Equation (i) can be written as:-

$$\frac{-d[KBrO_3]}{dt} = k[KBrO_3]^1 [\text{Pharmaceutical drug}]^0 [\text{Pd(II)}]^1 [H^+]^{n_4} [Cl]^{n_5} \text{………(iv)}$$

or

$$\frac{-d[KBrO_3]/dt}{[KBrO_3]} = k[Pd(II)]\ [H^+]^{n_4}\ [Cl^-]^{n_5}\ . \qquad \text{……..(iii)}$$

or
$$\frac{-d[KBrO_3]/dt}{[KBrO_3]} = k_1 [H^+]^{n_4} \text{………..(iv)}$$

where $k_1 = k[Pd(II)]\ [Cl^-]^{n_5}$

............(v)

where k_1 is first order rate constant.

3.5A: Determination and effect of variation in hydrogen ion concentration on the rate of Pd(II) catalyzed oxidation of gabapentin by acid bromate.

The concentration of hydrogen perchlorate was varied from 0.83×10^{-3} M to 5.00×10^{-3} M. The results obtained are presented in Table 3.5A(a). It is clear from Table 3.5A(a) that the reaction follows first order kinetics which is further verified by plotting a graph between (-dc/dt) values and $[HClO_4]$ as shown in Fig. 3.5A(a).

A straight line is obtained and these results are further confirmed by "least-square method" Table 3.5A(b) and Fig. 3.5A(b)

Table: 3.5A (a)

[GB]	= 1.00×10^{-2} M	[KCl]	= 1.00×10^{-3} M
[Pd(II)]	= 11.20×10^{-5} M	[$Hg(OAc)_2$]	= 1.25×10^{-3} M
[$KBrO_3$]	= 1.00×10^{-3} M	Temperature	= 35^0C.

[$HClO_4$] / 10^{-3} M →	0.83	1.00	1.25	1.67	2.5	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.77	9.60	9.42	9.10	8.73	8.10
10	9.23	9.00	8.40	8.23	8.00	7.21
15	9.00	8.20	8.00	7.82	7.20	6.58
20	8.62	8.00	7.53	7.23	6.80	6.00
25	8.21	7.45	7.12	7.00	6.40	5.24
35	7.45	7.00	6.10	5.63	5.50	4.62
45	7.00	6.55	5.53	5.20	5.00	4.00
60	6.50	6.00	5.00	4.68	4.10	3.42
(-dc/dt) / 10^{-7} Ms^{-1} →	1.00	1.27	1.62	2.10	3.05	6.92
$k_1 = \frac{(-dc/dt)}{[HClO_4]}$ / 10^{-4} s^{-1} →	1.20	1.27	1.29	1.25	1.22	1.38

C* = Volume of hypo used (N/400) in ml.

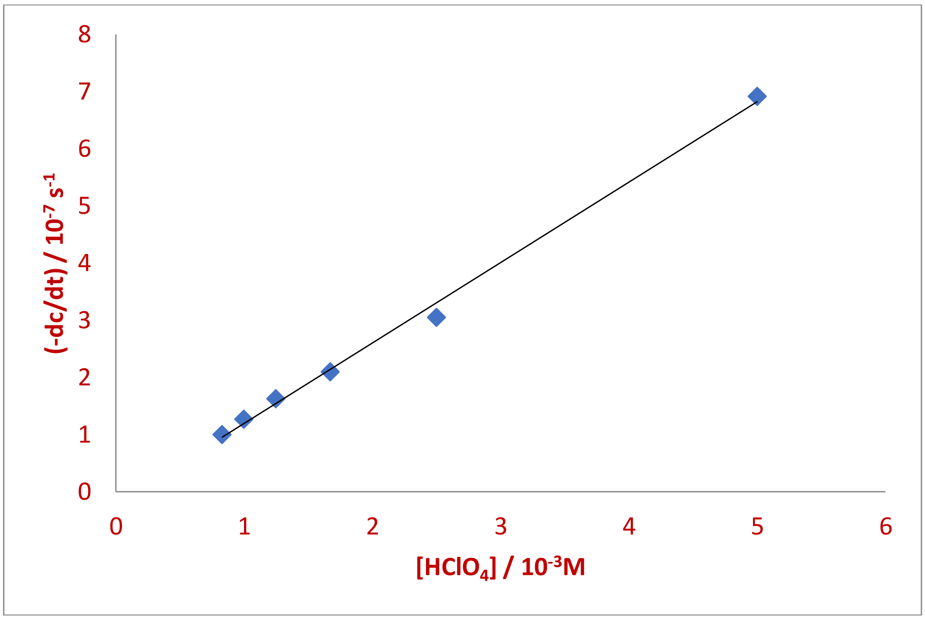

Figure3.5A(a): Plot between rate of reaction (-dc/dt) vs [HClO$_4$] for the oxidation of gabapentin at 35^{0}C. [KBrO$_3$] = 1.00 x 10^{-3}M, [KCl] = 1.00 x 10^{-3} M, [Hg(OAc)$_2$] = 1.25 x 10^{-3} M, [GB] = 1.00 x 10^{-2} M, [Pd(II)] =11.20 x 10^{-5} M

Table: 3.5A(b)

[HClO$_4$] / 10^{-3}(M)	(-dc/dt) (Y)	x (conc. – n)	x^2	xy	(a + bx)
0.83	1.00	-1.21	1.46	-1.21	0.95
1.00	1.27	-1.04	1.08	-1.32	1.19
1.25	1.62	-0.79	0.62	-1.27	1.54
1.67	2.10	-0.37	0.13	-0.77	3.18
2.50	3.05	0.46	0.21	1.40	3.30
5.00	6.92	2.96	8.76	20.48	6.83
12.25/6 n = 2.04	Σy = 15.96	Σx = 0.00	Σx^2 = 12.26	Σxy = 17.31	

$\Sigma y = Na + b\Sigma x$

$15.96 = 6a + 0$

$a = 15.96/6$

$a = 2.66$

$\Sigma xy = a\Sigma x + b\Sigma x^2$

$17.31 = 0 + b \times 12.26$

$b = 17.31/12.26$

$b = 1.41$

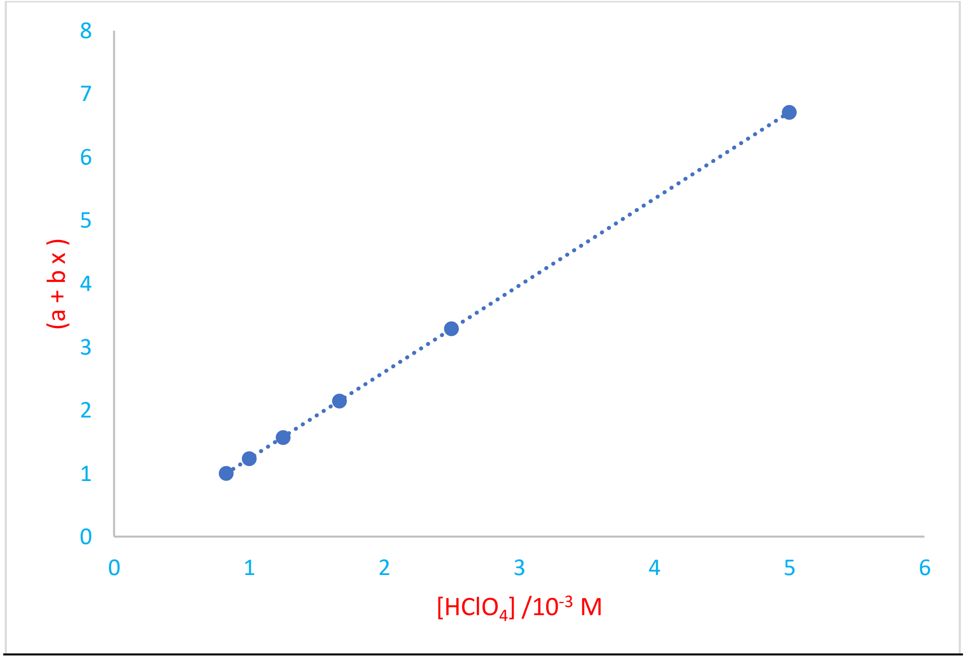

Figure: 3.5A(b) Plot between rate of reaction (a+bx) vs [$HClO_4$] for the oxidation of gabapentin at 35^{0}C. [KCl] = 1.00 X 10^{-3} M, [$Hg(OAc)_2$] = 1.25 X 10^{-3}M, [GB] = 1.00 x 10^{-2} M, [Pd(II)] = 11.20 x 10^{-5} M, [$KBrO_3$] = 1.00 x 10^{-3} M

3.5B: Effect of variation in hydrogen ion concentration on the rate of Pd(II) catalyzed oxidation of paracetamol by potassium bromate in acidic medium.

To justify the role of hydrogen ion in the Pd(II) catalyzed oxidation of paracetamol by bromate in acidic medium, various experiments were performed at 35^0C.

The hydrogen perchlorate concentration was varied from 0.83 x 10^{-3} M to 5.00 x 10^{-3} M. The result observed is presented in Table 3.5B(a). A perusal of (-dc/dt) values shows decreasing trend in the figure. It is clear from Table 3.5B(a) that addition of [$HClO_4$] has negative impact on reaction rate. In each kinetic run on enhancing the concentration of $HClO_4$, the (-dc/dt) values decrease as seen in fig-3.5B (a). When a plot of (-dc/dt) values is drawn against concentration of $HClO_4$ a negative curve is obtained with negative slope -0.41

<u>Table: 3.5B (a)</u>

[PA] = 1.00 x 10^{-2} M
[Pd(II)] = 11.20 x 10^{-5} M
[$KBrO_3$] = 1.00 x 10^{-3} M
[KCl] = 1.00 x 10^{-3} M
[$Hg(OAc)_2$] = 1.25 x 10^{-3} M
Temperature = 35^0C.

[$HClO_4$] / 10^{-3} M →	0.83	1.00	1.25	1.67	2.5	5.00
Time (Min.)	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	7.50	9.25	8.50	9.00	9.15	9.50
10	6.80	8.78	8.00	8.50	8.78	9.00
15	6.18	8.22	7.25	8.02	8.22	8.52
20	5.54	7.30	7.00	7.52	7.72	7.98
25	4.70	6.70	6.25	7.25	7.30	7.60
35	3.80	6.25	5.00	6.00	6.28	7.00
45	3.00	5.25	4.25	5.12	5.22	6.50
60	2.50	4.50	3.50	4.00	4.50	6.00
(-dc/dt) / 10^7 Ms^{-1} →	2.90	2.60	2.41	2.10	1.78	1.00

C* = Volume of hypo used (N/400) in ml.

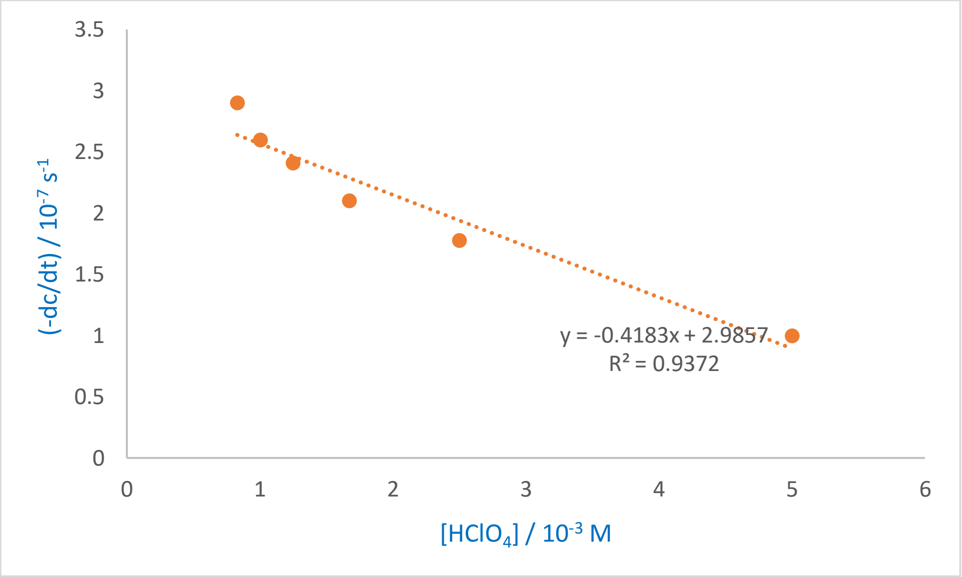

Figure:3.5B.(a): Plot between rate of reaction (-dc/dt) vs [$HClO_4$] for the oxidation of paracetamol at 35^0C. [$KBrO_3$] = 1.00 x 10^{-3} M, [KCl] = 1.00 x 10^{-3}M, [$Hg(OAc)_2$] =1.25 x 10^{-3}M, [PA]= 1.00 x 10^{-2} M,[Pd(II)] = 11.20 x 10^{-5} M

3.6: Impact of mercuric acetate on reaction rate in oxidation of pharmaceutical drugs by $KBrO_3$ in presence of Pd(II) as homogeneous catalyst in acidic medium.

In the proposed research, $Hg(OAc)_2$ is not acting as an oxidant because reaction does not initiate without addition of $KBrO_3$. Various experiments were performed with constant conc. of $KBrO_3$. and varing conc. of $Hg(OAc)_2$. It was observed that the reaction rate is unaffected which means $Hg(OAc)_2$ is neither acting as oxidant nor as a catalyst.

This rules out possibility of mercuric acetate being involved as catalyst in the reactions. Hence it only functions as a scavenger for bromide ion.

3.6A: Impact of variation in mercuric acetate on the reaction rate for oxidation of gabapentin by $KBrO_3$ in presence of Pd(II) as homogeneous catalyst in acidic medium.

A number of experiments were performed by varying the concentration of mercury(II) acetate in the range 0.83 x 10^{-3}M to 5.00 x 10^{-3} M and the results displayed in the Table 3.6A(a) which reveals that the values of (-dc/dt) are nearly constant throughout the variation in conc. of $Hg(OAc)_2$. This confirms that $Hg(OAc)_2$ has no significant impact on reaction rate. Therefore its role is neither as oxidant nor as catalyst. It follow zero order kinetics.

Table: 3.6A(a)

$[KBrO_3]$ = 1.00×10^{-3} M

[GB] = 1.00×10^{-2} M

[Pd(II)] = 11.20×10^{-5} M

$[HClO_4]$ = 1.00×10^{-3} M

[KCl] = 1.00×10^{-3} M

Temperature = 35^0C.

$[Hg(OAc)_2]$ / 10^{-3} M →	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.)	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.50	9.56	9.25	9.26	9.46	9.20
10	9.15	9.08	8.78	9.00	8.95	885
15	8.52	8.67	8.22	8.50	8.15	8.18
20	8.02	8.00	7.30	8.05	7.81	7.82
25	7.40	7.55	6.70	7.50	7.40	7.35
35	6.65	6.50	6.25	6.45	6.20	6.55
45	6.12	6.27	5.25	6.10	5.85	5.90
60	5.82	6.00	4.50	5.50	5.70	5.50
(-dc/dt) → / 10^{-7} Ms^{-1}	1.30	1.38	1.27	1.24	1.20	1.32

C* = Volume of hypo used (N/400) in ml.

3.6B: Impact of variation of mercuric acetate on the reaction rate of Pd(II) catalyzed oxidation of paracetamol drug by potassium bromate in acidic medium.

To elucidate the role of mercuric acetate on the rate of oxidation of paracetamol by potassium bromate, using palladium(II) chloride as catalyst in acidic medium, concentration of mercuric acetate has been varied from 0.83 x 10^{-3} M to 5.00 x 10^{-3} M at constant concentration of all other reactants. All experiments were carried out at constant temperature 35^0C and the results have been recorded in Tables 3.6B(a).

A perusal of Table 3.6B(a), indicates thar the values of (-dc/dt) remain almost constant throughout the variation of mercuric acetate concentration. This shows insignificant effect of mercuric acetate on the rate of reaction. Thus it is obvious from the results that neither mercuric acetate acts here as an oxidant nor as a catalyst.

Table: 3.6B(a)

[$KBrO_3$]	= 1.00 x 10^{-3} M	[$HClO_4$]	= 1.00 x 10^{-3} M
[PA]	= 1.00 x 10^{-2} M	[KCl]	= 1.00 x 10^{-3} M
[Pd(II)]	= 11.20 x 10^{-5} M	Temperature	= 35^0C.

[$Hg(OAc)_2$] / 10^{-3} M	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.)	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.00	9.25	9.15	9.20	9.40	9.21
10	8.50	8.70	8.78	8.80	8.85	8.21
15	8.12	8.02	8.22	8.21	8.00	8.00
20	7.50	7.72	7.72	7.65	7.25	7.50
25	7.25	7.36	7.30	7.15	7.00	7.25
35	6.42	6.30	6.28	6.25	6.05	6.25
45	5.75	5.23	5.22	5.65	5.30	5.50
60	5.00	4.60	4.50	5.22	4.60	5.00
(-dc/dt) / 10^{-7} Ms^{-1}	2.21	2.60	2.60	3.00	2.42	2.51

C* = Volume of hypo used (N/400) in ml.

3.7: Impact of variation in ionic strength of the medium on the rate of palladium(II) catalyzed oxidation of pharmaceutical drugs (i.e. gabapentin and paracetamol) by potassium bromate in acidic medium.

With the help of ionic strength we can ascertain the nature of active species involved in the slow step of the proposed mechanism. So it was note worthly to evaluate the impact of ionic strength on proposed reaction mechanism. In this section our main attempt has been to determine the effect of ionic strength which has been varied by the addition of suitable amounts of sodium perchlorate in the reaction mixture. The ionic strength of the solution has been varied by addition of $NaClO_4$ of concentration from 0.83 x 10^{-3} M to 5.00 x 10^{-3} M at the constant concentration of all other reactants, and at constant temperature 35^0C. All experimental results are displayed in Table 3.7A(a) for gabapentin and 3.7B(a) for paracetamol rand summarized in Tables 3.7.

The value of (-dc/dt) does not show any appreciable change, which shows that in all the cases, there is negligible effect of variation in ionic strength (µ) of the medium on the reaction rate.

Ionic strength (µ) has been calculated taking sum of concentration of those reactants which ionize in solution i.e. $KBrO_3$, $HClO_4$, KCl and $Hg(OAc)_2$. Known concentration of $NaClO_4$ has been used to change the ionic strength of the medium and keeping the concentration of all other reactants constant. The choice of $NaClO_4$ for varying ionic strength has been made because it does not initiate any reaction with other reactants taking part in the reaction and only changes the ionic strength of the medium.

Table: 3.7A(a)

[$KBrO_3$]	= 1.00×10^{-3} M	[$HClO_4$]	= 1.00×10^{-3} M
[GB]	= 1.00×10^{-2} M	[KCl]	= 1.00×10^{-3} M
[Pd(II)]	= 11.20×10^{-5} M	Temperature	= 35^0C.
[$Hg(OAc)_2$	= 1.25×10^{-3} M		

[$NaClO_4$] → / 10^{-3} M	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.)	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.50	9.60	9.25	9.52	9.45	9.50
10	8.75	9.00	8.65	9.00	8.75	8.80
15	8.25	8.20	8.00	8.53	8.10	8.10
20	8.00	8.00	7.54	8.10	7.66	7.54
25	7.54	7.45	7.25	7.80	7.32	7.00
35	7.00	7.00	6.53	7.21	6.58	6.25
45	6.52	6.55	5.85	6.45	5.94	5.70
60	5.52	5.74	5.25	5.80	5.30	5.22
(-dc/dt) → / 10^{-7} Ms^{-1}	1.11	1.27	1.00	1.14	1.20	1.12

C* = Volume of hypo used (N/400) in ml.

Table: 3.7A(b)

[$KBrO_3$]	= 1.00 x 10^{-3} M	[$HClO_4$]	= 1.00 x 10^{-3}M
[GB]	= 1.00 x 10^{-2} M	[KCl]	= 1.00 x 10^{-3} M
[Pd(II)]	= 11.20 x 10^{-5} M	Temperature	= 35^0C.
[$Hg(OAc)_2$	== 1.25 x 10^{-3} M		

[$NaClO_4$] / 10^{-3} M	μ / 10^{-3} M	(-dc/dt) / $10^{-7}$$Ms^{-1}$
0.00	6.75	1.27
0.83	7.58	1.11
1.00	7.75	1.27
1.25	8.00	1.00
1.67	8.42	1.14
2.50	9.25	1.20
5.00	11.75	1.12

Table: 3.7B (a)

[$KBrO_3$]	= 1.00 x 10^{-3} M	[$HClO_4$]	= 1.00 x 10^{-3} M
[PA]	= 1.00 x 10^{-2} M	[KCl]	= 1.00 x 10^{-3} M
[Pd(II)]	= 11.20 x 10^{-5} M	Temperature	= 35^0C.
[$Hg(OAc)_2$	= 1.25 x 10^{-3} M		

[$NaClO_4$] → / 10^{-3} M	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.00	9.25	9.53	9.50	9.75	9.50
10	8.50	8.78	9.05	9.12	9.00	8.50
15	8.12	8.22	8.60	8.75	8.50	8.25
20	7.25	7.50	7.98	7.75	7.51	8.00
25	6.54	6.70	7.52	7.00	7.25	7.45
35	5.68	6.25	6.60	6.34	6.55	6.70
45	5.20	5.25	6.00	5.60	5.95	5.80
60	4.55	4.50	4.98	4.88	5.20	5.14
(-dc/dt) → / 10^{-7} Ms^{-1}	2.41	2.60	2.80	2.52	2.62	2.50

C* = Volume of hypo used (N/400) in ml.

Table: 3.7B(b)

[$KBrO_3$]	= 1.00 x 10^{-3} M	[$HClO_4$]	= 1.00 x 10^{-3}M
[PA]	= 1.00 x 10^{-2} M	[KCl]	= 1.00 x 10^{-3} M
[Pd(II)]	= 11.20 x 10^{-5} M	Temperature	= 35^0C.
[$Hg(OAc)_2$	= 1.25 x 10^{-3} M		

[$NaClO_4$] / 10^{-3} M	μ / 10^{-3} M	(-dc/dt) / $10^{-7}Ms^{-1}$
0.00	6.75	2.60
0.83	7.58	2.41
1.00	7.75	2.60
1.25	8.00	2.80
1.67	8.42	2.52
2.50	9.25	2.62
5.00	11.75	2.50

3.8: Effect of addition of D_2O on the reaction rate of Pd(II) catalyzed reaction between potassium bromate and each of the reducing pharmaceutical drugs Gabapentin and Paracetamol

In order to investigate the solvent isotope effect on the reaction velocity of the title reaction, a number of experiments containing different percentages of D_2O : H_2O (volume/volume) and with fixed concentrations of remaining reactants, were performed. The experiments were repeated similarly with different pharmaceutical drugs mentioned in the title. The results obtained are summarized in following Table 3.8A(a). It is obvious from the results of the summarized table, collected from the experiments performed with each of the title pharmaceutical drug that the reaction rate remains unaffected in all cases at different D_2O – H_2O ratios (values of (- dc/dt) remain almost constant at different D_2O – H_2O ratios). This shows that in the present reactions the rate determining step does not involve protonated reducing pharmaceutical drugs.

Table: 3.8A(a)

$[KBrO_3]$	$= 1.00 \times 10^{-3}$ M	$[HClO_4]$	$= 1.00 \times 10^{-3}$M
[Substrate]	$= 1.00 \times 10^{-2}$ M	[KCl]	$= 1.00 \times 10^{-3}$ M
[Pd(II)]	$= 11.20 \times 10^{-5}$ M	$[Hg(OAc)_2]$	$= 1.25 \times 10^{-3}$ M
		Temperature	$= 35^0$C.

[SUBSTRATE]	D_2O – H_2O (%) (v/v)	(-dc/dt) / 10^{-7} Ms^{-1}
GB	00 – 100	1.27
GB	05 – 95	1.20
GB	10 – 90	1.50
GB	20 – 80	1.42
PA	00 – 100	2.60
PA	05 – 95	2.20
PA	10 – 90	2.65
PA	20 – 80	2.50

Summary:

Following kinetic results have been obtained on the basis of experiments performed for oxidation of Gabapentin and Paracetamol by acidic bromate in presence of Pd(II) chloride as a catalyst.

Gabapentin	**Reaction order**	**Paracetamol**	**Reaction order**
Reactants		**Reactants**	
[$KBrO_3$]	1st order	[$KBrO_3$]	1st order
[Pd(II)]	1st order	[Pd(II)]	1st order
Substrate	Zero order	Substrate	Positive effect
[KCl]	Positive effect	[KCl]	Zero order
[$HClO_4$]	1st order	[$HClO_4$]	Negative effect
$Hg(OAc)_2$	No effect	$Hg(OAc)_2$	No effect
[$NaClO_4$]	No effect	[$NaClO_4$]	No effect
D_2O	No effect	D_2O	No effect

CHAPTER- 4

EFFECT OF VARIATION IN TEMPERATURE ON THE RATE OF Pd(II) CATALYSED OXIDATION OF PHARMACEUTICAL DRUGS AND CALCULATION OF ACTIVATION PARAMETERS

4.0: Effect of variation in temperature on the rate of Pd(II) catalyzed oxidation of pharmaceutical drugs and calculation of activation parameters.

It is well known that increase in temperature frequently cause a marked increase in the rate of reaction. For homogeneous processes the specific rate is doubled or trebled for each 10^0 rise in temperature, generally expressed in the form of temperature coefficient:-

$$\text{Temperature coefficient} = K_{t+10} / K_t = 2 \text{ to } 3$$

where K_t is the specific rate at t^0 and K_{t+10} at 10^0 higher. An examination of the rate expression in the form:-

$$\text{Reaction rate} = \text{rate constant x (reactant concentration)}^{\text{order}}$$

shows that the rate constant is temperature dependent term, because of the following factors:-

(a) The reactant concentrations are virtually unaffected by temperature.

(b) Unless the mechanism changes, in which the reaction is no longer same, an increase in temperature will have no effect on the reaction order.

Thus, although the rate constant is independent of reactant concentration, it varies with temperature.

Arrhenius proposed an equation for calculation of energy of activation (E_a) of a reaction having rate constant 'k', at absolute temperature 'T', expressed as:-

$$k = A\, e^{-Ea/RT} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

where R is gas constant and A is a constant known as pre-exponential factor or Arrhenius frequency factor, which includes same energy unit as E_a. Both 'E_a' and 'A' are characteristic of a reaction. Equation (1) indicates that when $E_a = 0$ or $T = \infty$, then

$$k = A \quad \ldots\ldots\ldots\ldots\ldots(2)$$

Taking logarithm of equation (1), we have

$$\ln k = \ln A - E_a/RT \ldots\ldots\ldots\ldots\ldots\ldots (3)$$

$$\log k = \log A - E_a/2.303RT \ldots\ldots\ldots\ldots\ldots\ldots (4)$$

4.1A Impact of variation in Temperature on the rate of reaction for Pd(II) catalyzed oxidation of gabapentin and paracetamol by potassium bromate in acidic medium:

Equation (4) suggests that a plot of log k against 1/T should give a straight line and the slope of this straight line is equal to $-E_a/2.303R$ while intercept of straight line gives the value of logA Fig. 4.1A and Fig. 4.2B

In order to determine the effect of temperature on the rate of reaction, several experiments were performed under identical conditions at different temperature, viz. 30^0, 35^0, 40^0 and 45^0 respectively and their results have been given in Tables 4.1A[a], 4.1A[b], 4.1A[c] and summarized in Table 4.1A(d), for Gabapentin, while 4.2B(a), 4.2B(b), 4.2B(c) and summarized in Table 4.2B(d), for Paracetamol drug. It is evident from summarized tables that the values of (-dc/dt) or k_1 increases on increasing the temperature. Thus it is clear that the rate of reaction increases with rise in temperature.

Table: 4.1A(a)

$[KBrO_3]$ = 1.00×10^{-3} M
[GB] = 1.00×10^{-2} M
[Pd(II)] = 11.20×10^{-5} M
$[HClO_4]$ = 1.00×10^{-3} M
[KCl] = 1.00×10^{-3} M
$[Hg(OAc)_2]$ = 1.25×10^{-3} M
Temperature = 30 °C

Time (min.)	Vol. of Hypo used N/400 in ml.
0	10.00
5	9.05
10	8.40
15	7.86
20	7.24
25	6.80
35	6.25
45	5.70
55	5.35

(-dc/dt) = 1.00×10^{-7} Ms^{-1}

$[KBrO_3]$ = 1.00×10^{-3}M

$$k_1 = \frac{(-dc / dt)}{[KBrO_3]} = 1.00 \times 10^{-4}\ s^{-1}$$

Table: 4.1A(b)

$[KBrO_3]$ = 1.00×10^{-3}M
[GB] = 1.00×10^{-2}M
[Pd(II)] =11.20×10^{-5}M
$[HClO_4]$ = 1.00×10^{-3} M
[KCl] = 1.00×10^{-3} M
$[Hg(OAc)_2]$ = 1.25×10^{-3} M
Temperature = 40 °C

Time (min.)	Vol. of Hypo used N/400 in ml.
0	10.00
5	8.10
10	7.32
15	6.75
20	6.10
25	5.21
35	4.22
45	3.67
55	3.00

$[KBrO_3]$ = 1.00×10^{-3}M

(-dc/dt) =1.80×10^{-4} s^{-1}

$$k_1 = \frac{(-dc/dt)}{[KBrO_3]} = 1.80 \times 10^{-7} Ms^{-1}$$

Table: 4.1A(c)

$[KBrO_3]$ = 1.00×10^{-3} M

[GB] = 1.00×10^{-2} M

$[PdCl_2]$ = 11.20×10^{-5} M

$[HClO_4]$ = 1.00×10^{-3} M

[KCl] = 1.00×10^{-3} M

$[Hg(OAc)_2]$ = 1.25×10^{-3} M

Temperature = 45 ºC

Time (min.)	Vol. of Hypo used N/400 in ml.
0	10.00
5	7.90
10	7.00
15	6.21
20	5.57
25	5.00
35	4.00
45	3.24
55	2.23

(-dc/dt) = 2.42×10^{-7} M s^{-1}

$[KBrO_3]$ = 1.00×10^{-3} M

$k_1 = \frac{(-dc/dt)}{[KBrO_3\,]}$= 2.42×10^{-4} s^{-1}

Table 4.1 A(d)

$[KBrO_3] = 1.00 \times 10^{-3}M$ KCl = $1.00 \times 10^{-3}M$

$[GB] = 1.00 \times 10^{-2}M$ $[HClO_4] = 1.00 \times 10^{-3}M$

$[Pd(II)] = 11.20 \times 10^{-5}M$ $[Hg(OAc)_2 = 1.25 \times 10^{-3}M$

Temperature		$(-dc/dt)/10^{-7}Ms^{-1}$	$K/10^{-4}\ s^{-1}$	4 + log k
0	K			
30	303	1.00	1.00	0.000
35	308	1.27	1.27	0.1038
40	313	1.80	1.80	0.2553
45	318	2.42	2.42	0.3838

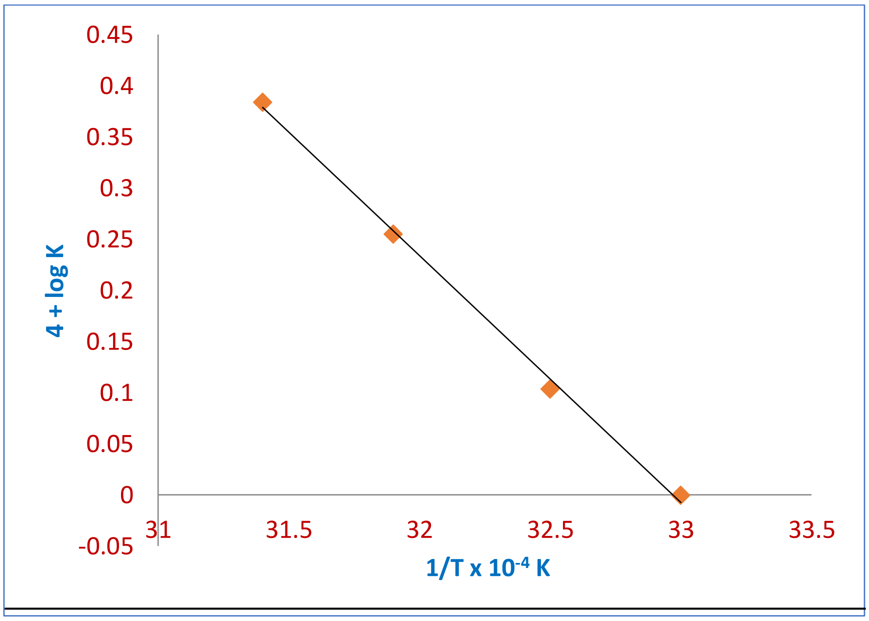

Figure 4.1A: Arrhenius plot for the oxidation of gabapentin by acidic bromate in presence of Pd(II) chloride as a catalyst. $[Pd(II)] = 11.20 \times 10^{-5}M$, $[KCl] = 1.00 \times 10^{-3}M$, $[Hg(OAc)_2] = 1.25 \times 10^{-3}M$, $[KBrO_3] = 1.00 \times 10^{-3}M$, $[GB] = 1.00 \times 10^{-2}M$, $[HClO_4] = 1.00 \times 10^{-3}$ M

Table: 4.1B(a)

[$KBrO_3$] = 1.00×10^{-3} M
[PA] = 1.00×10^{-2} M
[Pd(II)] = 11.20×10^{-5} M
[$HClO_4$] = 1.00×10^{-3} M
[KCl] = 1.00×10^{-3} M
[$Hg(OAc)_2$] = 1.25×10^{-3} M
Temperature = 30 ºC

Time (min.)	Vol. of Hypo used N/400 in ml.
0	10.00
5	9.25
10	8.52
15	7.95
20	7.30
25	6.85
35	6.00
45	5.35
55	4.90

(-dc/dt) = 1.85×10^{-7} M s^{-1}
[$KBrO_3$] = 1.00×10^{-3} M

$$k_1 = \frac{(-dc/dt)}{[KBrO_3]} = 1.85 \times 10^{-4} s^{-1}$$

Table: 4.1B(b)

[$KBrO_3$] = 1.00×10^{-3} M
[PA] = 1.00×10^{-2} M
[Pd(II)] = 11.20×10^{-5} M
[$HClO_4$] = 1.00×10^{-3} M
[KCl] = 1.00×10^{-3} M
[$Hg(OAc)_2$] = 1.25×10^{-3} M
Temperature = 40 ºC

Time (min.)	Vol. of Hypo used N/400 in ml.
0	10.00
5	8.15
10	7.10
15	6.24
20	5.50
25	5.00
35	4.35
45	3.70
55	3.25

(-dc/dt) = 3.74×10^{-7} M s^{-1}
[$KBrO_3$] = 1.00×10^{-3} M

$$k_1 = \frac{(-dc/dt)}{[KBrO_3]} = 3.74 \times 10^{-4} s^{-1}$$

Table: 4.1 B(c)

$[KBrO_3]$ = 1.00×10^{-3}M

[PA] = 1.00×10^{-2}M

[Pd(II)] = 11.20×10^{-5}M

$[HClO_4]$ = 1.00×10^{-3}M

[KCl] = 1.00×10^{-3}M

$[Hg(OAc)_2]$ = 1.25×10^{-3}M

Temperature = 45 ^{0}c

Time(min.)	Vol.of Hypo used N/400 in ml.
0	10.00
5	8.00
10	6.95
15	6.00
20	5.10
25	4.50
35	3.58
45	2.70
55	2.00

(-dc/dt) = $5.18 \times 10^{-7} Ms^{-1}$

$[KBrO_3]$ = 1.00×10^{-3}M

$$k_1 = \frac{(-dc/dt)}{[KBrO_3]} = 5.18 \times 10^{-4}\ s^{-1}$$

Table 4.1 B(d)

$[KBrO_3] = 1.00 \times 10^{-3}M$	$KCl = 1.00 \times 10^{-3}M$
$[PA] = 1.00 X 10^{-2}M$	$[HClO_4] = 1.00 \times 10^{-3}M$
$[Pd(II)] = 11.20 \times 10^{-5}M$	$[Hg(OAc)_2 = 1.25 \times 10^{-3}M$

Temperature		$(-dc/dt)/10^{-7}Ms^{-1}$	$K/10^{-4} s^{-1}$	4 + log k
0	K			
30	303	1.85	1.85	0.2672
35	308	2.60	2.60	0.4150
40	313	3.74	3.74	0.5729
45	318	5.18	5.18	0.7143

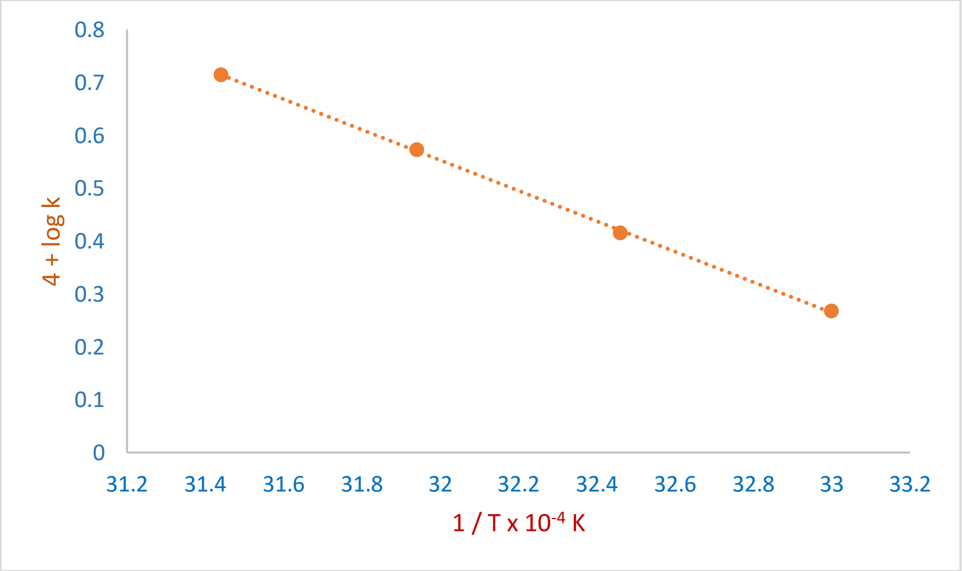

Figure 4.1B: Arrhenius plot for Pd(II) catalyzed oxidation of paracetamol by bromate. $[Pd(II)] = 11.20 \times 10^{-5}M$, $[KCl] = 1.00 \times 10^{-3}M$, $[Hg(OAc)_2]= 1.25 \times 10^{-3}M$, $[KBrO_3] = 1.00 \times 10^{-3}M$, $[PA] = 1.00$ **x** $10^{-2}M$,$[HClO_4] =1.00 \times 10^{-3}$ M

4.2: Calculation of thermodynamic activation parameters and their interpretation

In this chapter an attempt has been made to calculate different thermodynamic parameters such as entropy of activation (ΔS*), enthalpy of activation (ΔH*), free energy of activation (ΔG*), Arrhenius frequency factor (A) and specific rate constant (k_r). According to transition state theory the equation for specific rate constant k_r (i.e. the rate constant of reaction when concentration of each of the reactant is unity at a given temperature is given as:

$$k_r = \frac{KT}{h}\, K^{*} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (i)$$

where T is absolute temperature h is Plancks constant and K is boltzmann constant, The quantity KT/h is known as universal frequency factor and is independent of nature and type of reaction. K* is activation equilibrium constant for the process of formation of an activated complex, which is regarded as a normal molecule. Free energy change of activation ΔG* is related with equilibrium constant K* by equation.

$$\Delta G^* = -RT\ln K^* \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (ii)$$

According to Gibb’s Helmholtz equation

$$\Delta G^* = \Delta H^* - T\Delta S^* \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (iii)$$

substituting the value of ΔG* from equation (iii) to (ii) we get

$$\Delta H^* - T\Delta S^* = -RT\ln K^*$$

or

$$\ln K^* = \frac{-\Delta H^*}{RT} + \frac{\Delta S^*}{R}$$

or

$$K^* = e^{-\Delta H^*/RT} \cdot e^{\Delta S^*/R} \qquad \text{……….(iv)}$$

Substituting the value of K* from equation (iv) to equation (i)

$$k_r = \frac{KT}{h} e^{-\Delta H^*/RT} \cdot e^{\Delta S^*/R}$$

taking logarithms on both sides

$$\ln k_r = \frac{\ln K}{h} + \ln T - \frac{\Delta H^*}{RT} + \frac{\Delta S^*}{R} \qquad \text{……….(v)}$$

Differentiating the above equation with respect to temperature, we have

$$\frac{d}{dt}(\ln k_r) = \frac{1}{T} + \frac{\Delta H^*}{RT^2} \qquad \text{……….(vi)}$$

According to Arrhenius equation –

$$k_r = A e^{-E_a/RT}$$

Taking logarithm on both sides

$$\ln k_r = \ln A - \frac{E_a}{RT}$$

Differentiating above equation with respect to temperature, we get

$$\frac{d}{dt}(\ln k_r) = \frac{E_a}{RT^2} \qquad \text{.........(vii)}$$

comparing equation(vi) and (vii) we get:

$$\frac{1}{T} + \frac{\Delta H^*}{RT^2} = \frac{E_a}{RT^2}$$

$$\Delta H^* = E_a - RT \text{ ....(viii)}$$

Substituting the value of ΔH* from equation (viii) to equation (v)

$$k_r = \frac{KT}{h} e^{-(E_a - RT)/RT} . \; e^{\Delta S^*/R}$$

or

$$k_r = \frac{KT}{h} e^{-E_a/RT} . \; e^{RT/RT} . \; e^{\Delta S^*/R}$$

or

$$k_r = \frac{eKT}{h} e^{-E_a/RT} . \; e^{\Delta S^*/R}$$

taking logarithm on both sides we get

$$\ln k_r = \ln e + \ln K/h + \ln T - E_a/RT + \Delta S^*/R$$

or

$$\Delta S^*/2.303R = \log k_r - \log \frac{ek}{h} - \log T + E_a/2.303RT \text{......................(ix)}$$

The value of K is 1.3803 x 10^{-16} erg deg^{-1} mol^{-1}, R is 1.987 Cal $deg^{-1} mol^{-1}$ and h is 6.6238 x 10^{-27} erg sec^{-1} mol^{-1}. Substituting the value of K, h and R in equation (9) we get,

$$\Delta S^*/4.576 = \log k_r - 10.753 - \log T + E_a/4.576T \quad \text{............(x)}$$

ΔS^* has a unit of Cal deg^{-1} mol^{-1}. Equation (x) is valid only if the constant is based on the second as the unit of time. From the above equation ΔS^* can be calculated in entropy units. The free energy (ΔG^*) and Arrhenius factor (A) can be calculated from the following equation.

$$\Delta G^* = \Delta H^* - T\Delta S^* = E_a - RT - T\Delta S^* \text{..........................} (xi)$$

and

$$\log A = \log k_r + E_a/2.303RT$$

The specific rate constant k_r is calculated for the acidic medium as-

$$k_r = (-dc/dt)/[KBrO_3]^{n_1}[S]^{n_2}[Pd(II)]^{n_3}[H^+]^{n_4}$$

The E_a values obtained from the slope were used to calculate ΔS^*, ΔH^*, ΔG^* and A with the help of above equations. The value of activation parameters for oxidation of pharmaceutical drugs by bromate in presence of Pd(II) chloride as catalyst under investigation along are given in tabular form for acidic medium in table 4.2.

Evans and Polanyi(1) and Eyring(2) put forth the idea of formation of activated complex as a result of molecular collision between energized molecules and established that the chemical reaction involves first the formation of activated complex in a reversible process which then decomposes irreversibly to give the products of the reaction.

Table 4.2

Values of Activation Parameters for pharmaceutical drugs of Pd(II) catalyzed oxidation by potassium bromate in acidic medium

Arrhenius parameters	Gabapentin	Paracetamol
E_a KJ mol^{-1}	52.42	61.27
Log A	10.34	11.79
∆S* $JKmol^{-1}$	-56.87	-23.18
∆G* kJ mol^{-1}	70.18	68.42
∆H* kJ mol^{-1}	52.67	61.27

The phenomenon of entropy of activation plays a vital role in case of reactions between ions or neutral molecules forming ions. When a reaction occurs between two oppositely charged ions, it is usually observed that entropy increases in going from reactant to activated complex but on the other hand when the same takes place between two similarly charged ions, decrease in entropy is observed in terms of solvation of ions. An explanation for such a behavior of entropy can be given as follows for different reactions. It is well known that solvation generally increases with increase in charge on the ion. In other words, smaller ions are highly solvated. Neutral molecule is formed when two ions of opposite charge, result in a lowering of net charge and due to this some frozen solvent such as water molecules frozen around the incipient ions are released with an increase in entropy. On the other hand when reaction takes place between two similarly charged ions, the transition state or the activated state which is a more highly charged ion, is as expected, a highly solvated molecule. Consequently more solvent molecules for this transition state will be required as compared to that for separate ions which would lead to decrease in entropy, so for the reaction in solution, enthalpy of activation changes with the solvent and becomes less negative (i.e. increase) while free energy change of activation decreases, as the polarity of solvent increases. Table 4.2 for activation parameters shows high positive values of free energy of activation (ΔG^*) signifying the transition state to be highly solvated and negative value of entropy of activation (ΔS^*) indicates the formation of activated complex with reduction in degree of freedom of reactant molecules or ions.

Summary:

In this chapter several experiments were performed under identical conditions at different temperature viz 30 ⁰C, 35 ⁰C, 40 ⁰C, and 45 ⁰C respectively for Pd(II) catalysed oxidation of gabapentin and paracetamol by acidic bromate. It was observed that rate of reaction increased with increase in temperature. From the values of rate constant obtained Arrhenius plot was plotted, which gave a straight line. The value of energy of activation ΔE^* was obtained from the slope of the line by using the expression.

$$\text{Slope} = \frac{-\Delta E^*}{2.303R}$$

Using this value of ΔE^*, other activation parameters i.e. entropy of activation (Δs^*), enthalpy of activation (ΔH^*) free energy of activation (ΔG^*), and Arrhenius frequency factor (A) have been calculated.

References-

1. M.G. Evansand, M. Polanyi, *Trans. Far. Soc*. vol 31, 875, **1935**
2. H. Eyring: *J. Chem. Phys*., vol 3,107, **1935**

CHAPTER-5

ASCERTAINING ORDER OF REACTION WITH RESPECT TO VARIOUS REACTANTS IN Ir(III) CATALYZED OXIDATION OF PHARMACEUTICAL DRUGS BY POTASSIUM BROMATE IN ACIDIC MEDIUM

5.0: Determination of order of reaction with respect to Oxidant (potassium bromate) in Ir(III) catalyzed oxidation of pharmaceutical drugs by potassium bromate in acidic medium.

In this section, an attempt has been made to study the dependence of reaction rate on potassium bromate concentration i.e. [$KBrO_3$]. An experimental study of rate of reaction can be made by estimating the concentration(c) of the reactant as function of time (t) which will give the reaction rate i.e. (-dc/dt) at that instant of time. The relation between reaction rate and reactant concentrations will give rate equation for general reaction, as illustrated below:

$$\underset{\text{(Reactants)}}{A + B + C} \longrightarrow \text{Product}$$

The rate equation for the above reaction can be written as:

$$Rate = k[C_A]^{n_1} [C_B]^{n_2} [C_C]^{n_3} \cdots\cdots\cdots(1)$$

where k is the rate constant for the reaction and n_1, n_2 and n_3 indicate order with respect to the reactants A, B and C respectively. The total order (n) of the above reaction can be obtained as:-

$$n = n_1 + n_2 + n_3 \ldots\ldots\ldots\ldots (2)$$

In the present section for determination of order of reaction with respect to various reactants, we have followed isolation method in which the experiments have been carried out by taking all the reactants except one in fixed quantities, so that the concentration of other reactants remain constant throughout the investigation. Considering potassium bromate, pharmaceutical drugs, Ir(III) chloride, perchloric acid and potassium chloride as main reactants, the rate equation can be written in the following way:-

$$Rate = dc/dt = k\,[KBrO_3]^{n_1}\,[Pharmaceutical\ drugs]^{n_2}\,[Ir(III)]^{n_3}\,[H^+]^{n_4}\,[Cl^-]^{n_5} \ldots(3)$$

In proposed investigation, the order of reaction with respect to each reactant taking part in the reaction has been determined with the help of Ostwald isolation method, graphical and differential method.

In Ostwald isolation method, the concentration of the reactant whose order is to be determined is taken in a very small quantity in comparison to the concentration of other reactants, which is not taken in excess and the apparent order will be order with respect to the reactant isolated.

For the determination of order of reaction with respect to potassium bromate (n_1), concentration of potassium bromate is varied and the concentration of other reactants is kept constant, therefore the velocity of the reaction will mainly be determined by change in concentration of potassium bromate. Now rate equation will take the form:-

$$\text{Rate} = k_1\ [KBrO_3]^{n_1} \quad \ldots\ldots(4)$$

where $k_1 = k[Pharmaceutical\ drugs]^{n_2}[Ir(III)]^{n_3}[H^+]^{n_4}[Cl^-]^{n_5}$

Rate of reaction in terms of decrease in the concentration of potassium bromate, can be given as:-

$$\frac{-d[KBrO_3]}{dt} = k_1[KBrO_3]^{n_1}$$

If n=1

or

$$\frac{(-d[KBrO_3]/\mathrm{dt})}{[KBrO_3]} = k_1 \ldots\ldots(5)$$

where k_1 is the first order rate constant. Equation (5) shows that a plot between $d[KBrO_3]/dt$ and $[KBrO_3]$ will give a straight line passing through the origin.

5.1A: Determination of order of reaction with respect to potassium bromate in Iridium (III) catalyzed oxidation of gabapentin by potassium bromate in acidic medium:

Order of reaction with respect to potassium bromtae in [Ir(III)] catalyzed oxidation of gabapentin has been determined by performing a series of experiments at constant temperature 35^0C and constant concentration of other reactants. Results obtained for various kinetic runs are presented in Table 5.1A(a) Concentration of potassium bromate was varied from 0.83 x 10^{-3} M to 5.00 x 10^{-3} M at constant concentration of all other reactants and constant temperature 35^0C. Rate of reaction (-dc/dt) in each run was determined by slope of tangent at fixed time (5 min.)

A close perusal of Table 5.1A(a) indicates that the rate of reaction is almost directly proportional to the concentration of potassium bromate i.e., with increase in concentration of potassium bromate, rate of reaction increases in same proportion. Hence first order kinetics with respect to potassium bromate is confirmed. A plot of (-dc/dt) Vs. [$KBrO_3$] gives a straight line passing through the origin [Fig. 5.1A(a). Last row of Table 5.1A(a) shows almost constant values of k_1 throughout the variation of [$KBrO_3$] which also support the first order kinetics with respect to [$KBrO_3$]. First order kinetics is further confirmed by least square method from table 5.1 A(b) and Fig. 5.1A(b).

Table: 5.1A(a)

[GB] = 1.00×10^{-2} M [KCl] = 1.00×10^{-3} M
[Ir(III)] = 11.20×10^{-5} M [$Hg(OAc)_2$] = 1.25×10^{-3} M
[$HClO_4$] = 1.00×10^{-3} M Temperature = 35^0C

[$KBrO_3$] / 10^{-3} M →	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	8.33	10.00	12.50	16.70	25.00	50.0
5	8.08	9.62	11.75	15.03	21.25	42.50
10	7.91	9.10	10.87	13.69	19.30	37.00
15	7.49	8.50	10.00	12.52	18.00	35.15
20	7.16	8.21	9.50	11.84	17.04	31.05
25	6.91	8.00	8.75	10.90	16.25	29.25
35	6.24	7.25	7.75	9.68	15.00	26.00
45	5.83	6.43	7.20	9.18	13.75	21.50
60	5.00	5.85	6.80	8.35	11.25	17.60
(-dc/dt) → / 10^{-7} Ms^{-1}	1.30	2.00	2.10	3.20	4.60	9.10
[$KBrO_3$] / 10^{-3} M →	0.83	1.00	1.25	1.67	2.50	5.00
$k_1 = \frac{(-dc/dt)}{[KBrO_3]}$ / 10^{-4} s^{-1}	1.56	2.0	1.68	1.91	1.84	1.82

C* = Volume of hypo used (N/400) in ml.

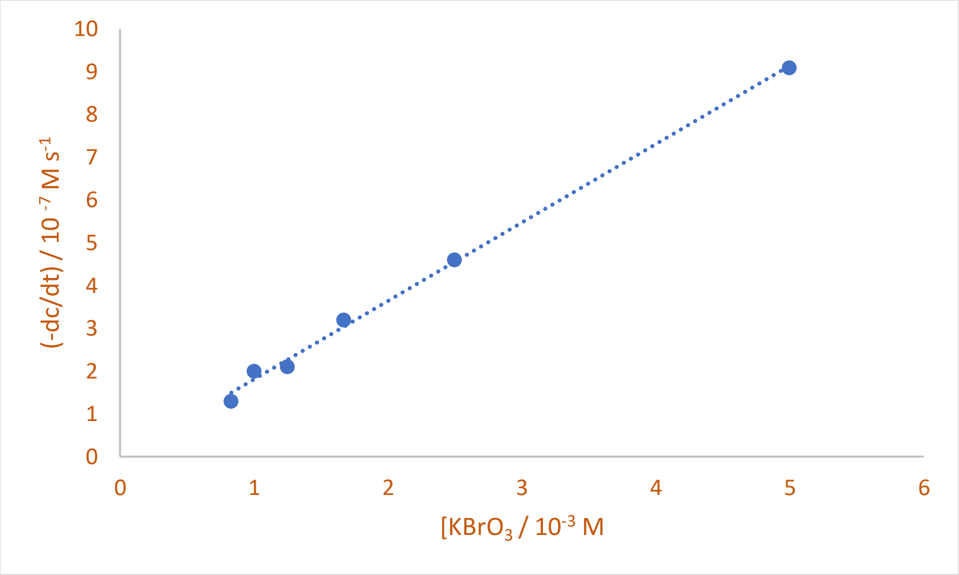

Figure: 5.1A(a): Plot between rate of reaction (-dc/dt) vs [$KBrO_3$] for the oxidation of gabapentin at 35^0C. [$HClO_4$] = 1.00 x 10^{-3}M, [KCl] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [GB] = 1.00 x 10^{-2} M, [Ir(III)]=11.20 x 10^{-5} M

Table: 5.1A(b)

[$KBrO_3$] / 10^{-3} (M)	(-dc/dt) (Y)	x (conc. – n)	x^2	xy	(a + bx)
0.83	1.30	-1.21	1.46	-1.57	1.48
1.00	2.00	-1.04	1.08	-2.08	1.79
1.25	2.10	-0.79	0.62	-1.65	2.25
1.67	3.20	-0.37	0.13	-1.18	3.02
2.50	4.60	0.46	0.21	2.11	4.55
5.00	9.10	2.96	8.76	26.93	9.15
12.25/6 n = 2.04	Σy = 22.3	Σx = 0.00	Σx^2 = 12.26	Σxy =22.56	

$\Sigma y = Na + b\Sigma x$

$22.3 = 6a + 0$

$a = 22.3/6$

$a = 3.71$

$\Sigma xy = a\Sigma x + b\Sigma x^2$

$22.56 = 0 + b \times 12.26$

$b = 22.56/12.26$

$b = 1.84$

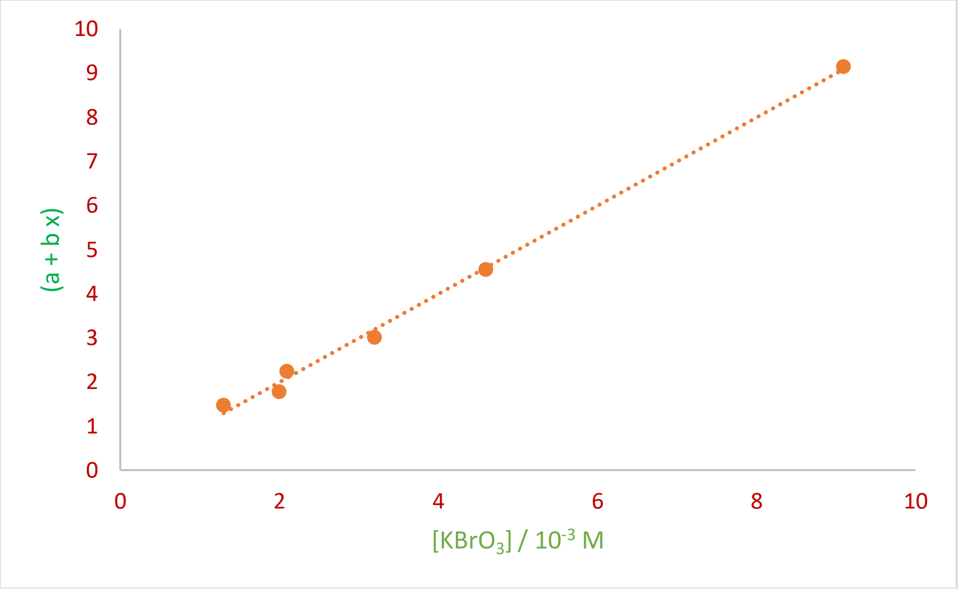

Figure: 5.1A(b) Plot between rate of reaction (a+bx) vs [KBrO$_3$] for the oxidation of gabapentin at 35^{0}C. [HClO$_4$] = 1.00 x 10^{-3} M, [KCl] = 1.00 x 10^{-3}M, [Hg(OAc)$_2$] = 1.25 x 10^{-3}M, [GB] = 1.00 x 10^{-2} M, [Ir(III)] = 11.20 x 10^{-5}M

5.1B: Determination of order of reaction with respect to oxidant in Iridium(III) catalyzed oxidation of paracetamol by potassium bromate in acidic medium.

To determine the order of reaction with respect to potassium bromate in the oxidation of paracetamol in acidic medium, a number of experiments were performed at constant temperature of 35^{0}C.The concentration of potassium bromate was varied from 0.83 x 10^{-3} M to 5.00 x 10^{-3} M. The results obtained are presented in Table 5.1B(a) It is clear from the last row of Table 5.1B(a) that the reaction follows first order kinetics. In each kinetic run upon increasing the concentration of potassium bromate the (-dc/dt) values also increase linearly. This result is further verified by plotting a graph between (-dc/dt) values and [KBrO$_3$] [Fig.5.1B(b)].

A straight line passing through the origin is obtained. This has also been confirmed by “least square method” Table 5.1B(b) and Fig. 5.1B(b).

Table: 5.1B (a)

[PA] = 1.00×10^{-2} M
[Ir(III)] = 11.20×10^{-5} M
[$HClO_4$] = 1.00×10^{-3} M
[KCl] = 1.00×10^{-3} M
[$Hg(OAc)_2$] = 1.25×10^{-3} M
Temperature = 35^0C

[$KBrO_3$] / 10^{-3} M →	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	8.33	10.00	12.50	16.70	25.00	50.00
5	7.99	9.25	11.37	14.52	20.00	43.50
10	7.49	8.62	10.00	12.85	18.75	36.85
15	6.99	8.10	9.37	11.69	16.75	29.98
20	6.44	7.50	8.75	10.70	15.30	25.00
25	5.98	7.00	8.12	10.02	14.05	21.75
35	5.24	6.12	7.50	8.84	12.58	15.00
45	4.74	5.40	6.25	7.84	10.00	10.50
60	4.16	4.80	5.25	6.68	8.00	8.05
(-dc/dt) → / 10^{-7} Ms^{-1}	4.30	5.20	6.45	8.65	12.80	25.50
[$KBrO_3$] / 10^{-3} M →	0.83	1.00	1.25	1.67	2.50	5.00
$k_1 = \frac{(-dc/dt)}{[KBrO_3]}$ / 10^{-4} s^{-1} →	5.18	5.20	5.16	5.17	5.12	5.10

C* = Volume of hypo used (N/400) in ml.

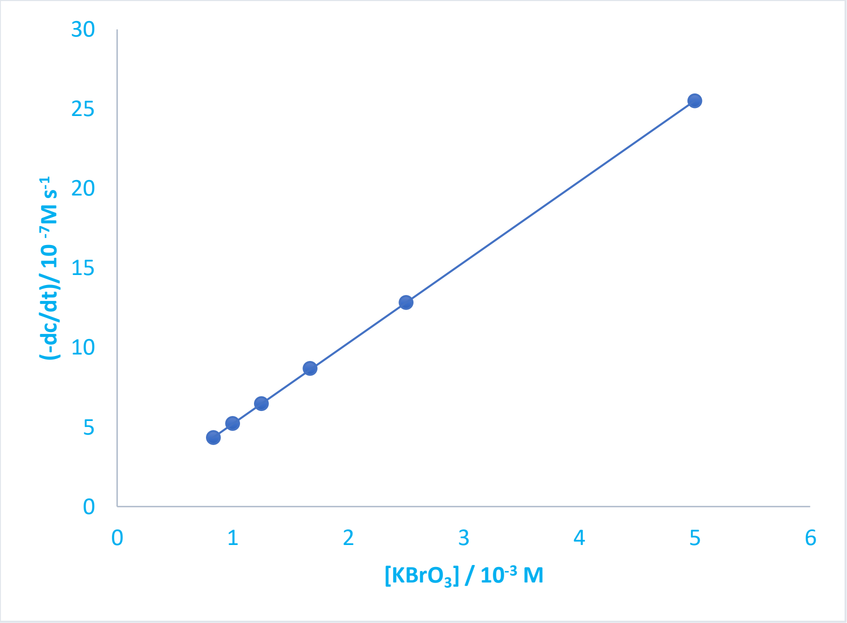

Figure: 5.1B(a) Plot between rate of reaction (-dc/dt) vs [$KBrO_3$] for the oxidation of paracetamol at 35^0C. [$HClO_4$] = 1.00 x 10^{-3}M, [KCl] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [PA] = 1.00 x 10^{-2} M, [Ir(III)]= 11.20 x 10^{-5} M

Table: 5.1B(b)

[$KBrO_3$] / 10^{-3} (M)	(-dc/dt) (Y)	x (conc. – n)	x^2	xy	(a + bx)
0.83	4.30	-1.21	1.46	-5.20	4.31
1.00	5.20	-1.04	1.08	-5.40	5.18
1.25	6.45	-0.79	0.62	-5.09	6.45
1.67	8.65	-0.37	0.13	-3.20	8.59
2.50	12.80	0.46	0.21	5.88	12.82
5.00	25.50	2.96	8.76	75.48	25.58
12.25/6 n = 2.04	Σy = 62.9	Σx = 0.00	Σx^2 = 12.26	Σxy =62.47	

Σy	=	Na + bΣx	Σxy	=	aΣx + $b\Sigma x^2$
62.9	=	6a + 0	62.47	=	0 + b x 12.26
a	=	62.9/6	b	=	62.47/12.26
a	=	10.48	b	=	5.10

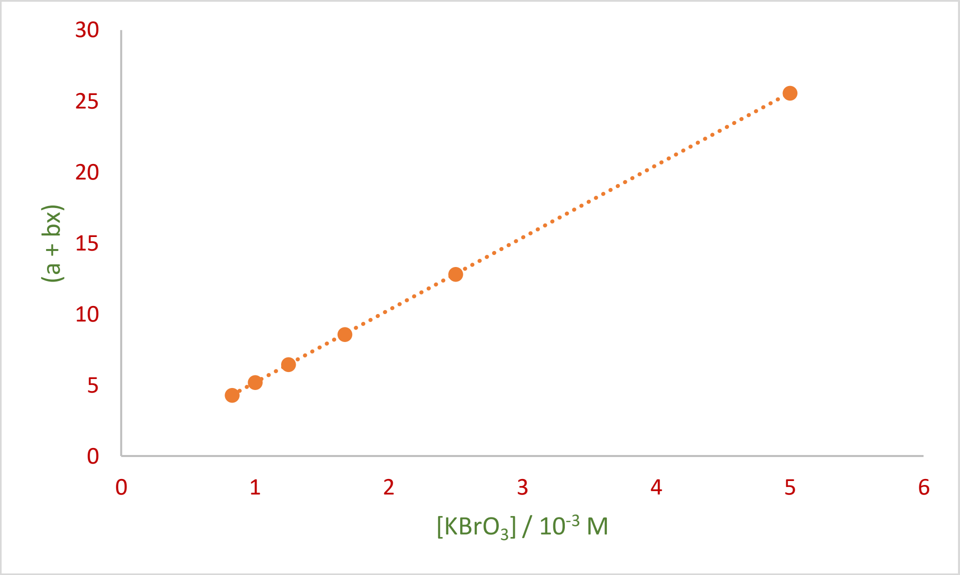

Figure: 5.1B(b) Plot between rate of reaction (a+bx) vs [KBrO$_3$] for the of paracetamol at 35^{0}C. [HClO$_4$] = 1.00 x 10^{-3} M, [KCl]= 1.00 x 10^{-3}M, [Hg(OAc)$_2$] = 1.25 X 10^{-3}M, [PA] = 1.00 x 10^{-2} M, [Ir(III)] = 11.20 x 10^{-5} M

5.2: Determination of order of reaction with respect to Ir(III) catalyzed oxidation of pharmaceutical drugs (gabapentin and paracetamol) by bromate in acidic medium.

The rate equation for Ir(III) catalyzed oxidation of pharmaceutical drugs by potassium bromate can be expressed as:-

$$Rate = \frac{-d[KBrO_3]}{dt} = k\,[KBrO_3]^{n_1}\,[Pharmaceutical\ drugs]^{n_2}\,[Ir(III)]^{n_3}\,[H^+]^{n_4}\,[Cl^-]^{n_5}$$

First order kinetics is observed with respect to potassium bromate i.e. [KBrO$_3$] (n_1 = 1). In the variation of Ir(III) chloride concentration, if other reactant were kept constant, then equation reduces to

$$k_1 = \frac{-d[KBrO_3]/dt}{[KBrO_3]} = k[Pharmaceutical\ drug]^{n_2}\,[Ir(III)]^{n_3}\,[H^+]^{n_4}\,[Cl^-]^{n_5}$$

$$k_1 = k'[Ir(III)]^{n_3}$$

where of $k' = k\,[KBrO_3]\,[Comp]^{n_2}\,[H^+]^{n_4}\,[Cl^-]^{n_5}$

values of k_1 have been calculated for each kinetic run to predict the order of reaction with respect to Ir(III) chloride.

5.2 A: Determination of order of reaction with respect to catalyst in Iridium(III) catalyzed oxidation of gabapentin by potassium bromate in acidic medium.

In order to determine the effect of Ir(III) chloride on the rate of reaction, its concentration has been varied from 5.60×10^{-5} M to 44.80×10^{-5} M at constant temperature 35^0C. All the results obtained are presented in Table 5.2A(a). For each run (-dc/dt) values have been calculated from the slopes of tangents drawn at fixed concentrations of all reactants. A close examination of Table 5.2A(a) suggests that with increase in the concentration of catalyst (-dc/dt) values also increase, showing that there is a linear relationship between (- dc/dt) values and [Ir(III)] (Fig. 5.2A(b). This linear relationship clearly indicates that the reaction follows first order kinetics with respect to catalyst. This has also been confirmed by “least-square method” as shown in Table 5.2A(b) and fig-5.2A(b)

Table: 5.2A

[GB]	= 1.00×10^{-2} M	[KCl]	= 1.00×10^{-3} M
[$KBrO_3$]	= 1.00×10^{-3} M	[$Hg(OAc)_2$]	= 1.25×10^{-3} M
[$HClO_4$]	= 1.00×10^{-3} M	Temperature	= 35^0C

[$IrCl_3$] / 10^{-5} M →	5.60	11.20	16.80	22.40	33.60	44.80
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.82	9.62	9.20	9.00	8.75	8.50
10	9.50	9.10	8.85	8.25	8.00	7.11
15	9.00	8.50	8.25	7.73	7.54	6.25
20	8.62	8.21	7.80	7.25	6.94	5.63
25	8.24	7.88	7.25	6.88	6.25	5.20
35	7.78	7.25	6.50	5.76	5.25	4.52
45	7.00	6.43	5.62	5.00	4.75	4..00
60	6.54	5.76	5.00	4.50	4.00	3.51
(-dc/dt) → / 10^{-7} Ms^{-1}	1.00	2.00	2.62	3.50	6.00	7.50
$k_1 = \frac{(-dc / dt)}{[Ir(III)]}$ / 10^{-2} s^{-1} →	1.78	1.79	1.56	1.56	1.79	1.67

C* = Volume of hypo used (N/400) in ml.

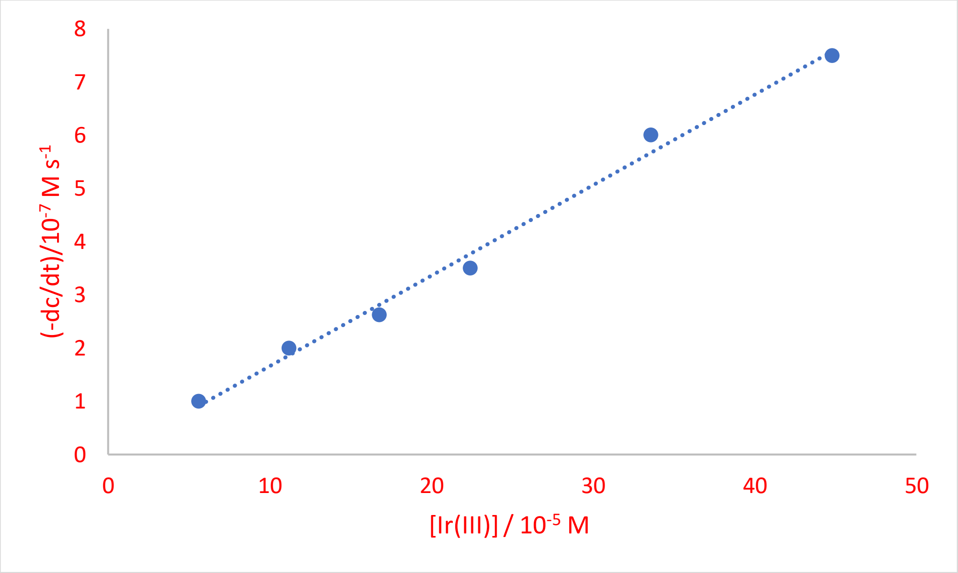

Figure: 5.2A(a) Plot between rate of reaction (-dc/dt) vs [IrCl$_3$] for the oxidation of gabapentin at 35^{0}C. [HClO$_4$] = 1.00 x 10^{-3}M, [KCl] = 1.00 x 10^{-3} M, [Hg(OAc)$_2$] = 1.25 x 10^{-3} M, [GB] = 1.00 x 10^{-2} M, [KBrO$_3$] = 1.00 x 10^{-3}M,

Table: 5.2A(b)

[IrCl$_3$] /10^{-5} M	(-dc/dt)/10^{-7}Ms^{-1} (Y)	x (conc. – n)	x^2	xy	(a + bx)
5.6	1.00	-16.8	282.24	-16.8	0.91
11.2	2.00	-11.2	125.44	-22.4	1.86
16.8	2.62	-5.6	31.36	-14.67	2.82
22.4	3.50	0.00	00.00	0.00	3.77
33.6	6.00	11.2	125.44	67.2	5.67
44.8	7.50	22.4	501.76	168	7.58
134.4/6 n =22.4	Σy = 22.62	Σx = 0.00	Σx^2 = 1066.24	Σxy =181.33	

Σy	=	$Na + b\Sigma x$	Σxy	=	$a\Sigma x + b\Sigma x^2$
22.62	=	6a + 0	181.33= 0 + b x 1461.35		
a	=	22.62/6	b	=	181.33/1066.24
a	=	3.77	b	=	0.17

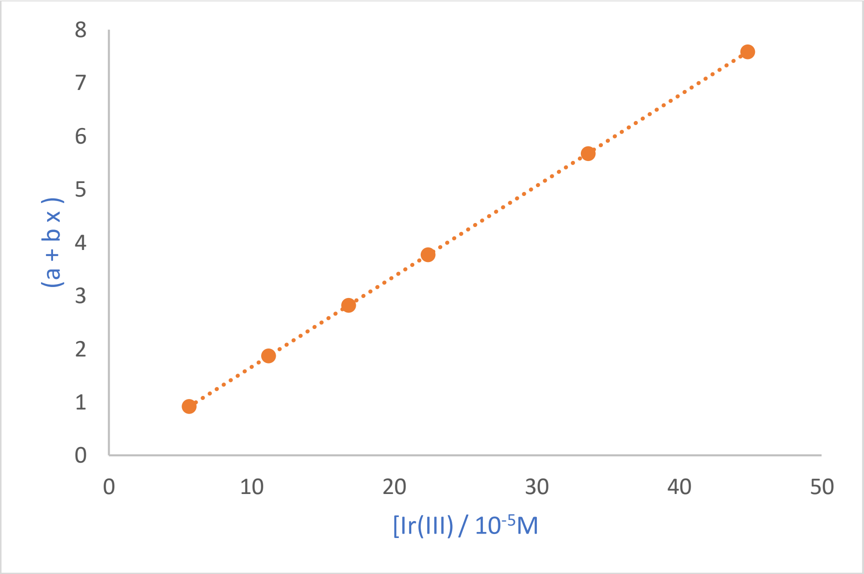

Figure: 5.2A(b) Plot between rate of reaction (a+bx) vs [IrCl$_3$] for the oxidation of gabapentin at 35^{0}C. [HClO$_4$] = 1.00 x 10^{-3} M, [KCl] = 1.00 x 10^{-3}M, [Hg(OAc)$_2$] = 1.25 x 10^{-3}M, [GB] = 1.00 x 10^{-2} M, [KBrO$_3$] = 1.00 x 10^{-3}M

5.2B: Thermodynamic investigation and order of reaction with respect to catalyst Ir(III) in Ir(III) catalyzed oxidation of paracetamol by KBrO$_3$ in acidic medium.

To determine the order of reaction with respect to Ir(III) chloride and its effect on the rate of reaction, its concentration has been varied from 5.60 x 10^{-5} M to 44.80 x 10^{-5} M keeping the concentration of all other reactants fixed at constant temperature 35^{0}C.

All the results obtained are presented in Table 5.2B(a). For each run (-dc/dt) values have been calculated from the slopes of tangents drawn at fixed concentrations of all reactants. A close examination of Table 5.2B(a) suggests that with increase in the concentration of catalyst there is an increase in (- dc/dt) values, showing that there is a linear relationship between (-dc/dt) values and [Ir(III)] Fig. 5.2B(b)].

This linear relationship clearly indicates that the reaction follows first order kinetics with respect to catalyst. This has also been confirmed by "least-square method" as obvious from Table 5.2B(b) and fig-5.2B(b)

Table: 5.2B(a)

[PA] = 1.00×10^{-2} M
[KBrO$_3$] = 1.00×10^{-3} M
[HClO$_4$] = 1.00×10^{-3} M
[KCl] = 1.00×10^{-3} M
[Hg(OAc)$_2$] = 1.25×10^{-3} M
Temperature = 35^0C

[IrCl$_3$] / 10^{-5} M →	5.60	11.20	16.80	22.40	33.60	44.80
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.50	9.25	9.12	8.50	8.20	8.00
10	9.00	8.62	8.50	8.00	7.00	7.25
15	8.65	8.10	8.00	7.35	6.40	6.78
20	8.20	7.50	7.25	6.75	5.42	6.25
25	7.94	7.00	6.65	6.25	5.00	5.35
35	7.52	6.12	6.00	5.20	4.56	4.50
45	6.95	5.40	5.25	4.45	4.00	3.52
60	6.30	5.00	4.50	3.50	3.10	2.50
(-dc/dt) → / 10^{-7} Ms^{-1}	2.56	5.20	7.80	10.30	15.40	20.20
$k_1 = \frac{(-dc/dt)}{[Pd(III)]}$ / 10^{-2} s^{-1} →	4.57	4.64	4.64	4.59	4.58	4.51

C* = Volume of hypo used (N/400) in ml.

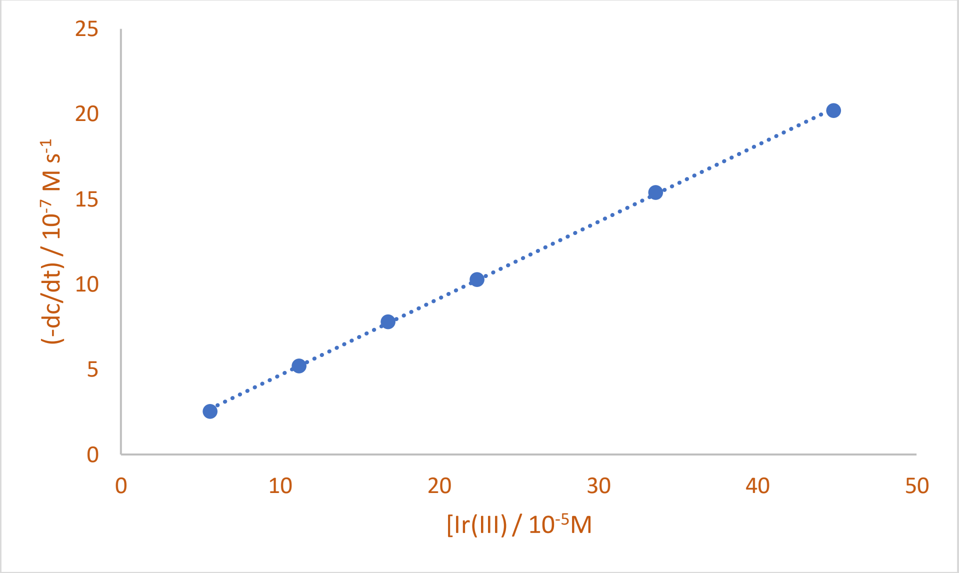

Figure: 5.2B(a) Plot between rate of reaction (-dc/dt) vs [$IrCl_3$] for the oxidation of paracetamol at 35^0C. [$HClO_4$] = 1.00 x 10^{-3}M, [KCl] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [PA] = 1.00 x 10^{-2} M, [$KBrO_3$] = 1.00 x 10^{-3} M

Table: 5.2B(b)

[$IrCl_3$] /10^{-5} (M)	(-dc/dt) (Y)	x (conc. – n)	x^2	xy	(a + bx)
5.60	2.56	-16.8	282.24	-43.00	2.68
11.20	5.20	-11.2	125.44	-58.24	5.20
16.80	7.80	-5.6	31.36	-43.68	7.80
22.40	10.30	0.00	00.00	00.00	10.24
33.60	15.40	11.2	125.44	172.48	15.28
44.80	20.20	22.4	501.76	452.48	20.32
134.4/6 n = 22.4	Σy = 61.46	Σx =00	Σx^2 = 1,066.24	Σxy =480.04	

$\Sigma y = Na + b\Sigma x$

$61.46 = 6a + 0$

$a = 61.46/6$

$a = 10.24$

$\Sigma xy = a\Sigma x + b\Sigma x^2$

$480.04 = 0 + b \times 1{,}066.24$

$b = 480.04/1{,}066.24$

$b = 0.45$

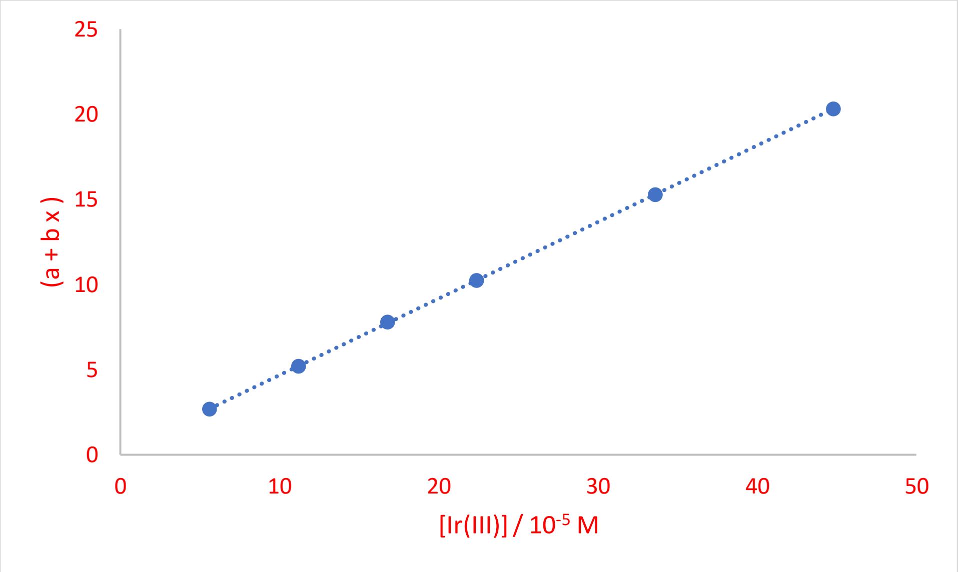

Figure: 5.2B(b) Plot between rate of reaction (a+bx) vs [$IrCl_3$] for the oxidation of paracetamol at 35^{0}C. [$HClO_4$]=1.00 x 10^{-3}M, [KCl]=1.00 x 10^{-3}M, [$Hg(OAc)_2$] = 1.25 x 10^{-3}M, [PA] = 1.00 x 10^{-2}M, [$KBrO_3$] = 1.00 x 10^{-3}M

5.3A Kinetic investigation and determination of order with respect to compound (substrate) in Ir(III) catalyzed oxidation of gabapentin by $KBrO_3$ in acidic medium.

To determine the order of reaction for Gabapentin on the rate of reaction, its concentration has been varied from 0.40 x 10^{-2} M to 4.00 x 10^{-2} M keeping the concentration of all other reactants fixed at constant temperature 35^{0}C.

All the results obtained are presented in Table 5.3A(a). For each run (-dc/dt) values have been calculated by the slopes of tangents drawn at fixed concentrations of all reactants. A close examination of Table 5.3A(a) suggests that with increase in the concentration of substrate there is no change seen in(-dc/dt) values of gabapentin.

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Table: 5.3A(a)

[$KBrO_3$] = 1.00 x 10^{-3} M [KCl] = 1.00 x 10^{-3} M

[Ir(III)] = 11.20 x 10^{-5} M [$Hg(OAc)_2$] = 1.25 x 10^{-3} M

[$HClO_4$] = 1.00 x 10^{-3} M Temperature = 35^0C

[GB] / 10^{-2} M→	0.40	0.50	0.66	1.00	2.0	4.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.52	9.62	9.85	9.62	9.75	9.82
10	9.08	9.10	9.15	9.10	9.20	9.25
15	8.50	8.50	8.75	8.50	8.75	8.64
20	8.14	8.21	8.25	8.21	8.25	8.30
25	7.92	7.90	7.75	7.67	7.87	7.96
35	7.45	7.37	7.25	7.25	7.50	7.58
45	6.63	6.43	6.50	6.63	6.89	6.85
60	6.18	6.20	6.08	6.20	6.14	6.10
(-dc/dt)→ / 10^{-7} M s^{-1}	2.21	2.00	2.10	2.00	2.10	2.22

C* = Volume of hypo used (N/400) in ml.

5.3:B Kinetic investigation and order with respect to compound (substrate) in Ir(III) catalyzed oxidation of paracetamol by $KBrO_3$ in acidic medium.

To determine the order of reaction for paracetamol and its impact on the rate of reaction, its concentration has been varied from 0.40 x 10^{-2} M to 4.00 x 10^{-2} M keeping the concentration of all other reactants fixed at constant temperature 35^0C. All the results obtained are presented in Table 5.3B. For each kinetic run (-dc/dt) values have been calculated from the slope of tangents drawn at fixed concentrations of all reactants. A close examination of Table 5.3B suggests that with increase in the concentration of substrate there is an increase in (-dc/dt) values. A plot of log k versus concentration of paracetamol gives a straight line with slope value of 0.38. This indicates fractional positive effect with respect to substrate paracetamol in its Ir(III) catalyzed oxidation by bromate.

Table: 5.3B

[$KBrO_3$] = 1.00×10^{-3} M
[KCl] = 1.00×10^{-3} M
[Ir(III)] = 11.20×10^{-5} M
[$Hg(OAc)_2$] = 1.25×10^{-3} M
[$HClO_4$] = 1.00×10^{-3} M
Temperature = 35^0C

[PA] → / 10^{-2} M	0.40	0.50	0.66	1.00	2.00	4.00
Time (Min.) ↑	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.80	9.50	9.20	9.25	9.00	8.52
10	9.25	9.00	8.75	8.62	8.10	7.82
15	9.00	8.67	8.25	8.10	7.25	6.95
20	8.50	8.25	7.90	7.50	6.52	6.00
25	8.00	7.50	7.25	7.00	5.90	5.62
35	7.65	7.25	6.45	6.12	5.20	5.00
45	7.25	6.50	6.00	5.40	4.50	4.10
60	7.00	6.00	5.50	4.80	4.00	3.25
(-dc/dt) → / 10^{-7} Ms^{-1}	3.98	4.30	4.62	5.20	6.65	8.25

C* = Volume of hypo used (N/400) in ml.

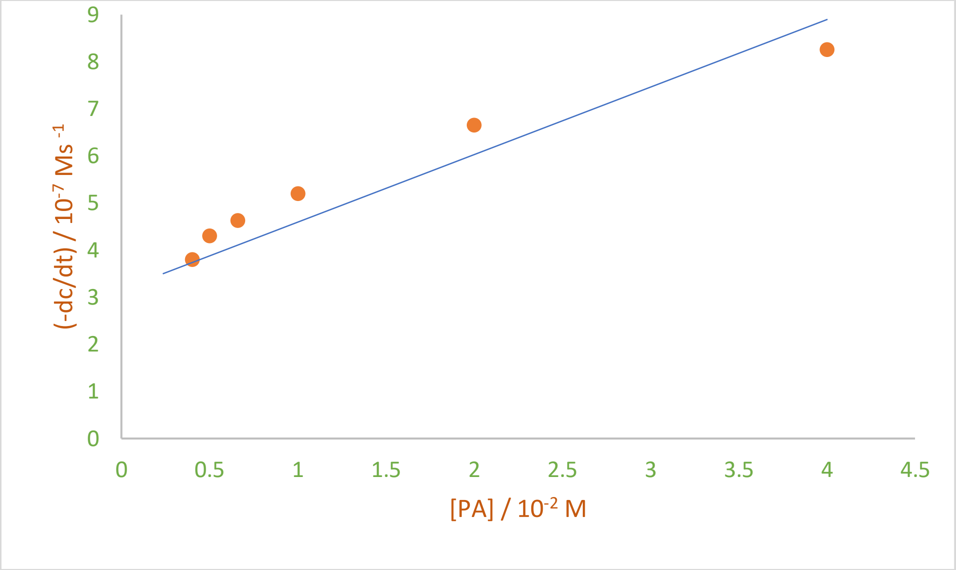


Figure: 5.3B Plot between rate of reaction (-dc/dt) vs [PA] for the oxidation of paracetamol at 35^{0}C. [$HClO_4$] = 1.00 x 10^{-3} M, [KCl] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [$KBrO_3$]=1.00 x 10^{-3} M, [Ir(III)] = 11.20 x 10^{-5} M

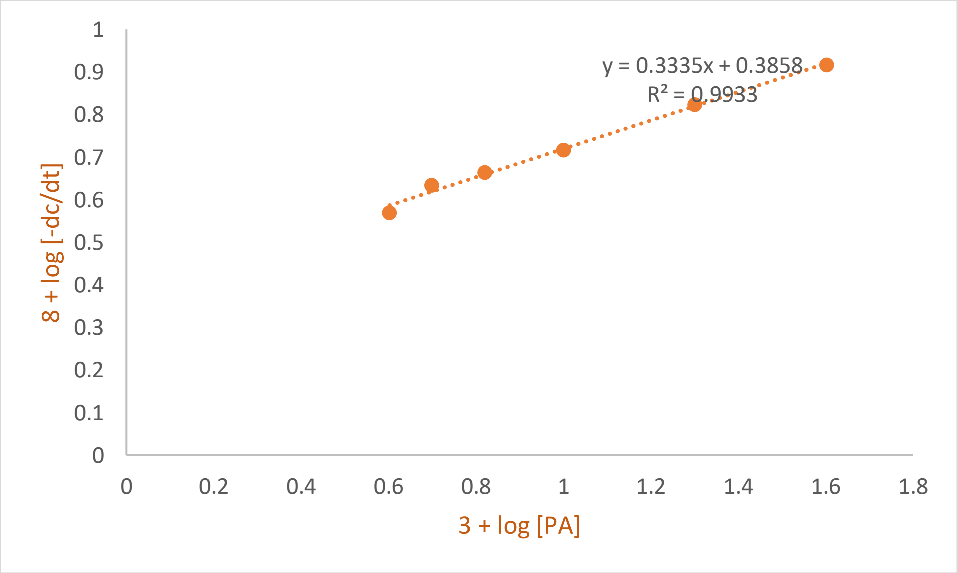


Figure: 5.3B Plot between rate of reaction log(-dc/dt) vs log[PA] for the oxidation of paracetamol at 35^{0}C. [$HClO_4$] = 1.00 x 10^{-3} M, [KCl] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [$KBrO_3$]=1.00 x 10^{-3} M, [Ir(III)] = 11.20 x 10^{-5} M

5.4: Thermodynamic study and Kinetic investigation of the effect of chloride ion in Ir(III) catalyzed oxidation of pharmaceutical drugs by $KBrO_3$ in acidic medium.

In order to study the effect of addition of chloride ion on the rate of Ir(III) catalyzed oxidation of pharmaceutical drugs by potassium bromate in acidic medium, different concentrations of KCl were taken into consideration. The concentration of KCl has been varied from 0.83 x 10^{-3} M to 5.00 x 10^{-3} M

5.4A: Effect of variation in chloride ion on the rate of Ir(III) catalyzed oxidation of gabapentin by potassium bromate in acidic medium.

To study the effect of alteration in chloride ion concentration on Ir(III) catalyzed oxidation of gabapentin by $KBrO_3$ in acidic medium, the concentration of KCl has been varied from 0.83 x 10^{-3} M to 5.00 x 10^{-3} M. The table 5.4A depicts that upon increasing the concentration of KCl, rate of reaction also increases. For each run (-dc/dt) values have been calculated by the slopes of tangents drawn at fixed concentrations of all reactants. This indicates a positive effect of KCl on the rate of reaction. A graph plotted between (-dc/dt) and [KCl] values gives a straight line with positive slope 0.88 which further confirms that KCl has positive effect on the rate of reaction. Fig 5.4A.

Table: 5.4A

[GB] = 1.00×10^{-2} M

[Ir(III)] = 11.20×10^{-5} M

[$HClO_4$] = 1.00×10^{-3} M

[$KBrO_3$] = 1.00×10^{-3} M

[$Hg(OAc)_2$] = 1.25×10^{-3} M

Temperature = 35^0C

[KCl] /10^{-3} M →	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.75	9.62	9.25	9.00	8.52	8.21
10	9.50	9.10	8.75	8.23	8.00	7.54
15	9.25	8.50	8.25	7.38	7.02	6.62
20	9.00	8.21	8.00	6.51	6.00	6.00
25	8.75	8.00	7.52	6.00	5.45	5.12
35	8.25	7.25	7.25	5.20	4.62	4.10
45	7.46	6.43	6.54	4.63	4.00	3.42
60	7.11	6.20	6.00	4.20	3.50	3.00
(-dc/dt) → / 10^{-7} Ms^{-1}	1.80	2.00	2.20	2.38	2.60	3.85

C* = Volume of hypo used (N/400) in ml

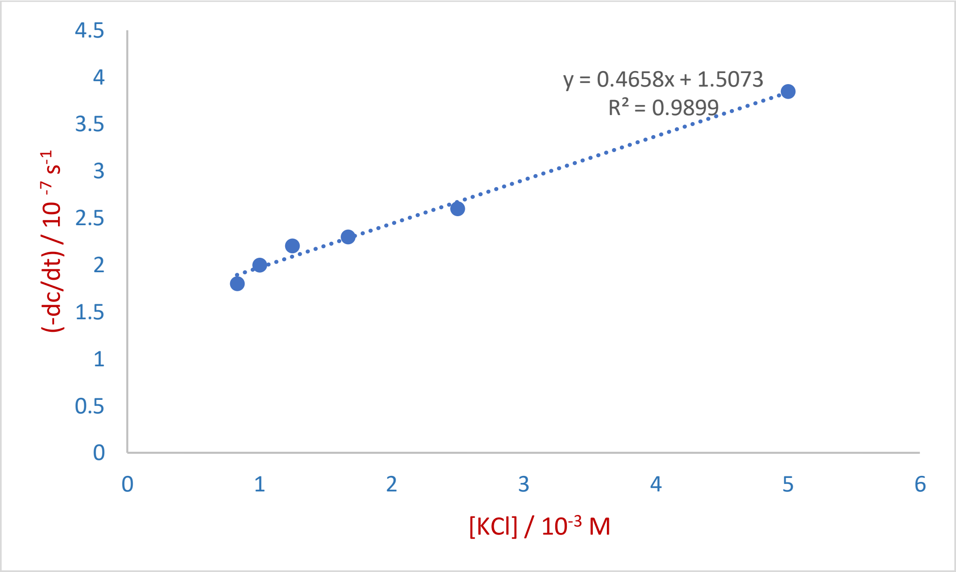


Figure: 5.4A(a) Plot between rate of reaction (-dc/dt) vs [KCl] for the oxidation of gabapentin at 35^0C. [$HClO_4$] = 1.00 x 10^{-3}M, [$KBrO_3$] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [GB] = 1.00 x 10^{-2} M, [Ir(III)] =11.20 x 10^{-5} M

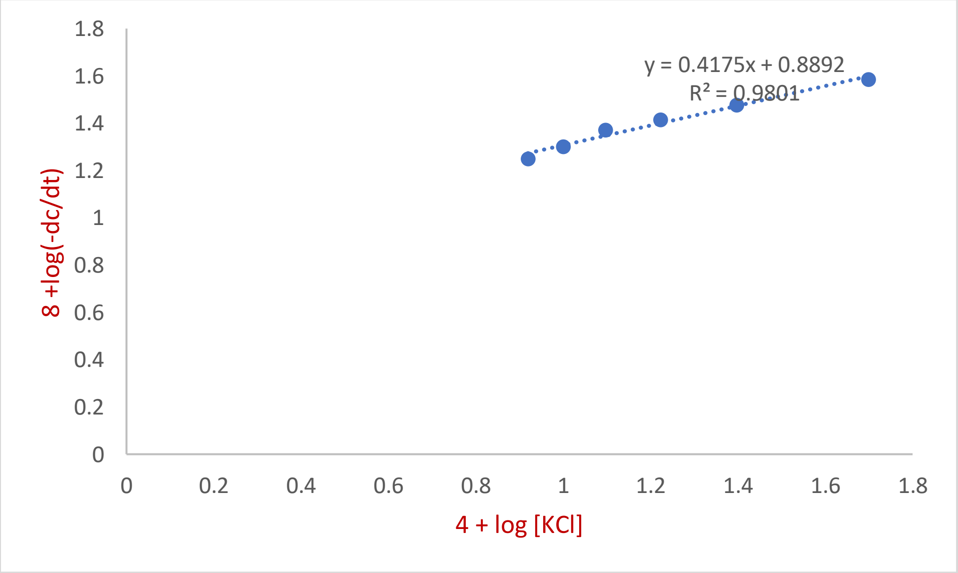


Figure: 5.4A(a) Plot between rate of reaction log (-dc/dt) vs log [KCl] for the oxidation of gabapentin at 35^0C. [$HClO_4$] = 1.00 x 10^{-3}M, [$KBrO_3$] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [GB] = 1.00 x 10^{-2} M, [Ir(III)] =11.20 x 10^{-5} M

5.4B: Kinetic investigation and study of the effect of chloride ion in Ir(III) catalyzed oxidation of paracetamol drug by $KBrO_3$ in acidic medium.

To study the effect of chloride ion in Ir(III) catalyzed oxidation of paracetamol by $KBrO_3$ in acidic medium, different concentration of KCl were added in various reaction mixture and the result have been presented in table 5.4B. The concentration of KCl has been varied from 0.83 x 10^{-3} M to 5.00 x 10^{-3} M. The table 5.4B shows that the rate remains almost constant upon increasing or decreasing the concentration of KCl. This indicates an insignificant effect of KCl on the reaction rate.

Table: 5.4B

[PA] = 1.00 x 10^{-2} M

[Ir(III)] = 11.20 x 10^{-5} M

[$HClO_4$] = 1.00 x 10^{-3} M

[$KBrO_3$] = 1.00 x 10^{-3} M

[$Hg(OAc)_2$] = 1.25 x 10^{-3} M

Temperature = 35^0C

[KCl] → / 10^{-3} M	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.00	9.25	9.00	9.38	9.50	9.25
10	8.56	8.62	8.70	8.80	9.00	9.00
15	8.00	8.10	8.25	8.25	8.50	8.25
20	7.48	7.50	7.56	7.58	8.00	8.00
25	7.00	7.00	6.80	6.60	7.56	7.40
35	6.25	6.12	6.50	5.12	6.20	6.00
45	5.20	5.40	5.00	4.90	6.00	5.25
60	4.60	4.80	4.28	4.66	5.00	4.50
(-dc/dt) → / 10^{-7} Ms^{-1}	4.90	5.20	4.82	5.25	5.12	4.72

C* = Volume of hypo used (N/400) in ml.

5.5: Kinetic investigation on the effect of variation in hydrogen ion concentration on the rate of Ir(III) catalyzed oxidation of pharmaceutical drugs by potassium bromate in acidic medium.

The effect of hydrogen ion concentration on the rate of reaction has been studied by varying concentration of perchloric acid which was used as a source of hydrogen ion$[H^+]$. In the reaction between potassium bromate and pharmaceutical drugs in presence of Ir(III) chloride, hydrogen ion and chloride ion, the rate of reaction may be expressed as:

$$\frac{d[KBrO_3]}{dt} = k[KBrO_3]^{n_1} [\textit{Pharmaceutical drug}]^{n_2} [Ir(III)]^{n_3} [H^+]^{n_4} [Cl^-]^{n_5}$$

In above equation (i), the values of n_1, n_2 and n_3 have already been found out to be one, positive & one respectively, in previous sections of this chapter. Equation (i) can be written as:-

$$\frac{-d[KBrO_3]}{dt} = k[KBro_3]^1 [\textit{Pharmaceutical drug}]^0 [Ir(III)]^1 [H^+]^{n_4} [Cl^-]^{n_5} \text{.............(ii)}$$

or

$$\frac{-d[KBrO_3]/dt}{[KBrO_3]} = k[Ir(III)]\,[H^+]^{n_4}\,[Cl^-]^{n_5}\ . \qquad \text{........(iii)}$$

or $$k_1 = k[Ir(III)]\,[H^+]^{n_4}\,[Cl^-]^{n_5}$$

............(iv)

where k_1 is first order Since concentrations of all other reactants except hydrogen ions, were kept constant, hence above equation (iv) can also be written as:-

$$k_1 = k'[H^+]^{n_4}$$

.........(v)

where $k' = k[Ir(III)]\,[Cl^-]^{n_5}$

5.5A: Effect of variation in hydrogen ion concentration on the rate of Ir(III) catalyzed oxidation of gabapentin by potassium bromate in acidic medium.

To determine the impact of variation in hydrogen ion concentration on Ir(III) catalyzed oxidation of gabapentin by acidic bromate, a number of experiments were performed at constant temperature of 35^0C.

The concentration of hydrogen perchlorate was varied from 0.83×10^{-3} M to 5.00×10^{-3} M. The results obtained are presented in Table 5.5A. It is clear from the Table 5.5A that with increase in the concentration of $[HClO_4]$ there is an increase in (-dc/dt) values, showing that there is a linear relationship between (-dc/dt) values and $[H^+]$ (Fig. 5.5A). This linear relationship clearly indicates that the reaction follows first order kinetics with respect to $[H^+]$ concentrations. This has also been confirmed by “least- square method” as revealed in Table 5.5A(b) and fig-5.5A(b).

Table: 5.5A

[GB]	= 1.00×10^{-2} M	[KCl]	= 1.00×10^{-3} M
[Ir(III)]	= 11.20×10^{-5} M	[$Hg(OAc)_2$]	= 1.25×10^{-3} M
[$KBrO_3$]	= 1.00×10^{-3} M	Temperature	= 35^0C.

[$HClO_4$] → / 10^{-3} M	0.83	1.00	1.25	1.67	2.5	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.78	9.62	9.20	9.00	8.52	8.00
10	9.50	9.10	8.75	8.40	8.00	7.26
15	9.00	8.50	8.21	7.98	7.54	6.40
20	8.50	8.21	7.56	7.54	7.00	5.98
25	8.25	8.00	7.25	7.00	6.42	5.40
35	7.85	7.47	6.60	6.25	5.22	4.75
45	7.21	6.93	6.00	5.45	4.00	3.88
60	7.00	6.20	5.54	4.48	3.52	3.00
(-dc/dt) → / 10^{-7} Ms^{-1}	1.60	2.00	2.40	3.30	4.90	9.70
$k_1 = \frac{(-dc/dt)}{[HClO_4]}$ → / 10^{-4} s^{-1}	1.93	2.00	1.92	1.97	1.96	1.94

C* = Volume of hypo used (N/400) in ml.

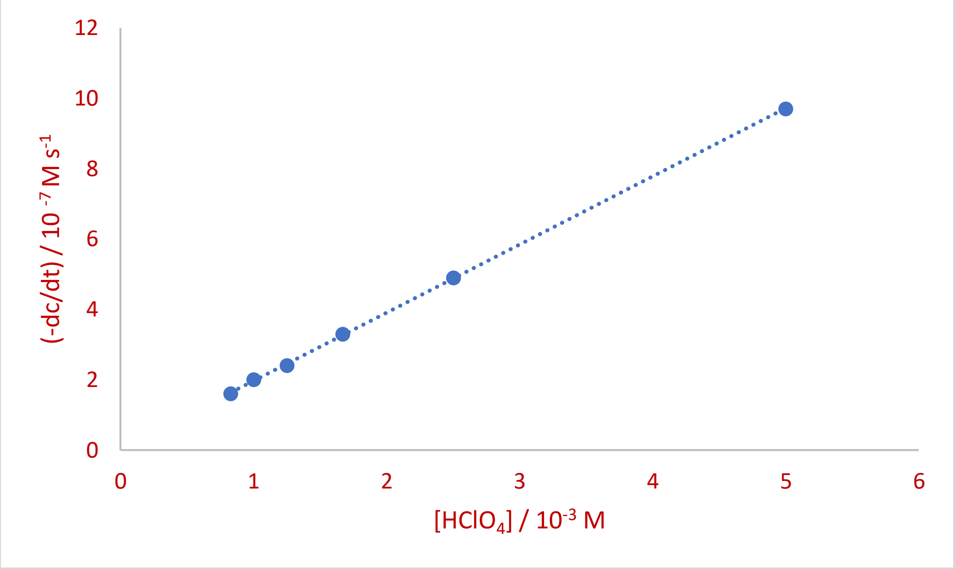


Figure: 5.5A Plot between (-dc/dt) vs [$HClO_4$] for the oxidation of gabapentin at 35^0C. [$KBrO_3$] = 1.00 x 10^{-3}M, [KCl] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3} M, [GB]= 1.00 x 10^{-2} M, [Ir(III)] =11.20 x 10^{-5} M

Table: 5.5A(b)

[$HClO_4$] / 10^{-3} (M)	(-dc/dt) (Y)	x (conc. – n)	x^2	xy	(a + bx)
0.83 1.00 1.25 1.67 2.50 5.00	1.60 2.00 2.40 3.30 4.90 9.70	-1.21 -1.04 -0.79 -0.37 0.46 2.96	1.46 1.08 0.62 0.13 0.21 8.76	-1.94 -2.08 -1.89 -1.22 2.25 28.71	1.62 1.95 2.44 3.26 4.88 9.75
12.25/6 n = 2.04	Σy = 23.90	Σx = 0.00	Σx^2 = 12.26	Σxy =23.83	

$\Sigma y = Na + b\Sigma x$ $\Sigma xy = a\Sigma x + b\Sigma x^2$

$23.90 = 6a + 0$ $23.83 = 0 + b \times 12.26$

$a = 23.90/6$ $b = 23.83/12.26$

$a = 3.98$ $b = 1.95$

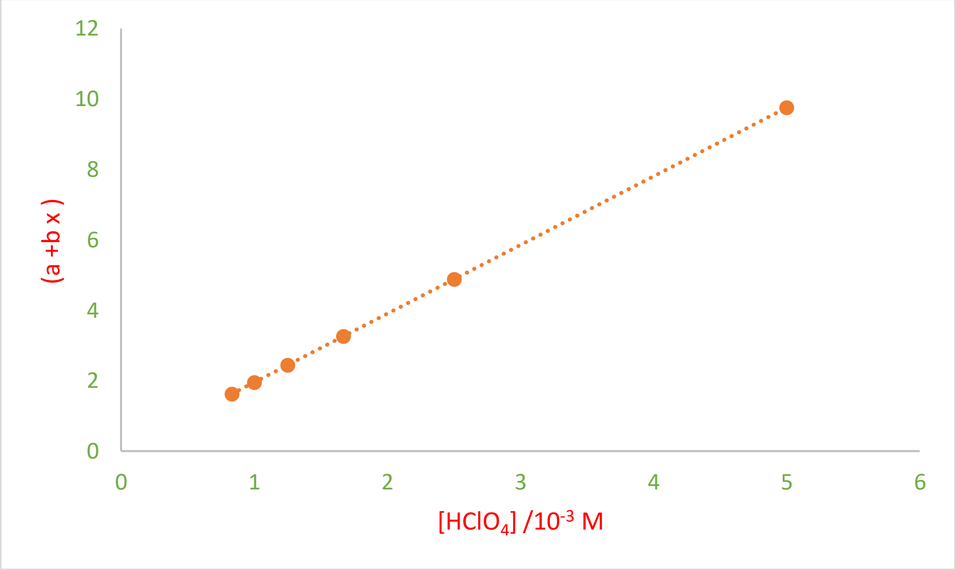


Figure: 5.5A(b) Plot between rate of reaction (a+bx) vs [$HClO_4$] for the oxidation of gabapentin at 35^{0}C. [$KBrO_3$]= 1.00 x 10^{-3} M, [KCl]= 1.00 x 10^{-3} M, [$Hg(OAc)_2$] = 1.25 x 10^{-3}M, [GB]= 1.00 x 10^{-2} M, [Ir(III)] = 11.20 x 10^{-5} M

5.5B: Effect of variation in hydrogen ion concentration on the rate of Ir(III) catalyzed oxidation of paracetamol by potassium bromate in acidic medium.

To determine the impact of variation in hydrogen ion for Ir(III) catalyzed oxidation of paracetamol by potassium bromate in acidic medium, a number of experiments were performed at constant temperature of 35^{0}C.

The concentration of hydrogen perchlorate was varied from 0.83 x 10^{-3} M to 5.00 x 10^{-3}M. The results obtained are presented in Table 5.5B. It is clear from Table 5.5B that the reaction follows negative effect of hydrogen ion concentration. In each kinetic run upon increasing the concentration of $HClO_4$, the (-dc/dt) values decreases. [fig- 5.5B]

Table: 5.5B

[PA] = 1.00×10^{-2} M
[Ir(III)] = 11.20×10^{-5} M
[$KBrO_3$] = 1.00×10^{-3} M

[KCl] = 1.00×10^{-3} M
[$Hg(OAc)_2$] = 1.25×10^{-3} M
Temperature = 35^0C.

[$HClO_4$] → / 10^{-3} M	0.83	1.00	1.25	1.67	2.5	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.00	9.25	9.45	9.50	9.65	9.70
10	8.15	8.62	9.20	9.30	9.45	9.50
15	7.15	8.10	8.50	8.60	9.10	9.15
20	6.90	7.50	8.00	8.50	8.50	8.80
25	6.25	7.00	7.55	7.85	8.25	8.45
35	5.70	6.12	7.00	7.35	7.60	8.00
45	5.02	5.40	6.30	6.90	7.15	7.50
50	4.20	4.80	5.50	6.50	6.95	7.20
(-dc/dt) / 10^{-7} Ms^{-1}	5.41	5.20	4.98	4.62	4.30	3.05

C*= Volume of hypo used (N/400) in ml.

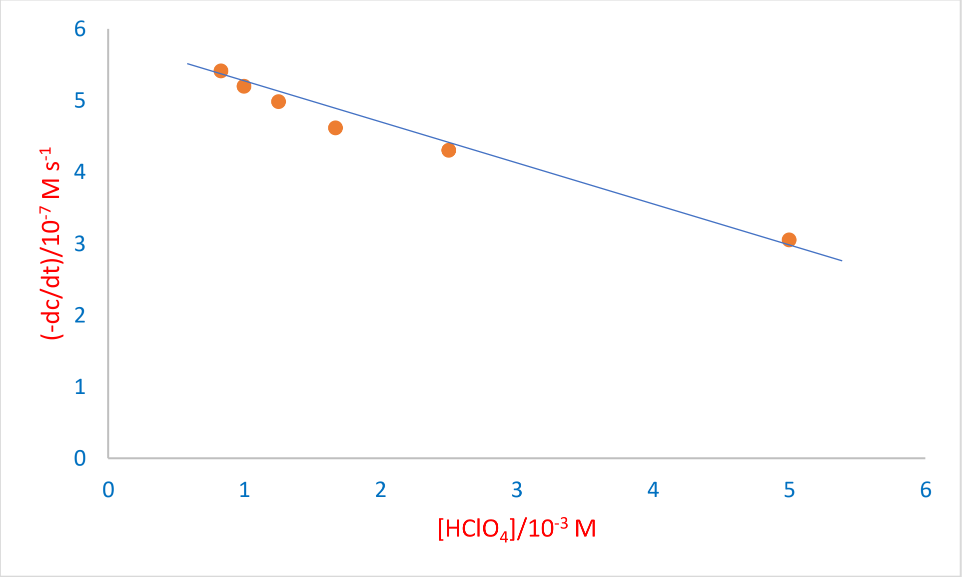


Figure:5.5B Plot between rate of reaction (-dc/dt) vs [$HClO_4$] for the oxidation of paracetamol at 35^0C. [$KBrO_3$]= 1.00 x 10^{-3}M, [KCl] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$]= 1.25 x 10^{-3} M, [PA]= 1.00 x 10^{-2} M, [Ir(III)]= 11.20 x 10^{-5} M

5.6: Effect of addition of mercuric acetate on the rate of Ir(III) catalyzed oxidation of pharmaceutical drugs by potassium bromate in acidic medium.

In the present thesis all the redox processes involving potassium bromate as an oxidant and pharmaceutical drugs as reducing agents have been studied in the presence of mercuric acetate as a scavenger, but mercury(II) can also act as an oxidant and catalyst as well. Hence in order to investigate the role of mercury(II) in the present investigation, various experiments, have been performed to ascertain whether mercuric acetate acts as an oxidant or a catalyst, in addition to its role as a bromide ion scavenger.

The preliminary investigations showed that mercuric acetate does not function here as an oxidant because without addition of potassium bromate the reaction does not proceed and it has been found during preliminary investigations that the reaction mixture develops pale yellow colour after few minutes of the progress of the reaction when mercuric acetate was not added to the reaction mixture. A set of experiments were performed in the presence of potassium bromate with varying amount of mercuric acetate under same physical conditions of experiment. It was observed that the reaction rate for all the redox processes, under the present investigation, were uninfluenced by successive addition of mercuric acetate in the reaction mixture.

This rules out possibility of mercuric acetate being involved as catalyst in the reactions. Hence it only functions as scavenger for bromide ion.

5.6A: Effect of addition of mercuric acetate on the rate of Ir(III) catalyzed oxidation of gabapentin drug by potassium bromate in acidic medium.

In order to study the effect of variation in mercuric acetate on the rate of oxidation of gabapentin by potassium bromate, in the presence of iridium(III) chloride in acidic medium, concentration of mercuric acetate has been varied from 0.83×10^{-3} M to 5.00×10^{-3} M at constant concentration of all other reactants. All experiments were carried out at constant temperature 35^0C and the results have been recorded in Tables 5.6A

A perusal of Table 5.6A, indicates that the values of first order rate constant k_1 or $(-dc/dt)/[KBrO_3]$ remain almost constant throughout the variation of mercuric acetate concentration. This shows insignificant effect of mercuric acetate on the rate of reaction. Thus it is obvious from the results that neither mercuric acetate acts here as an oxidant nor as a catalyst.

Table: 5.6A

$[KBrO_3]$ = 1.00 x 10^{-3} M
$[GB]$ = 1.00 x 10^{-2} M
$[IrCl_3]$ = 11.20 x 10^{-5} M

$[HClO_4]$ = 1.00 x 10^{-3} M
$[KCl]$ = 1.00 x 10^{-3} M
Temperature = 35^0C.

$[Hg(OAc)_2]$ / 10^{-3} M	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.)	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.50	9.10	9.00	9.50	9.10	9.50
10	9.00	8.50	8.32	9.00	8.50	8.75
15	8.51	8.21	7.50	8.50	8.00	8.10
20	8.00	8.00	7.12	8.05	7.67	7.74
25	7.58	7.67	6.52	7.64	7.25	7.10
35	6.95	7.05	6.00	6.95	6.63	6.70
45	6.50	6.43	5.50	6.30	6.20	6.15
60	5.95	5.90	5.00	5.80	5.85	5.70
(-dc/dt) / 10^{-7} Ms^{-1}	2.50	2.00	2.10	2.02	2.00	2.31

C* = Volume of hypo used (N/400) in ml.

5.6B: Effect of addition of mercuric acetate on the rate of Ir(III) catalyzed oxidation of paracetamol drug by potassium bromate in acidic medium.

In order to study the effect of variation in mercuric acetate on the rate of oxidation of paracetamol by potassium bromate, in the presence of Iridium(III) chloride in acidic medium, concentration of mercuric acetate has been varied from 0.83 x 10^{-3} M to 5.00 x 10^{-3} M at constant concentration of all other reactants.

All experiments were carried out at constant temperature 35^0C and the results have been recorded in Tables 5.6 B.

A perusal of Table 5.6B indicates that the values of (-dc/dt) remain almost constant throughout the variation of mercuric acetate concentration. This shows insignificant effect of change in concentration of mercuric acetate on the rate of reaction. Thus it is obvious from the results that neither mercuric acetate acts here as an oxidant nor as a catalyst.

Table: 5.6B

[$KBrO_3$] = 1.00×10^{-3} M
[PA] = 1.00×10^{-2} M
[$IrCl_3$] = 11.20×10^{-5} M
[$HClO_4$] = 1.00×10^{-3} M
[KCl] = 1.00×10^{-3} M
Temperature = 35^0C.

[$Hg(OAc)_2$] / 10^{-3} M →	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.40	9.25	9.35	9.00	9.35	9.20
10	8.50	8.62	8.50	8.15	8.55	8.60
15	7.80	8.10	7.90	7.40	7.90	8.00
20	7.25	7.50	7.40	6.80	7.35	7.25
25	6.90	7.00	7.00	6.00	6.84	6.65
35	6.21	6.12	6.92	5.15	6.17	6.00
45	5.50	5.40	5.50	4.50	5.75	5.50
60	4.25	4.75	4.85	4.00	4.95	5.14
(-dc/dt) → / 10^7 Ms^{-1}	4.82	5.20	4.94	5.04	5.55	5.32

C* = Volume of hypo used (N/400) in ml.

5.7: Effect of variation in ionic strength of the medium on the rate of Iridium(III) catalyzed oxidation of pharmaceutical drugs i.e. (gabapentin and paracetamol) by potassium bromate in acidic medium.

The effect of ionic strength variation helps in ascertaining the nature of the reactive species actually involved in the rate determining step. Therefore, it was thought worthwhile to investigate the effect of variation in ionic strength on the velocity of the title reaction. In this section our main attempt has been to determine the effect of ionic strength which has been varied by the addition of suitable amounts of sodium perchlorate in the reaction mixture. The ionic strength of the solution has been varied by addition of $NaClO_4$ with concentration varying from 0.83×10^{-3} M to 5.00×10^{-3} M at the constant concentration of all other reactants, at constant temperature 35^0C. All experimental results are displayed in Table 5.7A for gabapentin and 5.7B for paracetamol respectively.

It is evident from Table 5.7A for gabapentin and 5.7B for paracetamol and summarized table 5.7A(a) and 5.7B(b) respectively that the value of (-dc/dt) does not show any appreciable change, which reveals that in all the case, there is negligible effect of variation in ionic strength (µ) of the medium on the rate of reaction.

Ionic strength (µ) has been calculated taking sum of concentration of those reactants which ionize in solution i.e. $KBrO_3$, $HClO_4$, KCl and $Hg(OAc)_2$. Known concentration of $NaClO_4$ has been used to change the ionic strength of the medium. The choice of $NaClO_4$ for varying ionic strength has been made because it does not initiate any reaction with other reactants taking part in the reaction and only changes the ionic strength of the medium.

Table: 5.7A

$[KBrO_3]$ = 1.00 x 10^{-3} M

$[GB]$ = 1.00 x 10^{-2} M

$[IrCl_3]$ = 11.20 x 10^{-5} M

$[Hg(OAc)_2$ = 1.25 x 10^{-3} M

$[HClO_4]$ = 1.00 x 10^{-3} M

$[KCl]$ = 1.00 x 10^{-3} M

Temperature = 35^0C.

$[NaClO_4]$ / 10^{-3} M →	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.84	9.62	9.80	9.70	9.80	9.62
10	9.50	9.10	9.25	9.21	9.10	9.10
15	8.65	8.50	8.75	8.75	8.60	8.50
20	8.40	8.21	8.45	8.25	8.05	8.21
25	8.00	8.00	8.00	8.10	7.70	7.67
35	7.50	7.25	7.28	7.50	7.30	7.25
45	7.25	6.43	6.75	6.73	6.80	6.43
60	6.50	6.20	6.50	6.25	6.20	6.00
(-dc/dt) → / 10^{-7} Ms^{-1}	2.10	2.00	2.50	2.20	2.00	2.42

C* = Volume of hypo used (N/400) in ml.

Table: 5.7A(a)

[$KBrO_3$]	= 1.00×10^{-3} M	[$HClO_4$]	= 1.00×10^{-3}M
[GB]	= 1.00×10^{-2} M	[KCl]	= 1.00×10^{-3} M
[$IrCl_3$]	= 11.20×10^{-5} M	Temperature	= 35^0C.
[$Hg(OAc)_2$]	=1.25×10^{-3}M		

[$NaClO_4$] / 10^{-3} M	μ / 10^{-3} M	(-dc/dt) / 10^{-7} Ms^{-1}
0.83	7.58	2.10
1.00	7.75	2.00
1.25	8.00	2.50
1.67	8.42	2.20
2.50	9.25	2.00
5.00	11.75	2.42

Table: 5.7B

[$KBrO_3$] = 1.00×10^{-3} M

[PA] = 1.00×10^{-2} M

[$IrCl_3$] = 11.20×10^{-5} M

[$Hg(OA)_2$ = 1.25×10^{-3} M

[$HClO_4$] = 1.00×10^{-3} M

[KCl] = 1.00×10^{-3} M

Temperature = 35^0C.

[$NaClO_4$] → /10^{-3} M	0.83	1.00	1.25	1.67	2.50	5.00
Time (Min.) ↓	C*	C*	C*	C*	C*	C*
0	10.00	10.00	10.00	10.00	10.00	10.00
5	9.50	9.25	9.00	9.10	9.40	9.00
10	8.85	8.62	8.25	8.50	8.85	8.00
15	8.30	8.10	8.00	8.00	8.15	7.25
20	7.80	7.50	7.25	7.50	7.35	6.75
25	7.40	7.00	6.85	6.80	6.80	6.25
35	6.60	6.22	6.25	6.20	6.25	5.65
45	5.95	5.40	5.20	5.75	5.55	5.00
60	5.15	4.80	4.85	5.00	5.00	4.50
(-dc/dt) → / 10^{-7} Ms^{-1}	5.52	5.20	4.90	5.40	5.35	5.00

C* = Volume of hypo used (N/400) in ml.

Table: 5.7B(b)

$[KBrO_3]$ = 1.00 x 10^{-3} M
$[PA]$ = 1.00 x 10^{-2} M
$[IrCl_3]$ = 11.20 x 10^{-5} M
[Hg(OAc)] =1.25 x 10^{-3}M
$[HClO_4]$ = 1.00 x 10^{-3}M
[KCl] = 1.00 x 10^{-3} M
Temperature = 35^0C.

$[NaClO_4]$ / 10^{-3} M	μ / 10^{-3} M	(-dc/dt) / 10^{-7} Ms^{-1}
0.83	7.58	5.52
1.00	7.75	5.20
1.25	8.00	4.90
1.67	8.42	5.40
2.50	9.25	5.35
5.00	11.75	5.00

5.8: Effect of addition of D_2O on the reaction rate of Ir(III) catalyzed reaction between potassium bromate and each of the reducing pharmaceutical drugs gabapentin and paracetamol

In order to investigate the solvent isotope effect on the reaction rate of the title reaction, a number of experiments containing different percentages of D_2O: H_2O (volume/volume) and with fixed concentrations of remaining reactants, were performed. The experiments were repeated similarly with different pharmaceutical drugs mentioned in the title. The results obtained are summarized in following Table 5.8A.

It is obvious from the results of the summarized table, collected from the experiments performed with each of the title pharmaceutical drugs (gabapentin and paracetamol) that the reaction rate remains unaffected in all cases at different D_2O – H_2O ratios. (values of (- dc/dt) remain almost constant at different D_2O – H_2O ratio. This shows that in the present reactions the rate determining step does not involve protonated reducing pharmaceutical drug.

Table: 5.8A

$[KBrO_3]$	= 1.00×10^{-3} M	$[HClO_4]$	= 1.00×10^{-3}M
[Substrate]	= 1.00×10^{-2} M	[KCl]	= 1.00×10^{-3} M
[Ir(III)]	= 11.20×10^{-5} M	$[Hg(OAc)_2]$	= 1.25×10^{-3} M
		Temperature	= 35^0C.

[SUBSTRATE]/10^{-2}M	D_2O – H_2O (%) (v/v)	(-dc/dt) / 10^{-7} Ms^{-1}
GB	00 – 100	2.00
GB	05 – 95	2.37
GB	10 – 90	2.50
GB	20 – 80	2.32
PA	00 – 100	5.20
PA	05 – 95	5.48
PA	10 – 90	5.18
PA	20 – 80	5.50

Summary:

Following kinetic results have been obtained on the basis of experiments performed for oxidation of Gabapentin and Paracetamol by acidic bromate in presence of Ir(III) chloride as a catalyst.

Gabapentin	Reaction order	Paracetamol	Reaction order
Reactants		Reactants	
[$KBrO_3$]	1st order	[$KBrO_3$]	1st order
[Ir(III)]	1st order	[Ir(III)]	1st order
Substrate	Zero order	Substrate	Positive effect
[KCl]	Positive effect	[KCl]	No effect
[$HClO_4$]	1st order	[$HClO_4$]	Negative effect
$Hg(OAc)_2$	No effect	$Hg(OAc)_2$	No effect
[$NaClO_4$]	No effect	[$NaClO_4$]	No effect
D_2O	No effect	D_2O	No effect

CHAPTER 6

EFFECT OF VARIATION IN TEMPERATURE ON THE RATE OF Ir(III) CATALYZED OXIDATION OF PHARMACEUTICAL DRUGS BY ACIDIC POTASSIUM BROMATE AND DETERMINATION OF ACTIVATION PARAMETERS

6.0: Effect of variation in temperature on Ir(III) catalyzed oxidation of pharmaceutical drugs by acidic potassium bromate.

It is well known that increase in temperature frequently cause a marked increase in the rate of reaction. For homogeneous processes the specific rate is doubled or trebled for each 10^0 rise in temperature, generally expressed in the form of temperature coefficient:

$$K_{t\ +10} / K_t = 2 \text{ to } 3$$

K_t is the specific rate at t^0 and $K_{t\ +10}$ at 10^0 higher.

The temperature variation will have no effect on the reaction order. Thus, although the rate constant is independent of reactant concentration, it varies with temperature. Arrhenius proposed an equation for calculation of energy of activation (E_a) of a reaction having rate constant 'k', at absolute temperature 'T', expressed as:

$$k= A\ e^{-Ea/RT}$$

where R is gas constant and A is a constant known as pre- exponential factor or Arrehnius frequency factor, which includes same energy unit as E_a Both E_a and 'A' are characteristic of a reaction. Equation (1) indicates that when $E_a = 0$ or $T = \infty$, then

$$k \quad = \quad A \text{..................................} (2)$$

Taking logarithm of equation (1), we have

$$\ln k \quad = \quad \ln A - E_a / RT \text{ ....} (3)$$

6.1 Effect of variation in Temperature on the rate of reaction for Ir(III) catalyzed oxidation of gabapentin and paracetamol by potassium bromate in acidic medium.

$$\log k = \log A - E_a/2.303RT$$

The above equation suggests that a plot of log k against 1/T should give a straight line and the slope of this straight line is equal to $-E_a/2.303R$ while intercept of straight line gives the value of logA Fig. 6.1A and Fig. 6.2B. In order to determine the effect of temperature on the rate of reaction, several experiments were performed under identical conditions at different temperature, viz. 30^0, 35^0, 40^0 and 45^0 respectively and their results have been given in Tables 6.1A(a), 6.1A(b), and 6.1A(c) summarized in Tables 6.1A(d), for Gabapentin while 6.2B(a), 6.2B(b), and 6.2B(c) summarized in Table 6.2B(d), for Paracetamol drug. It is evident from summarized tables that the values of (-dc/dt) or k_1 increases on increasing the temperature. Thus it is clear that the reaction velocity goes on increasing with rise in temperature.

Table: 6.1A(a)

$[KBrO_3]$ = 1.00×10^{-3} M
[GB] = 1.00×10^{-2} M
[Ir(III)] = 11.20×10^{-5} M
$[HClO_4]$ = 1.00×10^{-3} M
[KCl] = 1.00×10^{-3} M
$[Hg(OAc)_2]$ = 1.25×10^{-3} M
Temperature = 30 ^{0}C

Time (min.)	Vol. of Hypo used N/400 in ml.
0	10.00
5	9.64
10	9.25
15	8.70
20	8.25
25	7.85
35	7.21
45	6.45
55	6.11

(-dc/dt) = $1.21 \times 10^{-7} Ms^{-1}$

$[KBrO_3]$ = 1.00×10^{-3}M

$$k_1 = \frac{(-dc/dt)}{[KBrO_3]} = 1.21 \times 10^{-4} s^{-1}$$

Table: 6.1A(b)

$[KBrO_3]$ = 1.00×10^{-3} M
[GB] = 1.00×10^{-2} M
[Ir(III)] = 11.20×10^{-5} M
$[HClO_4]$ = 1.00×10^{-3} M
[KCl] = 1.00×10^{-3} M
$[Hg(OAc)_2]$ = 1.25×10^{-3} M
Temperature = 40 ^{0}C

Time (min.)	Vol. of Hypo used N/400 in ml.
0	10.00
5	9.20
10	8.54
15	7.72
20	7.05
25	6.31
35	5.41
45	4.53
55	3.65

(-dc/dt) = $3.21 \times 10^{-7} Ms^{-1}$

$[KBrO_3]$ = 1.00×10^{-3}M

$$k_1 = \frac{(-dc/dt)}{[KBrO_3]} = 3.21 \times 10^{-4} s^{-1}$$

Table: 6.1A(c)

$[KBrO_3]$ = 1.00×10^{-3} M

[GB] = 1.00×10^{-2} M

[Ir(III)] = 11.20×10^{-5} M

$[HClO_4]$ = 1.00×10^{-3} M

[KCl] = 1.00×10^{-3} M

$[Hg(OAc)_2]$ = 1.25×10^{-3} M

Temperature = 45 ^{0}C

Time (min.)	Vol. of Hypo used N/400 in ml.
0	10.00
5	8.50
10	7.45
15	6.70
20	5.95
25	5.12
35	4.34
45	3.50
55	2.12

(-dc/dt) = 4.20×10^{-7} M s^{-1}

$[KBrO_3]$ = 1.00×10^{-3} M

$$k_1 = \frac{(-dc/dt)}{[KBrO_3]} = 4.20 \times 10^{-4}\ s^{-1}$$

Table: 6.1A(d)

[$KBrO_3$]	= 1.00 x 10^{-3} M	[$HClO_4$]	= 1.00 x 10^{-3} M
[GB]	= 1.00 x 10^{-2} M	[KCl]	= 1.00 x 10^{-3} M
[Ir(III)]	= 11.20 x 10^{-5} M	[$Hg(OAc)_2$]	= 1.25 x 10^{-3} M

Temperature		(-dc/dt)/ 10^{-7} Ms^{-1}	k_1 / 10^{-4} s^{-1}	4 + log K	1/T K^{-1} x 10^4
0^0C	K				
30	303	1.21	1.21	0.0828	33.00
35	308	2.00	2.00	0.3010	32.46
40	313	3.21	3.21	0.5065	31.94
45	318	4.20	4.20	0.6232	31.44

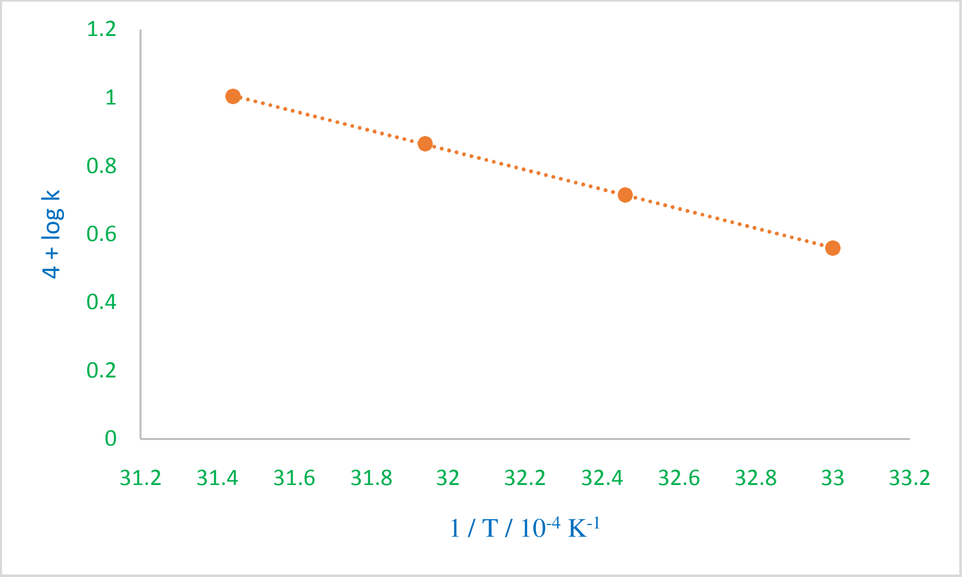


Figure:6.1A(d): Arrhenius plot for the oxidation by bromate in presence of [Ir(III)] catalyzed oxidation as catalyst. [Ir(III)] = 11.20 x 10^{-5} M, [KCl] = 1.00 x 10^{-3}M, [Hg(OAc)$_2$]= 1.25 x 10^{-3} M, [KBrO$_3$)] = 1.00 x 10^{-3} M, [GB] =1.00 x 10^{-2} M, [HClO$_4$] = 1.00 x 10^{-2} M

Table: 6.1B(a)

[$KBrO_3$] = 1.00×10^{-3} M
[PA] = 1.00×10^{-2} M
[Ir(III)] = 11.20×10^{-5} M
[$HClO_4$] = 1.00×10^{-3} M
[KCl] = 1.00×10^{-3} M
[$Hg(OAc)_2$] = 1.25×10^{-3} M
Temperature = 30 ^{0}C

Time (min.)	Vol. of Hypo used N/400 in ml.
0	10.00
5	9.50
10	9.00
15	8.50
20	8.20
25	7.95
35	7.25
45	6.54
55	6.00

(-dc/dt) = 3.70×10^{-7}Ms^{-1}

[$KBrO_3$] = 1.00×10^{-3}M

$$k_1 = \frac{(-dc/dt)}{[KBrO_3]} = 3.70\ x\ 10^{-4} s^{-1}$$

Table: 6.1B(b)

[$KBrO_3$] = 1.00×10^{-3} M
[PA] = 1.00×10^{-2} M
[Ir(III)] =11.20×10^{-5} M
[$HClO_4$] = 1.00×10^{-3} M
[KCl] = 1.00×10^{-3} M
[$Hg(OAc)_2$] = 1.25×10^{-3} M
Temperature = 40 ^{0}C

Time (min.)	Vol. of Hypo used N/400 in ml.
0	10.00
5	9.25
10	8.25
15	7.80
20	7.31
25	6.54
35	5.78
45	5.00
55	4.25

(-dc/dt) = 7.35×10^{-7}Ms^{-1}

[$KBrO_3$] = 1.00×10^{-3}M

$$k_1 = \frac{(-dc/dt)}{[KBrO_3]} = 7.35\ x\ 10^{-4} s^{-1}$$

Table: 6.1B(c)

$[KBrO_3]$ = 1.00×10^{-3} M

[P.A] = 1.00×10^{-2} M

[Ir(III)] = 11.20×10^{-5} M

$[HClO_4]$ = 1.00×10^{-3} M

[KCl] = 1.00×10^{-3} M

$[Hg(OAc)_2]$ = 1.25×10^{-3} M

Temperature = 45 ^{0}C

Time (min.)	Vol. of Hypo used N/400 in ml.
0	10.00
5	9.00
10	8.11
15	7.18
20	6.23
25	5.34
35	4.00
45	3.42
55	2.00

(-dc/dt) =10.12×10^{-7} M s^{-1}

$[KBrO_3]$ =1.00×10^{-3}M

$$k_1 = \frac{(-dc/dt)}{[KBrO_3]} = 10.12 \text{ x } 10^{-4} s^{-1}$$

Table: 6.1B(d)

[$KBrO_3$] = 1.00 x 10^{-3} M [$HClO_4$] = 1.00 x 10^{-3} M

[PA] = 1.00 x 10^{-2} [KCl] = 1.00 x 10^{-3} M

[Ir(III)] =11.20 x10^{-5} M [$Hg(OAc)_2$] = 1.25 x 10^{-3} M

Temperature		(-dc/dt)/$10^{-7}$$Ms^{-1}$	k_1 / 10^{-4} s^{-1}	4 +logk	1/T K^{-1} x 10^4
0^0C	K				
30	303	3.70	3.70.	0.5682	33.00
35	308	5.20	5.20	0.7160	32.46
40	313	7.35	7.35	0.8663	34.94
45	318	10.12	10.12	1.005	31.44

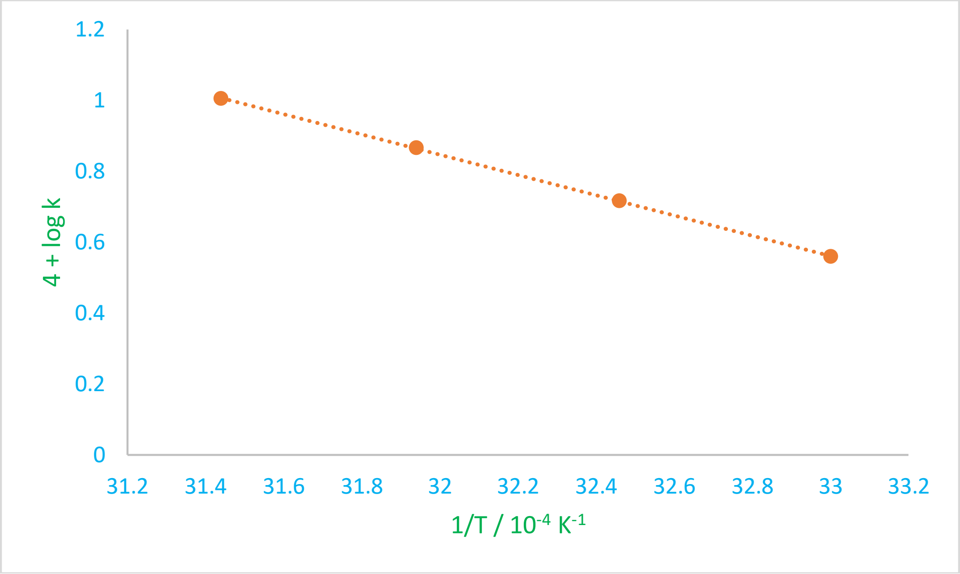


Figure: 6.1B: Arrhenius plot for the oxidation of paracetamol by bromate in presence of [Ir(III)] as catalyst. [Ir(III)] = 11.20 x 10^{-5} M, [KCl] = 1.00 x 10^{-3} M, [$Hg(OAc)_2$]= 1.25 x 10^{-3} M, [($KBrO_3$)] = 1.00 x 10^{-3} M, [PA] = 1.00 x 10^{-2}M, [$HClO_4$] = 1.00 x 10^{-3} M

6.2: Calculation of thermodynamic activation parameters and their interpretation-

In this section an attempt has been made to calculate different thermodynamic parameters such as entropy of activation (ΔS*), enthalpy of activation (ΔH*), free energy of activation (ΔG*), Arrhenius frequency factor (A) and specific rate constant (k_r). According to transition state theory the equation for specific rate constant k_r (i.e. the rate constant of reaction when concentration of each of the reactant is unity at a given temperature) is given as:

$$K_r = \frac{KT}{h} K^* \ldots\ldots\ldots\ldots\ldots\ldots\ldots (i)$$

where T is absolute temperature h is plancks constant and K is boltzmann constant, KT/h is known as universal frequency factor and is independent of nature and type of reaction. K* is activation equilibrium constant for the process of formation of an activated complex, which is regarded as a normal molecule.

Free energy change of activation ΔG* is related with equilibrium constant K* by equation.

$$\Delta G^* = -RT\ln K^* \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(ii)$$

According to Gibb's Helmholtz equation

$$\Delta G^* = \Delta H^* - T\Delta S^* \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(iii)$$

substituting the value of ΔG* from equation (iii) to (ii) we get

$$\Delta H^* - T\Delta S^* = -RT\ln K^*$$

or

$$\ln K^* = \frac{-\Delta H^*}{RT} + \frac{\Delta S^*}{R}$$

$$K^* = e^{-\Delta H/RT} . e^{\Delta S^*/R} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (iv)$$

Substituting the value of K* from equation (iv) to equation (i)

$$k_r = \frac{KT}{h} e^{-\Delta H^*/RT} . e^{\Delta S^*/R} \qquad \ldots\ldots\ldots..(v)$$

taking logarithms on both sides

$$\ln k_r = \frac{\ln K}{h} + \ln T - \frac{\Delta H^*}{RT} + \frac{\Delta S^*}{R}$$

Differentiating the above equation with respect to temperature, we have

$$\frac{d}{dt}(\ln k_r) = \frac{1}{T} + \frac{\Delta H^*}{RT^2} \qquad \text{……….(vi)}$$

According to Arrhenius equation –

$$k_r = A\,e^{-E_a/RT}$$

Taking logarithms on both sides

$$\ln k_r = \ln A - \frac{E_a}{RT}$$

Differentiating above equation with respect to temperature, we get

$$\frac{d}{dt}(\ln k_r) = \frac{E_a}{RT^2} \qquad \text{……….(vii)}$$

comparing equation (vi) and (vii) we get:

$$\frac{1}{T} + \frac{\Delta H^*}{RT^2} = \frac{E_a}{RT^2}$$

$$\Delta H^* = E_a - RT \text{...(viii)}$$

Substituting the value of ΔH* from equation (viii) to equation (v)

$$k_r = \frac{KT}{h}\, e^{-(E_a - RT)/RT} \,.\; e^{\Delta S^*/R}$$

or

$$k_r = \frac{KT}{h}\, e^{-E_a/RT} \,.\; e^{RT/RT} \,.\; e^{\Delta S^*/R}$$

or

$$k_r = \frac{eKT}{h} \quad e^{-E_a/RT} . \quad e^{\Delta S^*/R}$$

taking logarithms on both sides we get

$$\ln k_r = \ln e + \ln K/h + \ln T - E_a/RT + \Delta S^*/R$$

or

$$\Delta S^*/2.303R = \log k_r - \log e\frac{K}{h} - \log T + E_a/2.303RT \text{ ....(ix)}$$

The value of K is 1.3803 x 10^{-16} erg deg^{-1} mol^{-1}, R is 1.987 Cal $deg^{-1}mol^{-1}$ and h is 6.6238 x 10^{-27} erg sec^{-1} mol^{-1}, substituting the value of K, h and R in equation (9) we get,

$$\Delta S^*/4.576 = \log k_r - 10.753 - \log T + E_a/4.576T \text{ ....(x)}$$

ΔS^* has a unit of Cal deg^{-1} mol^{-1}. Equation (x) is valid only if the constant is based on second as the unit of time. From the above equation ΔS^* can be calculated in entropy units. The free energy (ΔG^*) and Arrhenius factor (A) can be calculated from the following equation.

$$\Delta G^* = \Delta H^* - T\Delta S^* = E_a - RT - T\Delta S^* \text{..........................(xi)}$$

and

$$\log A = \log k_r + E_a/2.303RT$$

The specific rate constant k_r is calculated for the acidic medium as-

$$k_r = (-dc/dt)/[KBrO_3]^{n_1}[S]^{n_2}[Ir(III)]^{n_3}[H^+]^{n_4}$$

The E_a values obtained from the slope of 1/T vs. log k plot were used to calculate ΔS^*, ΔH^*, ΔG^* and A with the help of above equations. The value of oxidation of organic substrates under investigation along with E_a values are given in tabular form for acidic medium.

Table 6.2

Values of Activation Parameters for pharmaceutical drugs of Ir(IIi) catalyzed oxidation by potassium bromate in acidic medium

Arrhenius Parameters	Ir(III) chloride Gabapentin	Ir(III) chloride Paracetamol
E_a kJ mol^{-1}	66.67	53.33
Log A	12.66	10.80
ΔS^* $JKmol^{-1}$	-6.51	-42.12
ΔG^* kJ mol^{-1}	68.71	66.60
ΔH^*kJmol^{-1}	66.67	53.62

The phenomenon of entropy of activation plays a vital role in case of reactions between ions or neutral molecules forming ions. When a reaction occurs between two oppositely charged ions, it is usually observed that entropy increases in going from reactant to activated complex but on the other hand when the same takes place

between two similarly charged ions, decrease in entropy is observed in terms of solvation of ions. An explanation for such a behavior of entropy can be given as follows for different reactions. It is well known that solvation generally increases with increase in charge on the ion. In other words smaller ions are highly solvated. Neutral molecule is formed when two ions of opposite charge combine and this results in a lowering of net charge and due to this some frozen solvent such as water molecules frozen around the incipient ions are released with an increase in entropy. On the other hand when reaction takes place between two similarly charged ions, the transition state or the activated state which is a more highly charged ion, is as expected, a highly solvated molecule. Consequently more solvent molecules for this transition state will be required as compared to that for separate ions which would lead to decrease in entropy, So for the reaction in solution, enthalpy of activation changes with the solvent and becomes less negative (i.e. increase) while free energy change of activation decreases, as the polarity of solvent increases. Table 6.3 for activation parameters shows high positive values of free energy of activation (ΔG^*) signifying the transition state to be highly solvated and negative value of entropy of activation (ΔS^*) indicates the formation of activated complex with reduction in degree of freedom of reactant molecules or ions.

Summary:

In this chapter several experiments were performed under identical conditions at different temperature viz 30 °C, 35 °C, 40 °C, and 45 °C respectively for Ir(III) catalysed oxidation of gabapentin and paracetamol by acidic bromate. It was observed that rate of reaction increased with increase in temperature. From the values of rate constant obtained Arrhenius plot was plotted, which gave a straight line. The value of energy of activation ΔE^* was obtained from the slope of the line by using the expression.

$$\text{Slope} = \frac{-\Delta E^*}{2.303R}$$

Using this value of ΔE^*, other activation parameters i.e. entropy of activation (Δs^*), enthalpy of activation (ΔH^*) free energy of activation (ΔG^*), Arrhenius frequency factor (A) have been calculated

CHAPTER-7

RESULT AND DISCUSSION OF KINETIC OUTCOMES

7.0 Result and Discussion of kinetic outcomes.

The study of a chemical reaction is of fundamental concern to a chemist from two aspects. Firstly for ascertaining the fastness or slowness of the reaction and secondly for investigating the effect of different factors like concentration, pressure, temperature, catalyst etc on the rate of reaction and thereby workout the optimum conditions for carrying out a process. For the fundamental chemist, these studies enable him to get an insight into the different steps through which the reaction proceeds and thus a reaction mechanism can be worked out for the process. An important milestone in understanding of chemical kinetics was the concept of molecular activation as a prerequisite to a chemical reaction first postulated by Arrhenius(1). The concept of molecular activation is now universally accepted and forms the basis of all subsequent theories of chemical reactions.

Evans and Polanyi(2) and Eyring(3) put forth the idea of formation of activated complex as a result of molecular collision between energized molecules and established that the chemical reaction involves first the formation of activated complex in a reversible process which then decomposes irreversibly to give the products of the reaction.

Thus according to Eyring for any chemical reaction to occur, it is necessary for the reacting atoms or molecules to approach each other and then to pass over a free energy barrier.

The molecular species corresponding to the top of such a free energy barrier are referred to as activated complex and the rate of reaction is controlled by the rate with which these complexes travel over the top of the barrier.

Amis(4), in his book "solvent effects on reaction rate and mechanism" has explained the role of the nature of solvent on rate of reactions occurring in solution. From the view point of solvent effect, the reaction may be broadly classified into many categories like ion-ion reactions, ion-dipolar molecular reaction, electron- exchange reaction etc.

In the previous chapters 3 to 6 an attempt has been made to collect the kinetic informations which deal with kinetic investigations of Pd(II) and Ir(III) catalyzed oxidation of pharmaceutical drugs in acidic medium by potassium bromate. These kinetic data have been utilized here to propose the reaction route of reactions investigated. In order to elucidate the mechanism for the redox system mentioned above, it is worthwhile to discuss the reactive species of various reactants i.e. $KBrO_3$, $PdCl_2$, $IrCl_3$, and reducing substrates in perchloric acid medium, in addition to ascertaining the role of $[Hg(OAc)_2]$ in the reaction in the light of experimentally observed data.

In the following sections, a summary of kinetic features observed, rationalization of reactive species of different reactants and more kinetic information have been presented.

7.1 Ascertaining the reactive species of potassium bromate in perchloric acid in the present investigation.

In this section, an efforts has been made to ascertain the reactive species of $KBrO_3$, on the basis of kinetic results. Potassium bromate being a strong electrolyte gives bromate ions as given below:-

$$KBrO_3 \longrightarrow K^+ + BrO_3^- \qquad \text{....................(i)}$$

It has been reported by earlier workers (5-6) that $KBrO_3$ exists in the following equilibria in acidic media.

$$BrO_3^- + H^+ \rightleftharpoons HBrO_3 \qquad \text{....................(ii)}$$

$$HBrO_3^- + H^+ \rightleftharpoons H_2Br^+O_3 \qquad \text{....................(iii)}$$

$$H_2Br^+O_3 \rightleftharpoons Br^+O_2 + H_2O \qquad \text{....................(iv)}$$

In acidic solutions Br(v) exists in unprotonated (BrO_3^-) and protonated forms ($HBrO_3$) and ($H_2Br^+O_3$/Br^+O_2) forms. Hence, the oxidation in the present study may be through interaction between the substrate and any one of these oxidant species. All the protonated and unprotonated species, appearing in the kinetic equilibria, may act as reactive species, but one of these species would be predominant in the reaction and may act as real reactive species of $KBrO_3$ in the present investigation.

If we assume BrO_3^- as such involved in the reaction, then the rate law derived on the basis mitigate the chances of unprotonated BrO_3^- to be the reactive species, because of the effect of solvent polarity and the acceleration in the rate with increase in [Gabapentin] and [Paracetamol]. Amis et al(7) proposed Br^+O_2 as the oxidizing species in acid bromate oxidation of iodide. Thus, the above species cannot play a dominant role in the reaction. When $H_2Br^+O_3$(8) is taken as reactive species, then it gives rate law which shows second order kinetics with respect to [H^+], which is not observed in the reactions studied, so $H_2Br^+O_3$ is discarded. In acidic solution of potassium bromate quick formation of $HBrO_3$ has been reported (9).

In case of pharmaceutical drugs BrO_3^- acts as the most reactive species of $KBrO_3$ in the reaction, which gives a rate law capable of explaining all the kinetic observations and other effects.

7.2: Ascertaining the reactive species of Palladium(II) chloride in acid medium in the present study.

Palladous chloride is very soluble in HCl and exists as $[PdCl_4]^{2-}$. The existence of different species of palladium chloride, specifically Pd^{2+}, $PdCl^+$, $PdCl_2$, $PdCl_3^-$ and $PdCl_4^{2-}$, has been observed in $HClO_4$ medium depending upon the $[Cl^-] / [Pd]$ ratio. It has been found that species(10) Pd^{++}, $PdOH^+$ and $PdCl^+$ were present when $[Cl^-] / [Pd]$ was up to 0.8; $PdCl^+$ and $PdCl_2$ were present when $[Cl^-] / [Pd]$ was 2.2 – 2.8, and only $PdCl_2$, $PdCl_3^-$ and $PdCl_4^{2-}$ were present(11-12) when $[Cl^-] / [Pd]$ was 4.0 to 4.8.

In our experiment $[Cl^-] / [Pd]$ was found to be in the range 2.2 to 2.8, so the reactive species might be $PdCl^+$ and $PdCl_2$. But on the basis of the results obtained Cl^- exists as the following equilibrium in acidic solution of palladium(II) chloride –

$$PdCl^+ + Cl^- \rightleftharpoons [PdCl_2]$$

The positive effect with respect to Cl^- in the present investigation suggests the equilibrium would shift to right. Therefore $[PdCl_2]$ is the reactive species of Palladium(II) chloride in acidic media.

7.3: Ascertaining the reactive species of Iridium(III) chloride in perchloric acid medium in the present kinetic study.

It has been reported that Ir(III) and Ir(I) ions are stable species(13) of iridium. Different reactive species of iridium trichloride viz $[IrCl_6]^{3-}$, $[IrCl_5.H_2O]^{2-}$, $[IrCl_4(H_2O)]^-$, $[IrCl_3(H_2O)]$ also exist(14-17). It has also been reported that in acidic medium Iridium trichloride exist(18) as $[IrCl_6]^{3-}$. Our experimental data indicate that addition of chloride ion has positive effect on the reaction velocity. If addition of chloride ion decreases the reaction velocity then probably the following equilibrium takes place.

$$[IrCl_6]^{3-} + H_2O \rightleftharpoons [IrCl_5H_2O]^{2-} + Cl^-$$

Thus either $[IrCl_6]^{3-}$ or $[IrCl_5.H_2O]^{2-}$ may act as reactive species but chloride ion has positive effect on the rate of reaction in the present investigation therefore $[IrCl_6]^{3-}$ can be safely assumed to be the reactive species.

7.4: Role of mercuric acetate in the present study.

The role of mercuric acetate as an oxidant, catalyst and Br^- ions scavenger(10) is well known. In the present investigation, mercuric acetate has been used as scavenger to eliminate Br^- which could have produced Br_2 in the reaction. The bromine thus produced might set another parallel oxidation and create complications in $KBrO_3$ oxidation. Mercuric acetate thus eliminates Br_2 oxidation and ensure that the oxidation proceeds purely through $KBrO_3$.

To ascertain the real role of $Hg(OAc)_2$ in addition to Br^- scavenger, several experiments were studied with $Hg(OAc)_2$ in absence of $KBrO_3$ under identical experimental conditions. It has been observed that the reaction does not proceed in such cases. This rules out the possibility of Hg(II) acting as an oxidant under present conditions of the experiments.

Thus we found that Mercuric acetate has been used as a trapping agent or scavenger(19) for bromide ions in the form of either unionized $HgBr_2$ or as complex $[Hg(Br)_4]^{2-}$ in the oxidation of pharmaceutical drugs by potassium bromate catalyzed by Pd(II) and Ir(III) in perchloric acid medium. In this way bromine formation and in turn parallel bromine oxidation is eliminated. Addition of mercuric acetate poses another problem. It has been reported to act as a catalyst and as an oxidant as well. In order to see its role as a catalyst the reaction were studied with fixed Pd(II) chloride/Ir(III) chloride and varying $[Hg(OAc)_2]$. The results of various experiments did not show any change in the reaction rate. This rules out the possibility of mercuric acetate to act as a catalyst. It was observed that reaction did not proceed in absence of potassium bromate which clearly demonstrates that mercuric acetate does not act as an oxidant as well. In view of the above discussion, now it can be clearly claimed that mercuric acetate neither acts as a catalyst nor as an oxidant but its role is only as bromide ion scavenger in the present work.

7.5: Stoichiometry and mechanism discussion for Pd(II) / Ir(III) catalyzed oxidation of Gabapentin by acid bromate.

7.5A: Various experiments with different concentration of Potassium bromate and substrates ([$KBrO_3$]: [Substrate]) ratio under the experimental condition were carried out for 48 hours in acidic medium. Iodometric titration of unconsumed [$KBrO_3$] revealed that, in acidic medium for the oxidation of one mole of each substrate two moles of potassium bromate were consumed in case of drug i.e, Gabapentin.

Table : 7.5A

Stoichiometric ratio for oxidation of gabapentin by acidic bromate in presence of Pd(II) / Ir(III) chloride as catalyst

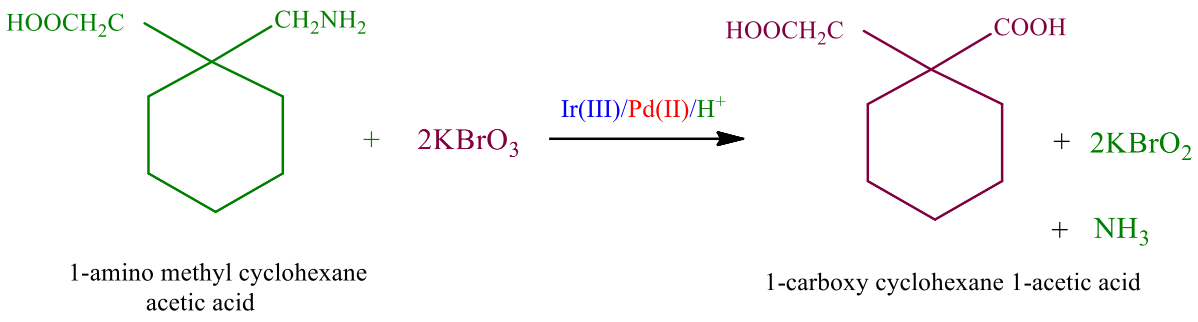
[$KBrO_3$] x 10^{-3}M	Substrate x 10^{-3}M	[$KBrO_3$]$^{*}_{residual}$		[$KBrO_3$]* / [Substrate]	
		Gabapentin [Pd(II)] catalyzed	Gabapentin [Ir(III)] catalyzed	Gabapentin [Pd(II)] catalyzed	Gabapentin [Ir(III)] catalyzed
12.50	1.00	10.35	10.50	2.15	2.00
10.00	1.00	8.05	7.95	1.95	2.05
5.00	1.00	2.90	2.85	2.10	2.15
2.50	1.00	0.45	0.55	2.05	1.95
12.50	2.00	8.60	8.30	1.95	2.10
12.50	3.00	6.40	6.45	2.03	2.02
12.50	4.00	4.55	4.25	1.99	2.06
12.50	5.00	2.40	2.60	2.02	1.98

[$KBrO_3$]* = [$KBrO_3$] left consumed after 48 h. i.e. [$KBrO_3$] – [$KBrO_3$]$^{*}_{residual}$

7.5B: Stoichiometry and product analysis for gabapentin

As revealed from Table 7.5A one mole of substance consumes two moles of potassium bromate in case of Gabapentin. Therefore, accordingly the stoichiometric equations may be given as below.

1-Determination of stoichiometry and product analysis for Gabapentin in acidic medium.



A solution containing pharmaceutical drug (Gabapentin), $KBrO_3$, Catalyst, Mercuric acetate, Potassium chloride (calculated amount) were made up to 50 ml. in perchloric acid and was left overnight for completion of the reaction. A concentrated solution of sodium bicarbonate was added to the solution kept on a watch glass. Evolution of carbon dioxide indicates that the products were corresponding acids. The products obtained were identified by TLC and by conventional methods.

According to the above reaction the oxidation product of gabapentin is 1-carboxycyclohexane1-acetic acid, which was identified and confirmed by paper chromatography. 1-carboxy cyclohexane1-acetic acid was identified and confirmed by IR spectral analysis. The bands at 1760cm^{-1} and 1710cm^{-1} corresponds to two C=O group and 3550 cm^{-1} corresponds to two –OH group clearly confirms 1- carboxy cyclohexane1-acetic acid.

7.5C: Kinetic summary observed in potassium bromate oxidation of Gabapentin catalyzed by Pd(II) chloride in perchloric acid medium .

Following kinetic results are obtained for oxidation oxidation of Gabapentin by bromate calayzed by Pd(II) chloride in perchloric acid medium .

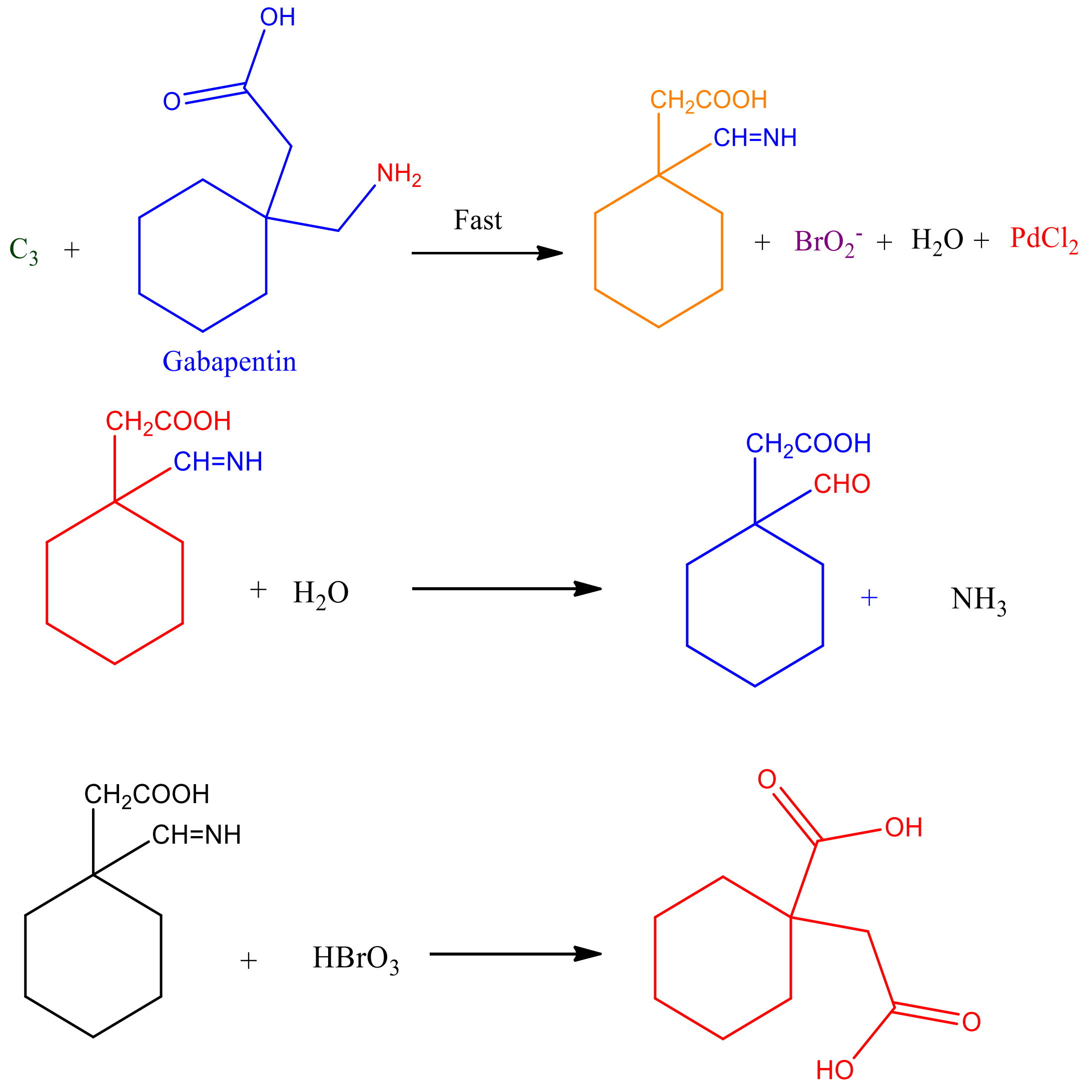
1. The reaction follows first order kinetics with respect to oxidant i.e potassium bromate.
2. First order kinetics with respect to catalyst i.e., palladium(II) chloride was observed.
3. Zero order kinetics with substrate i.e. Gabapentin.
4. The reaction rate shows positive effect with respect to [KCl].
5. The reaction rate shows first order kinetics with variation in $[H^+]$.
6. Insignificant effect of ionic strength of the medium on the reaction rate was observed.
7. Addition of mercuric acetate did not bring about any appreciable change in the reaction rate.
8. Addition of D_2O to the reaction mixture showed negligible effect on the reaction rate.
9. Increase in temperature markedly increases the rate of reaction.

7.5 (D): Mechanism of oxidation of gabapentin by acidic potasssium bromate in presence of micro amount of Pd(II) chloride acting as catalyst.

$$\underset{[C_1]}{PdCl^+} + Cl^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{[C_2]}{PdCl_2}$$

$$H^+ + BrO_3^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} HBrO_3$$

$$\underset{[C_2]}{[PdCl_2]} + HBrO_3 \xrightarrow[\text{slow step}]{k_3} \underset{[C_3]}{[PdCl_2\ldots\ldots\ldots HBrO_3]}$$



1-carboxy cyclohexane 1-acetic acid

Considering the proposed mechanism for oxidation of gabapentin by acidic potassium bromate in presence of micro amount of Pd(II) chloride acting as catalyst and applying the steady state approximation, the rate law may be written as follows.

$$Rate=k_3[C_2]\,[HBr0_3] \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(1)$$

$$[Pd(II)]_T=[C_1]+[C_2] \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

$$\frac{d[C_1]}{dt}=k_{-1}\,[C_2]-k_1\,[C_1][Cl^-]\ldots\ldots\ldots \quad (3)$$

According to steady state approximation $\frac{d[C_1\,]}{dt} = 0$

$$[C_1]=\frac{k_{-1}\,[C_2]}{k_1\,[Cl^-]} \quad \ldots\ldots\ldots\ldots\ldots. \quad (4)$$

$$[C_1]=\frac{[C_2]}{K_1\,[Cl^-]} \quad \ldots\ldots\ldots\ldots \quad (5)$$

(*where* $K_1 = k_1/\,k_{-1}$)

Putting the value of $[C_1]$ from eq. (5) in eq. (2) we get

$$[Pd(II)]_T=[C_2]\left[\frac{1+K_1\,[Cl^-]}{K_1\,[Cl^-]}\right]$$

$$[C_2]=\frac{K_1[Pd(II)]_{T_1}\,[Cl^-]}{1+K_1\,[Cl^-]}\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(6)$$

From step (2)

$$\frac{d[HBrO_3]}{dt}= \ k_2\,[H^+]\,[BrO_3]-\ k_{-2}[HBrO_3]$$

$$[HBrO_3]=K_2\,[H^+][BrO_3{}^-]\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(7)$$

Where $K_2 \ = \ \frac{k_2}{k_{-2}}$

Puting the values of $[C_2]$ and $[HBrO_3]$ from eq. (6) and (7) in equation (1), we get:

$$Rate = \frac{K_1\, K_2 k_3 [Pd(II)]_T [Cl^-][H^+][BrO_3{}^-]}{1 + K_1\,[Cl^-]}$$

This rate law is in full agreement with all the kinetic results obtained.

7.6A: Kinetic summary of results observed in potassium bromate oxidation of Gabapentin catalyzed by Ir(III) chloride in perchloric acid medium .

Kinetic results obtained for Gabapentin catalyzed by Ir(III) chloride in perchloric acid medium are as follows:-

1. The reaction follows first order kinetics with respect to oxidant i.e potassium bromate.
2. First order kinetics with respect to catalyst i.e., Iridium(III) chloride.
3. Zero order kinetics with respect to substrate i.e. Gabapentin.
4. The reaction rate shows positive effect with respect to [KCl].
5. The reaction rate shows first order kinetics with variation in $[H^+]$.
6. Insignificant effect of ionic strength of the medium on the reaction rate was observed.
7. Addition of mercuric acetate did not bring about any appreciable change in the reaction rate.
8. Addition of D_2O to the reaction mixture showed negligible effect on the reaction rate.
9. Increase in temperature markedly increases the rate of reaction.

7.6(B): Mechanism of Ir(III) catalyzed oxidation of Gabapentin by potasssium bromate in acidic medium.

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 iridium tri chloride and $KBrO_3$ and other kinetic features with respect to [Substrate], $[H^+]$, [Hg(II)], $[Cl^-]$ and ionic strength of the medium, the following mechanistic steps are proposed.

In acidic solution of the oxidant $KBrO_3$, quick formation of $HBrO_3$ has been reported.

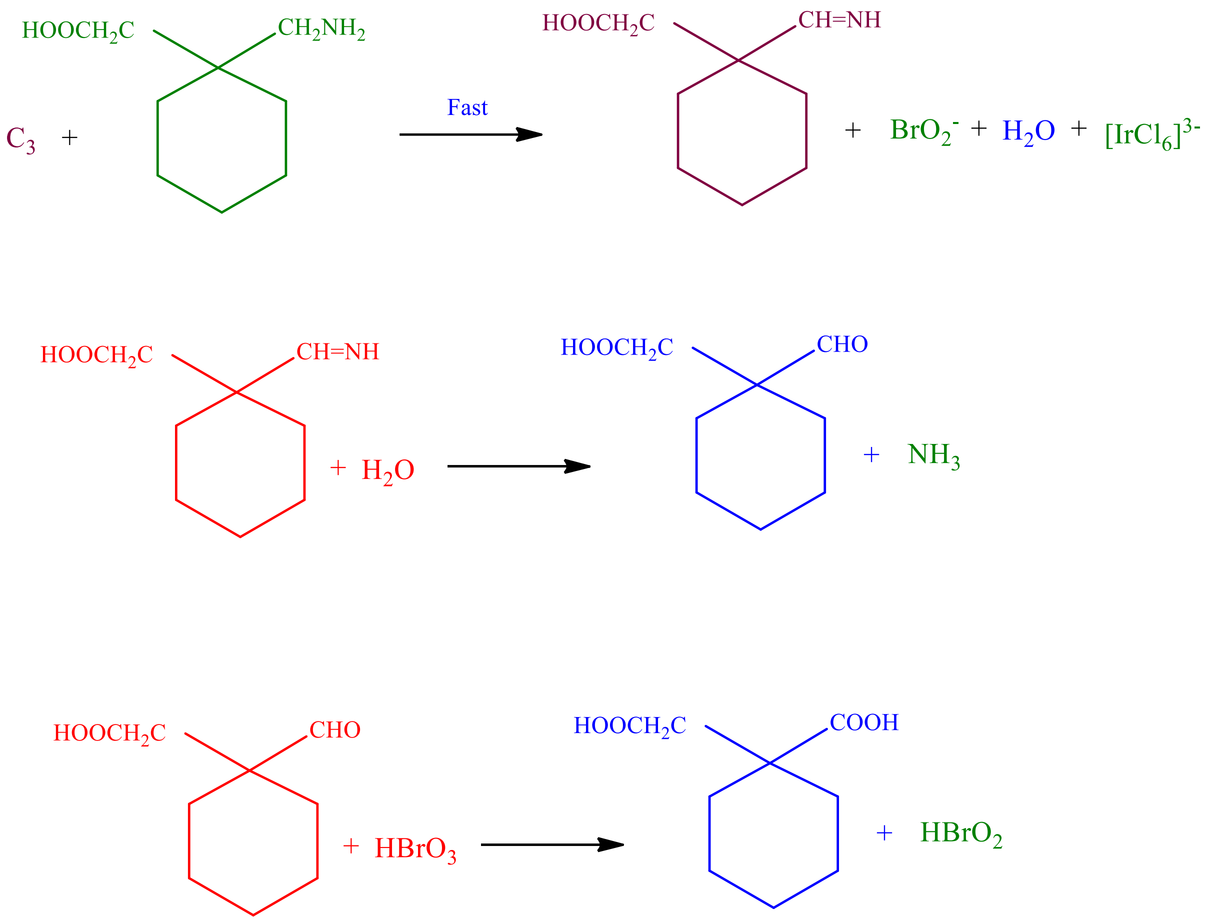
$$HBrO_3 \longrightarrow H^+ + BrO_3^- \qquad \text{....................(i)}$$

The BrO_3^- species formed in solution has been reported to act as an oxidising agent in acidic as well as in alkaline medium (Singh and Srivastava, 1991). Ir(III) chloride dependent on pH of the solution, under the experimental pH range in the present investigation $[Ir(CI)_5(H_2O)]^{2-}$ has been proposed. This is further confirmed as the reactive species dominant in the pH range 1.0 to 3.0. has already been reported as $[Ir(CI)_5(H_2O)]^{2-}]$ by other workers.

$$\underset{[C_1]}{[IrCl_5H_2O\ ]^{2-}} + Cl^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{[C_2]}{[IrCl_6\ ]^{3-}} + H_2O$$

$$H^+ + BrO_3^- \underset{k_2}{\overset{k_2}{\rightleftharpoons}} HBrO_3$$

$$\underset{[C_2]}{[IrCl_6\ ]^{3-}} + HBrO_3 \xrightarrow[k_3]{\text{slow}} \underset{[C_3]}{[IrCl_{6.}............HBrO_3]^{3-}}$$



1-carboxy cyclohexane 1-acetic acid

Considering the above reaction steps and applying the steady state approximation, the rate law may be written as equation.

$$Rate = k_3[C_2][HBrO_3] \qquad \text{………. (1)}$$

$$[Ir(III)]_T = [C_1] + [C_2] \qquad \text{……….(2)}$$

$$\frac{d[C_1]}{dt} = k_{-1}\,[C_2] - k_1\,[C_1][Cl^-] \qquad \text{…………….. (3)}$$

$$[C_1] = \frac{k_{-1}\,[C_2]}{k_1\,[Cl^-]} \qquad \text{…………… (4)}$$

$$[C_1] = \frac{[C_2]}{K_1\,[Cl^-]} \qquad \ldots\ldots\ldots\ldots\ldots.. \qquad (5)$$

(where $K_1 = k_1/ k_{-1}$)

$$[Ir(III)]_T = [C_2]\left[\frac{1 + K_1\,[Cl^-]}{K_1\,[Cl^-]}\right]$$

$$[C_2] = \frac{[Ir(III)]_T\,K_1\,[Cl^-]}{1 + K_1\,[Cl^-]}$$

$$\frac{d[HBrO_3]}{dt} = \frac{k_2\,[H^+][BrO_3{}^-]}{k_{-2}\,[HBrO_3]}$$

$$[HBrO_3] = K_2\,[H^+][BrO_3{}^-]$$

(where $K_2 = k_2/ k_{-2}$)

Puting the values of $[C_2]$ and $[HBrO_3]$ in equation (1), we get:

$$Rate = \frac{K_1\,K_2 k_3[Ir(III)]_T[Cl^-][H^+][BrO_3{}^-]}{1 + K_1\,[Cl^-]}$$

7.7: Stoichiometry and mechanism discussion for Pd(II)/Ir(III) catalyzed oxidation of Paracetamol by bromate in acidic medium.

7.7A: Various experiments with different concentration of Potassium bromate and substrates ([$KBrO_3$]: [Substrate]) ratio under the experimental condition were carried out for 48 hours in acidic medium. Iodometric titration of unconsumed [$KBrO_3$] revealed that, in acidic medium for the oxidation of one mole of each substrate two moles of potassium bromate were consumed in case of drug i.e, paracetamol.

Table : 7.7(A)

Stoichiometric ratio for oxidation of Paracetamol by acidic bromate in presence of Pd(II) / Ir(III) chloride as catalyst

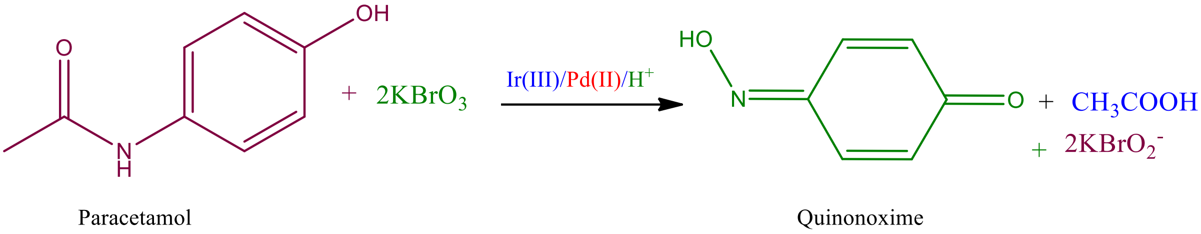
[$KBrO_3$] x 10^{-3}M	Substrate x 10^{-3}M	[$KBrO_3$]$^*_{\text{residual}}$		[$KBrO_3$]* / [Substrate]	
		Paracetamol [Pd(II)] catalyzed	Paracetamol [Ir(III)] catalyzed	Paracetamol [Pd(II)] catalyzed	Paracetamol [Ir(III)] catalyzed
12.50	1.00	10.45	10.25	2.05	2.25
10.00	1.00	7.85	8.15	2.15	1.85
5.00	1.00	3.10	3.10	1.90	1.90
2.50	1.00	0.30	0.40	2.20	2.10
12.50	2.00	8.20	7.95	2.15	2.28
12.50	3.00	6.65	6.70	1.95	1.93
12.50	4.00	4.30	4.60	2.05	1.98
12.50	5.00	2.20	2.15	2.06	2.07

[$KBrO_3$]* = [$KBrO_3$] consumed after 48 h. i.e. [$KBrO_3$] - [$KBrO_3$]$^*_{\text{residual}}$

7.7B: Stoichiometry and product analysis for Paracetamol

As revealed from Table 7.7A one mole of substrate consumes two moles of potassium bromate in case of Paracetamol. Therefore accordingly the stoichiometric equations may be given as below.

1-Determination of stoichiometry and product analysis for Paracetamol in acidic medium:-



A solution including pharmaceutical drug (Paracetamol), $KBrO_3$, Catalyst, Mercuric acetate, Potassium chloride (calculated amount) were made up to 50 ml. in perchloric acid and was left for 48 hourss to ensure that the reaction is complete.

Analysis of unconsumed $KBrO_3$ iodometrically for 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 extriacted 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 $KBrO_2$ was the reduction product of $KBrO_3$.

7.8: Kinetic summary of result observed in potassium bromate oxidation of Paracetamol catalyzed by Pd(II) chloride in perchloric acid medium .

The title of reaction shows following kinetic results. Similar kinetic results for oxidation of paracetamol by bromate catalyzed by Pd(II) chloride in perchloric acid medium .

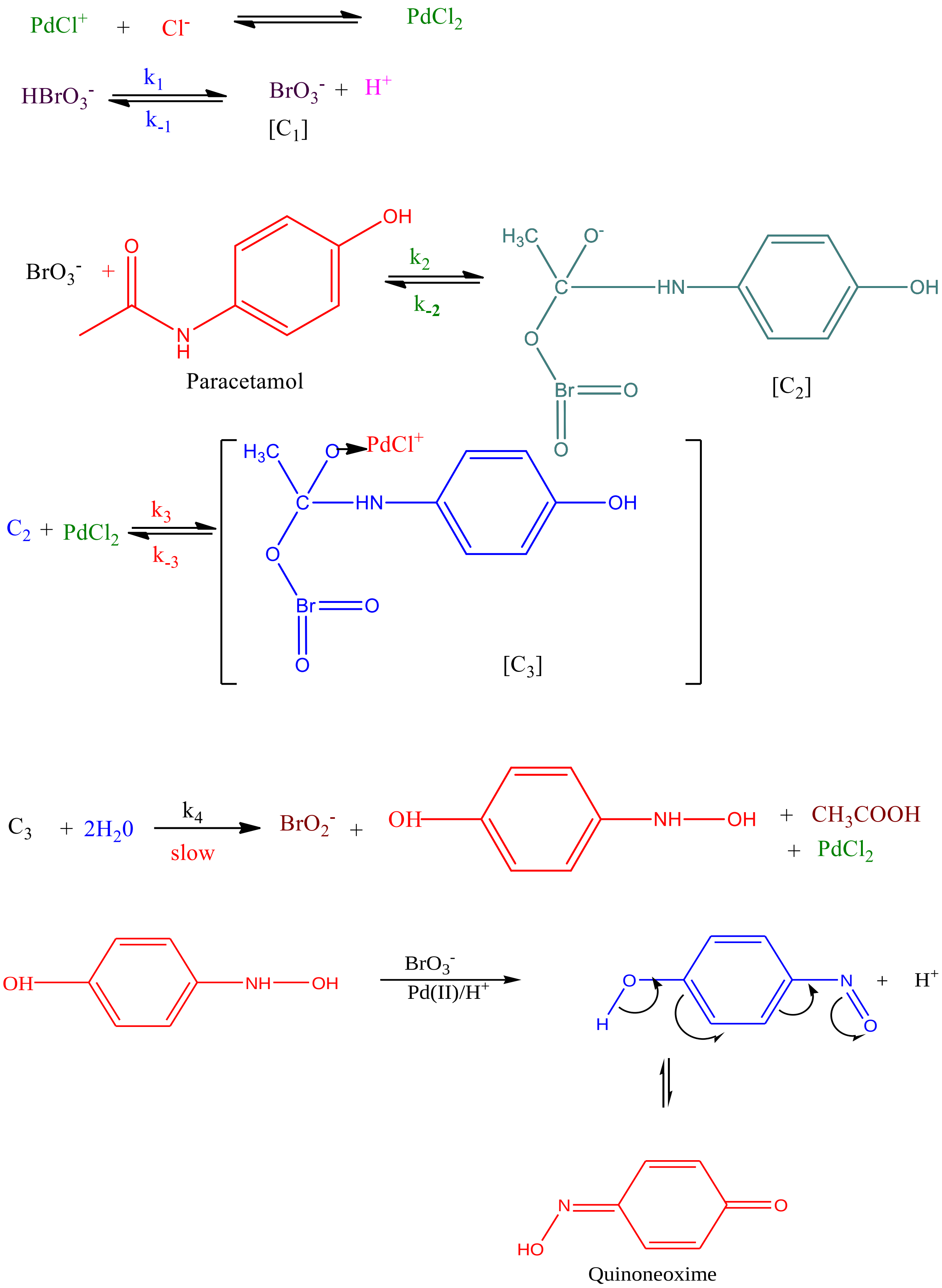
1. The reaction follows first order kinetics with respect to oxidant i.e. potassium bromate.
2. First order kinetics with respect to catalyst i.e., Pd(II) chloride on the rate of reaction.
3. The reaction rate shows positive effect with respect to [substrate].
4. Addition of chloride ion to the reaction mixture depicts no change in the reaction rate.
5. The reaction shows negative effect of [H^+] on the rate of reaction.
6. Insignificant effect of ionic strength of the medium on the rate of reaction.
7. Addition of mercuric acetate did not bring about any appreciable change in the reaction rate.
8. Addition of D_2O to the reaction mixture showed negligible effect on the reaction rate.
9. Increase in temperature markedly increases the rate of reaction.

7.8A: Mechanism of Pd(II) catalyzed oxidation of paracetamol by potasssium bromate in acidic medium.

It has been already discussed that $[PdCl]^+$ is the reactive species of palladium chloride in acidic medium. In view of the reactive species of Pd(II) chloride and $KBrO_3$ and other kinetic features with respect to [Substrate], $[H^+]$, [Hg(II)], $[Cl^-]$ and ionic strength of the medium, the following mechanistic steps are proposed. In acidic solution of $KBrO_3$, quick formation of $HBrO_3$ has been reported (9).

- **Mechanism and derivation of rate law-**

The reaction mechanism involves interaction of $KBrO^-_3$ with the substrate and 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) chloride has been reported to give a number of possible chloro species dependent on pH of the solution. As $[Cl^-]$ is in excess equilibrium shifts towords right.



Considering the fact that 1 mole of paracetamol is oxidised by 2 mole of bromate and applying the steady state treatment, with reasonable approximation, the rate law may be written as equation.

$$\text{Final} \qquad \text{Rate} = k_4[C_3] \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

On the basis of the proposed scheme we can be obtain in the following equations.

$$\frac{d[C_3]}{dt} = k_3[C_2]\,[PdCl_2] - k_{-3}\,[C_3]$$

Applying steady state approximation

$$[C_3] = K_3[C_2]\,[PdCl_2]$$

$$\frac{d[C_2]}{dt} = k_2\,[C_1]\,[PA]\ - k_{-2}\,[C_2]\ - k_3\,[C_2]\,[PdCl_2] + k_{-3}\,[C_3]$$

$$\frac{d[C_2]}{dt} = k_2[C_1][PA] - k_{-2}[C_2] - k_3[C_2][PdCl_2] + k_{-3}(\,k_3[C_2][PdCl_2])$$

$$k_2\,[C_1]\,[PA] = [C_2](\,k_{-2} - k_3[PdCl_2)] + k_{-3}\ x\ \tfrac{k_3}{k_{-3}}[PdCl_2]\,)$$

$$k_2[C_1]\,[PA] = [C_2](k_{-2})$$

$$[C_2] = K_2\,[PA]\,[C_1]$$

$$\frac{d[C_1]}{dt} = k_1\,[HBrO_3] - k_{-1}\,[C_1][H^+] - k_2\,[C_1]\,[PA] + k_{-2}\,[C_2]$$

$$\mathrm{k}_1[HBrO_3] = k_{-1}\,[C_1][H^+]$$

$$[C_1] = K_1\frac{[HBrO_3]}{[H^+]}$$

$$Rate = \frac{\mathrm{k}_1\,\mathrm{k}_2\,\mathrm{k}_3\,\mathrm{k}_4[PdCl_2]\,[PA][HBrO_3]}{[H^+]} \ldots\ldots\ldots\ldots\ldots (2)$$

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

$$[\mathrm{HBr0_3}]_T = [\mathrm{HBr0_3}] + [C_1] + [C_2] + [C_3] \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

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

$$[\mathrm{HBr0_3}]_T = [\mathrm{Br}O_3] + \frac{K_1[HBrO_3]}{[H^+]}$$

$$+K_2[PA]\frac{K_1[HBrO_3]}{[H^+]} + K_3[(PdCl_2]K_1K_2[PA]\frac{[HBrO_3]}{[H^+]}$$

$$[\mathrm{HBr0_3}]_T = [HBrO_3]\ (1 + \frac{K_1}{[H^+]} + \frac{K_1K_2[PA]}{[H^+]} + \frac{K_1K_2K_3[PdCl_2][PA]}{[H^+]})$$

$$[HBrO_3] = \frac{[HBrO_3]_T\ [H^+]}{[H]^+ + K_1 + K_1K_2[PA] + K_1K_2\ k_3\ [PdCl_2][PA]} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots. (4)$$

Substituting the value of $[HBrO_3]$ from eq.(4) in eq.(2) we get

$$\text{Final}\quad Rate = \frac{K_1K_2\ K_3k_4[PdCl_2]\ [PA][HBrO_3]_T\ \cancel{[H^+]}}{\cancel{[H^+]}\ \{\ [H^+] + K_1 + K_1\ K_2[PA] + \ K_1\ K_2\ K_3[PdCl_2]\ [PA]\ \}}$$

The value of $K_1\ K_2\ K_3[PdCl_2]\ [PA]$ is negligible so it can be neglected.

$$\text{Therefore, Final } Rate = \frac{K_1K_2\ K_3k_4[PdCl_2][PA][HBrO_3]_T}{[H^+] + k_1(1 + \ k_2[PA])}$$

The rate law explains all observed effects.

7.8B: Kinetic summary observed in potassium bromate oxidation of Paracetamol catalyzed by Ir(III) chloride in perchloric acid medium .

The title of reaction shows following kinetic results. Similar kinetic results are obtained for paracetamol catalyzed by Ir(III) chloride in perchloric acid medium .

1. The reaction follows first order kinetics with respect to oxidant i.e. potassium bromate.
2. First order kinetics with respect to catalyst i.e., Ir(III) chloride on the rate of reaction.
3. The reaction shows positive effect with respect to [substrate] on the reaction rate.
4. Addition of chloride ion to the reaction mixture depicts no change in the reaction rate
5. The reaction shows negative effect of $[H^+]$ on the rate of reaction.
6. Insignificant effect of ionic strength of the medium on the reaction rate was observed.
7. Addition of mercuric acetate did not bring about any appreciable change in the reaction rate.
8. Addition of D_2O to the reaction mixture showed negligible effect on the reaction rate.
9. Increase in temperature markedly increases the rate of reaction.

7.8C: Mechanism and derivation of rate law:

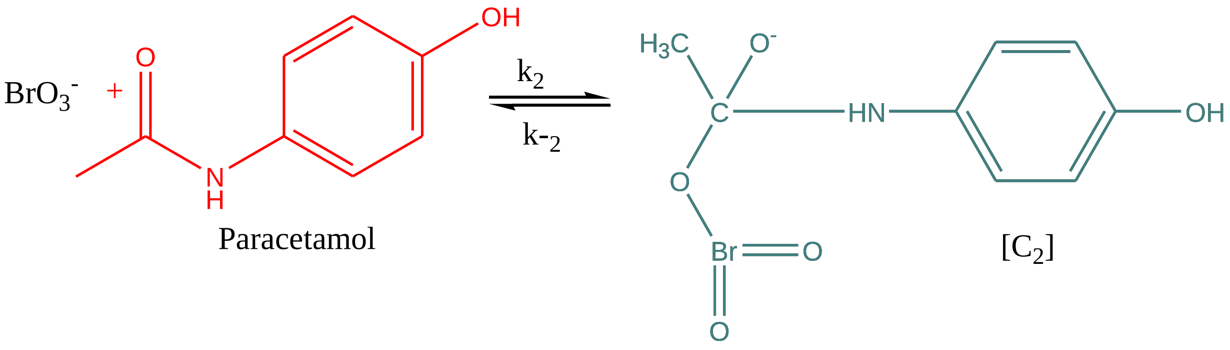
In alkaline and acidic medium, potassium bromate is ionised:

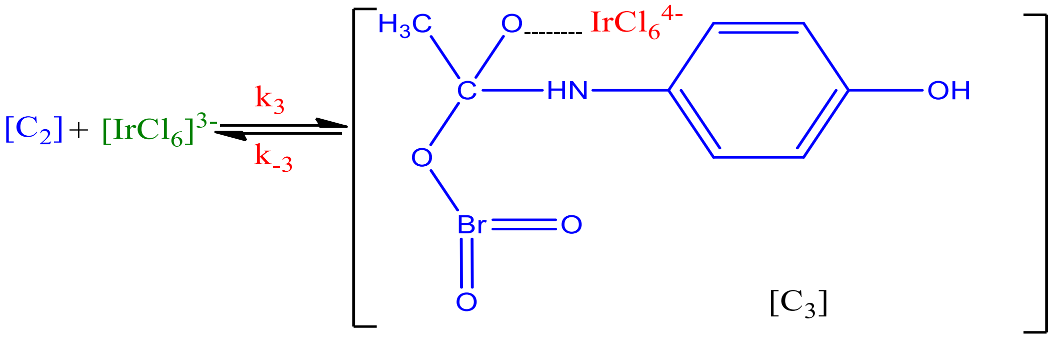
$$KBrO_3 \longrightarrow K^+ + BrO_3^- \quad \text{....................(i)}$$

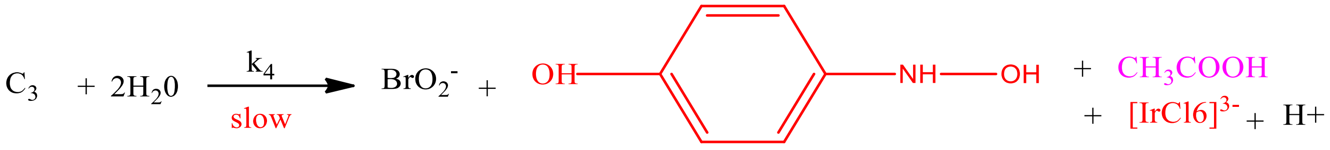
The BrO_3^- species has been reported to act as an oxidising agent in acidic as well as in alkaline medium (Singh and Srivastava, 1991). Ir(III) chloride has been reported to give a number of possible chloro species dependent on pH of the solution presence of [Cl^-] in excess shifts the equilibrium to right.

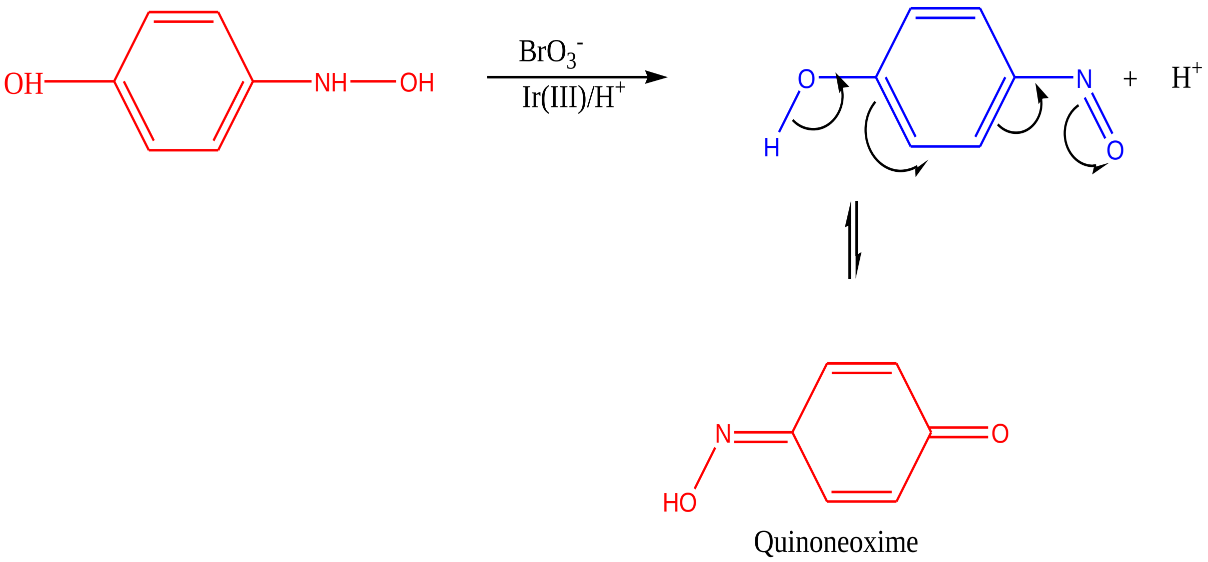
$$[IrCl_5(H_2O)]^{2-} + Cl^- \rightleftharpoons [IrCl_6]^{3-} + H_2O$$

$$HBrO_3 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{[C_1]}{BrO_3^-} + H^+$$









Quinoneoxime

Considering the proposed mechanism for oxidation of paracetamol by acidic potassium bromate in presence of micro amount of [Ir(III)] chloride acting as catalyst and applying the steady state approximation, the rate law may be written as equation.

$$\text{Final Rate} = k_4[C_3] \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

On the basis of scheme above step (1) we can be obtained in the following form respectively as-

$$\frac{d[C_3]}{dt} = k_3[C_2]\,[IrCl_3] - k_{-3}\,[C_3]$$

$$[C_3] = K_3[C_2]\,[IrCl_3]$$

$$\frac{d[C_2]}{dt} = [k_2][C_1][PA] - k_{-2}[C_2] - k_3[C_2][IrCl_3] + k_{-3}[C_3]$$

Substituting the value of [C_3] we get

$$\frac{d[C_2]}{dt} = k_2\,[C_1]\,[PA]\; - k_{-2}\,[C_2]\; - k_3\,[C_2]\,[IrCl_3] + k_{-3}(k_3[C_2]\,[IrCl_3])$$

$$[C_2] = K_2\ [PA]\ [C_1]$$

$$\frac{d[C_1]}{dt} = k_1\ [HBrO_3] - k_{-1}\ [C_1][H^+] - k_2\ [C_1]\ [PA] + k_{-2}\ [C_2]$$

Substituting the value of $[C_2]$ we get

$$\frac{d[C_1]}{dt} = k_1\ [HBrO_3] - k_{-1}\ [C_1][H^+] + \cancel{k_2\ [C_1]\ [PA]} + k_{-2}\frac{k_2}{\cancel{k_{-2}}}\ \cancel{[PA]}\ [C_1]$$

$$\mathrm{k}_1[HBrO_3] =\ k_{-1}\ [C_1][H^+]$$

$$[C_1] = K_1\frac{[HBrO_3]}{[H^+]}$$

$$Rate = \frac{\mathrm{k}_1\ \mathrm{k}_2\ \mathrm{k}_3\ \mathrm{k}_4[IrCl_3]\ [PA][HBrO_3]}{[H^+]} \ldots\ldots\ldots\ldots\ldots(2)$$

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

$$[\mathrm{HBr0_3}]_T = [\mathrm{HBr0_3}] +\ [\mathrm{C_1}] + [\mathrm{C_2}] + [\mathrm{C_3}] \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(3)$$

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

$$[\mathrm{HBr0_3}]_T = [\mathrm{HBr}O_3] + \frac{K_1[HBrO_3]}{[H^+]}$$

$$+K_2[PA]\frac{K_1[HBrO_3]}{[H^+]} + K_3([IrCl_3]K_1K_2[PA]\frac{[HBrO_3]}{[H^+]}$$

$$[\mathrm{HBr0_3}]_\mathrm{T} = [HBrO_3]\ (1 + \frac{K_1}{[H^+]} + \frac{K_1K_2[PA]}{[H^+]} + \frac{K_1K_2K_3[IrCl_3][PA]}{[H^+]})$$

$$[HBrO_3] = \frac{[HBrO_3]_T\ [H^+]}{[H]^+ + K_1 + K_1K_2[PA] + K_1K_2\ k_3\ [IrCl_3][PA]} \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots.(4)$$

Substituting the value of [HBrO$_3$] from eq.(4) in eq.(2) we get

$$\text{Final} \quad Rate = \frac{K_2\ K_3k_4[IrCl_3]\ [PA][HBrO_3]_T\ \cancel{[H^+]}}{\cancel{[H^+]}\ \{\ [H^+] + K_1 + K_1\ K_2[PA] +\ K_1\ K_2\ K_3[IrCl_3]\ [PA]\ \}}$$

The value of $K_1\ K_2\ K_3[IrCl_3]\ [PA]$ is negligible so it can be neglected.

$$\text{Therefore, Final } Rate = \frac{K_1K_2\ K_3k_4[IrCl_3][PA][HBrO_3]_T}{[H^+] + k_1(1 +\ k_2[PA])}$$

The derived rate law explains all the observed kinetic results.

Table 8.0

Values of Activation Parameters for pharmaceutical drugs in Pd(II) and Ir(III) catalyzed oxidation by potassium bromate in acidic medium

Arrhenius Parameters	Pd(II) chloride		Ir(III) chloride	
	Gabapentin	Paracetamol	Gabapentin	Paracetamol
E_a kJ mol^{-1}	52.42	61.27	66.67	53.33
Log A	10.34	10.79	12.66	10.80
ΔS^* JKmol^{-1}	-56.99	-23.18	-6.51	-42.12
ΔG^* kJ mol^{-1}	70.18	68.42	68.71	66.60
ΔH^* kJ mol^{-1}	52.67	61.27	66.67	53.62

The entropy of activation plays an important role in case of reactions between ions or neutral molecules forming ions. When reaction takes place between two oppositely charged ions, there is generally an entropy increase in going from reactant to activated complex but on the other hand when it takes place between two similarly charged ions, there is entropy decrease in terms of solvation of ions, the explanation of entropy can be given as follows for different reactions. It is well known that solvation in general increases with charge on the ion (smaller ions are highly solvated). In case of reaction between two ions of opposite charge, their union forms a neutral molecule which will result in a lowering of net charge and due to this some frozen solvent (such as water molecules frozen around the incipient ions) molecule will be released with an increase in entropy. But on the other hand when reaction takes place between two similarly charged ions, the transition state will be a more highly charged ion, which will be expected to be strongly solvated, so that more solvent molecules will be required than for separate ions which would lead to decrease in entropy, this is due to desolvation of activated state rather than the reactants. So for the reaction in solution enthalpy of activation changes with the solvent and becomes less negative (i.e. increase) while free energy change of activation decreases, as the polarity of solvent increases. Table for activation parameters shows high positive values of free energy of activation (ΔG^*) indicating transition state to be highly solvated and negative value of entropy of activation (ΔS^*) suggests the formation of activated complex with reduction in degree of freedom of reactant molecules or ions.

8.1: Conclusion

The experimental results as detailed in the previous chapters of this thesis depict that the reaction rate doubles when the concentration of the catalyst is made two times. The rate law in case of Gabapentin and Paracetamol are in accordance with all kinetic observations and proposed mechanistic steps are reinforced by the insignificant effect of ionic strength, which also explains the participation of a dipole in the slow and rate determining step. From the present explorations, it is deduced that $HBrO_3$ (in case of pharmaceutical drugs) and $[PdCl^+]$ and $[IrCl_6]^{3-}$ are the reactive species of $KBrO_3$ and Pd(II)/Ir(III) chloride catalyst respectively in acid medium.

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PUBLICATIONS
AND
CONFERENCES

Publications and Conferences

1. **Reena Patel, Shailesh Kumar, Arvind Kumar Pandey and Sheila Srivastava,** "A Thermodynamic and Comparative Study of Pharmaceutical Drug by Ir(III) and Pd(II) Catalyzed Oxidation in Acidic Medium ($HClO_4$): Kinetic Model", Journal of Applicable Chemistry: 8 (3), 1337-1349, (2019).

2. **Reena Patel, Deepak Kumar, Arvind Kumar Pandey, Shailesh kumar, Sheila Srivastava and Puneet Kumar:** "Mechanistic and Thermodynamic study of Iridium (III) Catalyzed Oxidation of Paracetamol Drug by Acidic Solution of Potassium Bromate ($KBrO_3$): A Kinetic Study" Journal of Applicable Chemistry: 7 (5), 1418-1427, (2018).

3. **Reena Patel, Shailesh kumar, Abhishek Verma, Sheila Srivastava,** Thermodynamic properties and Mechanism of Aquachloro iridium (III) catalyzed Oxidation of Pharmaceutical drug (Paracetamol) by Acidic solution of Potassium Bromate ($KBrO_3$): A kinetic study", International Journal for Research in Applied Science & Engineering Technology, Volume 6 Issue I, January (2018)

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Papers presented in International Conferences

1. Presented a paper entitled “Kinetic and thermodynamic properties of pharmaceutical drug (Gabapentin) oxidized by potassium bromate ($KBrO_3$) in presence of micro amount of Ir(III) chloride as catalyst in acidic medium” in International Conference on **Multifuctional Materials For Future Applications (ICMFA)** held at Department of Chemistry, IIT , Banaras Hindu University from October 27-29, (2015)

2. Presented paper entitled “Pd(II) catalyzed oxidative cleavage of Paracetamol by potassium bromate in acidic medium- A kinetic approach” in International Conference on **Futuristic materials and emerging trends in chemical sciences(ICOFMATICS)** held at Department of Chemistry , D.B.S college, Kanpur from February 8-10, (2016)

Papers presented in National Conferences/ Workshop/ Symposium

1. Presented paper entitled “Studies on kinetic and Mechanism……..in Acidic Medium” in National Conference on **3rd Lucknow Science Congress (LUSCON)** held at Babasaheb Bhimrao Ambedkar University, Lucknow from October 31- November 2 , (2015)

2. Presented a paper entitled “Mechanistic investigation of Enviroment friendly Pd(II) catalyzed oxidation of Paracetamol by potassium bromate ($KBrO_3$) in presence of $HClO_4$ acid medium” in National conference on **Recent advances and innovations in chemical and materials sciences** (RAICMS) held in Department of Chemistry, Shri Jai Narain PG college, Lucknow from 23-24 February , (2017)

3. Presented paper entitled “Assesment of Fluoride Content in Ground water and its Enviromental important at some blocks of Distt. Raebareli India” in National Seminar on **Enviromental Pollution and its Impact on Modern Society** held at Indira Gandhi Rajkeeya Mahila Mahavidyalaya Raebareli from February 24 - 25, 2015

4. Presented a paper entitled “Mechanistic study of Palladium(II) catalyzed oxidation of Aspirin by Sodium Periodate [$NaIO_4$] in perchloric acid medium” in National Conference on **Nano Chemistry** held in Department of Chemistry Sam Higginbottom Institute of Agriculture, Technology and Sciences from November 11-12, 2014

5. Workshop on “**Excitement in Chemical Sciences**” at Department of Chemistry, Feroze Gandhi College, Raebareli on September 13-14, 2014 organized by **The National Academy of Sciences, India**.

6. 8th NIPER(RBL)-CSIR-CDRI Symposium on **Current Trends In Medicinal Chemistry and Pharmaceutical Sciences in Drug Discovery** held at National Institute of Pharmaceutical Education and Research, Raebareli from March 18-19, 2016

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

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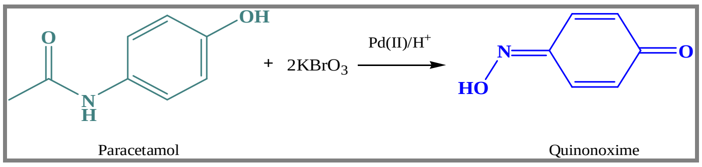
ABSTRACT

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 [KCl] 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 [PA]. 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 catalyzed 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

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Mechanistic Investigation on Pd (II) Catalyzed Oxidation of Paracetamol by Potassium Bromate ($KBrO_3$) in Presence of $HClO_4$ Acid Medium: A Kinetic Model

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Abstract: The present paper deals with the kinetic and mechanistic investigation of pd(II) catalyzed oxidation of paracetamol by potassium bromate ($KBrO_3$) in presence of perchloric acid medium at 303 K. The experimental result shows a first order kinetics with respect to [Palladium] and [bromate]. The reaction showed negative effect for [H^+]. Paracetamol positively influenced the rate of reaction. Negligible effect of [$HgOAc)_2$] and ionic strength of the medium was observed. Variation of [Cl^-] does not show any significant change on the rate of reaction. The values of rate constants observed at different temperatures (30 to 45^0C) were utilized to calculate the activation parameters. Quinoneoxime and acetic acid have been identified as main oxidation products of the reactions. Feasible mechanism has been proposed conforming with the kinetics, stochiometry and product of the reaction. The rate law has been derived from obtained kinetic data.

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

1. INTRODUCTION

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.[1-9]. 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. Paracetamol (4-hydroxyacetanilide or acetmidophenol) is a well known drug that is having extensive appliction in pharmaceutical industries. It is antipyretic and analgesic compound of high therapeutic value[10-11]. It is also used as an intermediate for pharmeceutical (as a precursor in penicillin) and azo dye [112-15]. Oxidation reactions are important in the synthesis of organic compounds, create new functional groups or modify existing functional groups in a molecule[16-17]. Various advanced oxidation processes such as electrochemical[18-20] ozonation and H_2O_2 / UV oxidation[21-24] have been employed to remove aqueous paracetamol.

The oxidation kinetics of Paracetamol drug by oxidant like organic haloamines, metal ion oxidants, metal complex, use of catalyst, variation of media, product effect, is of importance to understand the mechanism of metabolic conversion of paracetamol in biological systems and also identify the reactive species of the oxidant in aqueous acid/ base. Till date the action of paracetamol at a molecular level is not completely understood but could be related to production of reactive metabolites by the peroxidase function of COX-2, which could deplete glutathione, a cofactor of enzymes such as PGE synthase[25]. which has high therapeutic value. The results of various studies are interpreted and consolidated. In recent years have been metal platinum group metal ion including Ru(III), Os(VIII), Ir(III), Rh(III), and Pd(II) widely used as catalyst due to their strong catalytic influence in various reactions. Palladium (II) chloride is the most important salt in the catalytic chemistry of palladium. Several authors have performed studies using Pd(II) because of the commercial importance of reactions catalyzed by Pd(II). The kinetics for the oxidation of ethylene by aqueous Pd (II) is an example[26-27]. 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 [28-29]. 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 catalytic techniques have been reported for the detection of biomolecules[30-32]. The present study examines, in detail the kinetic and mechanistic aspects of the Pd(II) catalyzed oxidation of paracetamol by $KBrO_3$ in acidic media with the following objective.

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Kinetic and thermodynamic properties of pharmaceutical drug (Gabapentin) by potassium bromate ($KBrO_3$) in presence of micro amount of Ir(III) chloride as catalyst in acidic medium

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ABSTRACT

The kinetic and thermodynamic properties of pharmaceutical drug (gabapentine) by potassium bromate ($KBrO_3$) in presence of Micro amount of Ir(III) chloride as catalyst in acidic medium was studied in the temperature range 30 to 45^0 C. The reaction is carried out in the presence of mercuric acetate as a scavenger for chloride 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 GBP respectively. The reaction followed first order with respect to Ir(III) chloride and $[H^+]$.Negligible effect of $[Hg(OAc)_2]$ and ionic strength of the medium was observed. Chloride ion positively influenced the rate of reaction. The values of rate constants observed at different temperatures (30 to 45^0C) were utilized to calculate the activation parameters. Feasible mechanism is proposed which are be composed with the kinetics, stochiometry and product of the reaction. The rate law has been derived from obtained kinetic data.

Capsule Summary: Effect of Ir(III) chloride and temperature on kinetic and thermodynamic properties of gabapentine was studied and study revealed that both catalyst and temperature affected both kinetic and thermodynamic properties considerably.

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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 catalyze a wide variety of reactions like hydrogenation, oxidation and polymerization. The applications of transition metal catalyst such as Ru(III)(Singh et al., 2007; Hosahalli et al., 2012), Rh(III) (Singh et al., 2009 and 2010), Cu(II) (Li et al., 2009; Olusanya and Odebunmi, 2011) and Pd(II) (Koli and Nandibewoor, 2000; Singh et al., 2010) 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

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Thermodynamic properties and Mechanism of Aquachloro iridium (III) Catalyzed Oxidation of Pharmaceutical drug (Paracetamol) by Acidic solution of Potassium Bromate ($KBrO_3$): A kinetic study

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Abstract: The thermodynamic properties and mechanism of a quachloroiridium(III) Catalyzed oxidation of pharmaceutical drug(Paracetamol) by acidic solution of potassium bromated(KBrO3) at 350C. The reaction followed first order kinetics with respect to Ir (III) and potassium bromated (KBrO3). Rate of reaction exhibits zero order and fractional positive order kinetics with respect to [KCl] and [PA] respectively. The rate of reaction decreased with increasing [H+] was observed for the oxidation of paracetamol. Negligible effect of [Hg(OAC)2] and ionic strength of the mediumwas observed at different temp.(300 C to 450 C) were utilized to calculate the activation parameters. The reaction between potassium bromate and paracetamol in acid medium exhibits 1:2 stoichiometry. Quinoneoxime and acetic acid have been identified as main oxidation products of the reactions. Feasible mechanism has been proposed conforming to the kinetics, stochiometry and product of the reaction. The rate law has been derived from obtained kinetic data.

Key words: Kinetics, oxidation, Paracetamol, Potassium bromate, Ir (III) chloride, Acidic medium.

I. INTRODUCTION

Cataysis by transition metal ions, plays an important role in understanding the mechanistic aspects of a particular redox reaction. Ir(III) chloride is a strong catalyst and is more conveniently prepared either by the action of chlorine on iridium powder at 600-620^0[1-2] or from the tetrahydroxideIr $(OH)_4$ by the action of chlorine at 600^0, Or hydrogen chloride at 310^0[2]. It has a large range of stability. It is formed from its elements at a temperature below 100^0, and it does not decompose until 760^0. The rate of chlorination of metal is greater in presence of sunlight or ultraviolate light; the addition of a trace of carbon monoxide diminishes the rate of reaction in the dark, but increases it in ultraviolate light.[2] The kinetics of redox reactions incorporating certain transition metal ions like osmium(VIII), ruthenium(VIII), ruthenium(III), and palladious ions as homogeneous catalyst has been extremely investigated.[3-8] These are non toxic and homogeneous catalyst reported by several workers.[9-10] Scant attention has been paid on catalytic role of ruthenium(III) chloride with potassium bromated as oxidant.[11-12]Ir(III) chloride is seen to be a good catalyst in recent years. It has been investigated very little as a homogeneous catalyst with N-bromosuccinimide.[13] Iridium(III) chloride has also been used as catalyst in N-bromoacetamide oxidation[14] of some organic compounds. Kinetics of Ir(III) catalysis have also been reported[15]. Oxidant chosen for the present work is potassium bromated ($KBrO_3$) which has been reported to be a powerful oxidant with redox potential of 1.44 volt in acidic media. $KBrO_3$ hasbeen widely used in oxidation of alcohols[16], ketones[17], aniline[18], phenols, aldehydes[19], tartaric acid[20], some labile substrate[21], nitrites[22], pyrogallic acid[23], amino acids[24], diols[25], unsaturated corboxlyic acids[26] and n-substituted phenyl methyl sulphides[27] with ruthenium (III) chloride as catalyst. 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 has also been reported. Ir(III) catalyzed cyclicalcohols[32], cyclic ketones[33] oxidation by potassium bromate has also been reported. Comparatively Ir(III) catalyzed 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

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Mechanistic and Thermodynamic study of Iridium (III) Catalyzed Oxidation of Paracetamol Drug by Acidic Solution of Potassium Bromate ($KBrO_3$): A Kinetic Study

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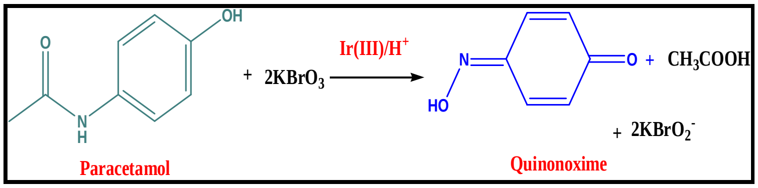
ABSTRACT

Mechanistic and thermodynamic study of Iridium(III) Catalyzed Oxidation Of Paracetamol drug by Acidic solution of Potassium Bromate ($KBrO_3$) at 35°C. The reaction followed first order kinetics with respect to Ir(III) and potassium bromated ($KBrO_3$). Rate of reaction exhibits zero order and fractional positive order kinetics with respect to [KCl] and [PA] respectively. The rate of reaction decreased with increasing [H^+] was observed for the oxidation of paracetamol. Negligible effect of [$Hg(OAC)_2$] and ionic strength of the medium was observed at different temperature (30°C to 45°C) were utilized to calculate the activation parameters. The reaction between potassium bromate and paracetamol in acid medium exhibits 1:2 stoichiometry. Quinoneoxime and acetic acid have been identified as main oxidation products of the reactions. Feasible mechanism has been proposed conforming with the kinetics, stochiometry and product of the reaction. The rate law has been derived from obtained kinetic data.

Graphical abstract



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

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