INTERNATIONAL JOURNAL OF CURRENT RESEARCH IN CHEMISTRY AND PHARMACEUTICAL SCIENCES

(p-ISSN: 2348-5213: e-ISSN: 2348-5221)

www.ijcrcps.com

DOI: 10.22192/ijcrcps Coden: IJCROO(USA) Volume 7, Issue 1 - 2020

Research Article

DOI: http://dx.doi.org/10.22192/ijcrcps.2020.07.01.001

Kinetics and mechanism of oxidation of Rabeprazole sodium by potassium permanganate in alkaline medium

Ramyashree H[1], Vidyavati Shastry[1*]

SEA College of Engineering and Technology, Bangalore-560049

E-mail: *ramyashree732@gmail.com*

Abstract

The oxidation of Rabeprazole sodium by Potassium permanganate has been studied by spectrophotometrically in the presence of alkaline medium at 298 K at 525nm.

The oxidation kinetics was also studied by varying the ionic strength of the medium. The reaction was studied at different temperatures and products of oxidation were analyzed by LCMS. By the experimental observations, rate law was derived and mechanism was suggested.

Keywords: Potassium permanganate, Rabeprazole sodium, oxidation, spectrophotometry

Introduction

Rabeprazole sodium is a proton pump inhibitor(PPI) to reduce stomach acid and is used for the treatment of gastroesophageal reflux disease[GERD],duodenal ulcers, and used in combination with antibiotics to treat Helicobacter pylori[H. Pylori] bacterial infections in the stomach. It exhibits polymorphism and present article summarize the different polymorphic forms of rabeprazole sodium [1]. Rabeprazole sodium is chemically known as 2-[{4-(3-methoxypropoxy)-3-methylpyridin-2- yl}-methylsulphinyl]-1H-benzimidazole sodium.

It suppresses secretion of gastric acid by inhibiting the enzyme system of hydrogen/potassium adenosine triphosphatase (H^+ /K^+ ATPase), the proton pump of the gastric parietal cell. It is used in conditions where inhibition of gastric acid secretion is required, including aspiration syndromes, dyspepsia, gastro-oesophageal reflux, peptic ulcer and the Zollinger-Ellison syndrome [2]. It has an empirical formula of $C_{18}H_{20}N_3NaO_3S$ and molecular weight of 381.42. It is very soluble in water. Rabeprazole sodium rapidly degrades in acid media and is more stable under alkaline conditions[3].

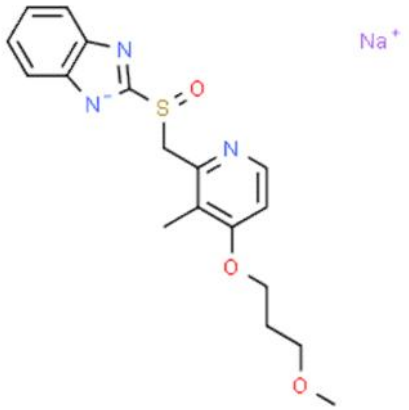


Fig 1. Structure of Rabeprazole sodium

Another great activity rabeprazole has, is against Helicobacter pylori, an organism strongly associated with peptic ulcer disease.[4]It is used to treat gastroesophagal reflux disease (GERD), a condition in which backward flow of acid from the stomach causes heartburn and possible injury of the esophagus (the tube that connects the throat and the stomach). It is a proton pump inhibitor that decreases the amount of acid produced in the stomach thus relieves symptoms such as heart burn, difficulty swallowing and persistent cough. Since it is an acid labile drug, it is commercialize as enteric coated tablet[5]. The literature survey reveals a crescent number of publications related to rabeprazole sodium determination in biological fluids [6-11] and also in pharmaceutical formulation by different methods, this drug is not studied for its kinetics behaviour in the presence of $KMnO_4$.

Potassium permanganate is widely used as a oxidizing agent in synthetic as well as in analytical chemistry and also as a disinfectant. The reactions with permanganate are governed by pH of the medium. Among six oxidation states of manganese from 2+ to +7,permanganate, Mn(VII) is the most potent oxidation state in acid as well as alkaline
medium [12].

Experimental

Materials

All chemicals used in this investigations were of Analytical Grade. The substrate pure Rabeprazole sodium was purchased from Everest organics limited, Hyderabad, India and was used as received. Solutions were prepared by dissolving requisite amount of RBZ [$1X10^{-3}$] and potassium permanganate[$1X10^{-4}$] is prepared in distilled water. NaOH [$1X10^{-2}$], KCl[$1X10^{-1}$] and were also prepared in doubly distilled water and standardized by standard methods.

Kinetic measurements

All kinetics measurements were performed under pseudo first order conditions, where [Rabeprazole sodium]>>[$KMnO_4$].Experiment has been done by using UV/Vis spectrophotometer at room temperature. The reaction progress was followed by spectroscopically at 525nm by monitoring decrease in absorbance due to $KMnO_4$.The first order rate constants calculated from the linear plots of log [Absorbance] v/s time were reproducible within $\pm$ 5%.

Results

Stiochiometry and product analysis

In order to analyse obtained kinetic results, the stiochiometry of $KMnO_4$ [$1x10^{-4}$] and Rabeprazole [$1X10^{-3}$] were determined spectrophotometrically. Reaction mixture was kept over 24 hours at room temperature and after the completion of reaction excess of potassium permanaganate was measured spectrophoto metrically at 525nm. The stoichiometry of the reaction was found to be 1:1. The product was identified by LC-MS spectra which give M^+H + peak at 375mHz.The result indicated that 1 mole of RBZ reacts with 1 mole permanganate. The product was identified as Rabeprazole sulphone[2-[[4-(3-methoxypropoxy)-3-methylpyridin-2-yl]methylsulfonyl]-1H-benzimidazole by using LCMS.

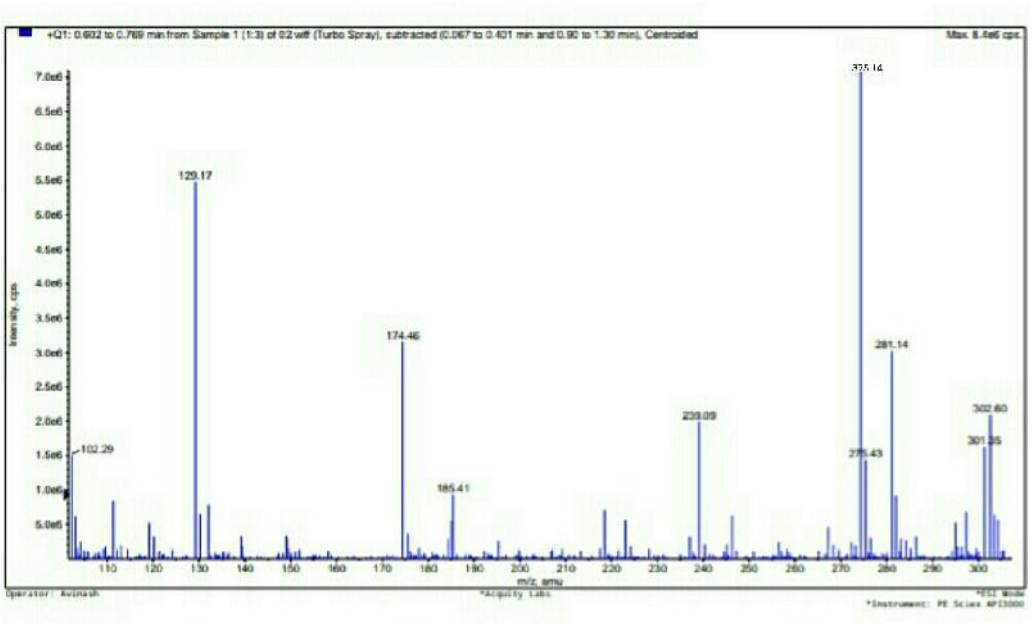
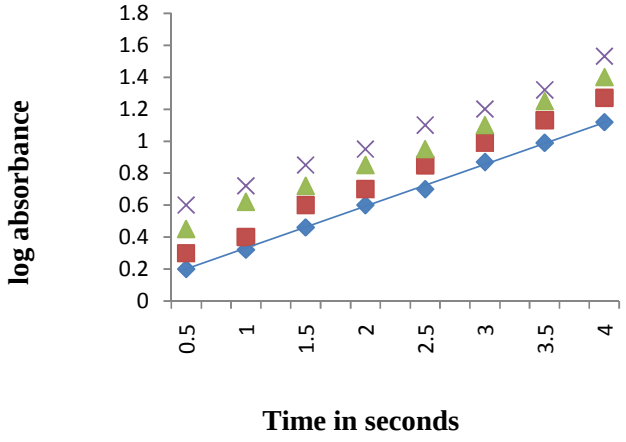


Fig 2. LCMS Spectra of oxidation product of Rabeprazole

Reaction order

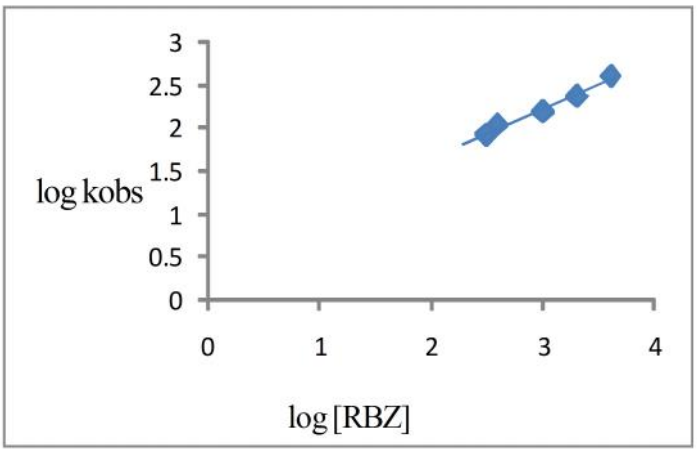
Effect of permanganate concentration

Potassium permanganate varied from $0.25X10^{-4}$ to $3X10^{-4}$ mol dm^{-3} keeping RBZ[$1X10^{-3}$], NaOH[$1X10^{-2}$], and KCl[$1X10^{-1}$] constant. The linear plots obtained by plotting the graph of log absorbance versus time indicates the reaction is first order with respect to permanganate.



Effect of Rabeprazole

Effect of Rabeprazole was varied its concentration from [0.25X10^{-3}] to [3X10^{-3}] keeping potassium permanganate [1X10^{-4}], NaOH[1X10^{-2}], KCl [1X10^{-1}] at constant. The plot log Kobs versus log [RBZ] for the different concentration is linear.



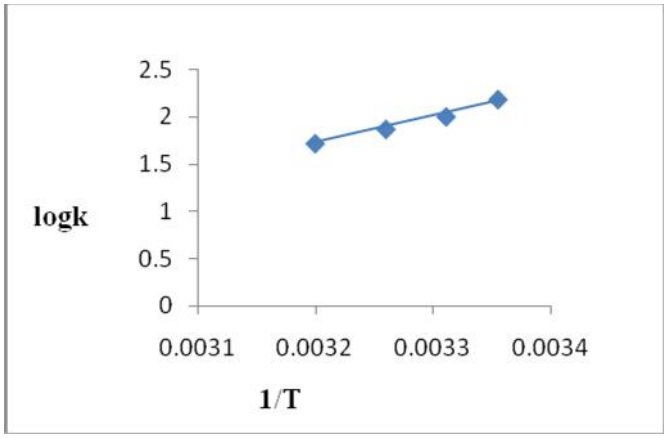
A graph of Log [RBZ] against log Kobs shows fractional order with respect to Rabeprazole

Effect of Sodium hydroxide

The effect of alkali on the reaction has been studied at constant concentration of rabeprazole and potassium permanganate. The concentration of sodium hydroxide 0.012 to 0.2 moldm^{-3} and the rate constant increases with an increase in [alkali].

Effect of temperature

To determine the temperature coefficient and thermodynamic activation parameters such as energy of activation, free energy of activation, entropy of activation and enthalpy of activation, the reaction was carried out at three different temperatures 298,302,306,312 at fixed concentration of rabeprazole [1X10^{-3}]and potassium permanaganate [1X10^{-4}], NaOH[1X10^{-2}], KCl[1X10^{-1}] were at constant condition. Rate k and activation quantities were tabulated in table I and table II.



Arrhenius plot for variation of temperature

Table I. Rate constants with respect to temperature

Temperature in (K)	Kobs $10^{-3}(S^{-1})$
298	6.50
302	9.00
306	13.2
312	19.1

Table II: Activation quantities

Parameters	Values
Ea	608.4
$\Delta H^{\#}$	-1.869
$\Delta G^{\#}$	1.866
$\Delta S^{\#}$	-6.27

Effect of potassium chloride

The effect of KCl was studied by varying concentration of potassium chloride was from 0.05 to 0.4 moldm^{-3} at fixed concentration of rabeprazole, $KMnO_4$ and NaOH. It was negligible effect on the rate of reaction.

Test for free radicals

The small amount of the oxidation reaction mixture to the aqueous acryl amide did not initiate polymerization, shows the absence of free radicals.

Table III: Effect of varying concentration of OMZ [1X10^{-3}], KMnO4 [1X10^{-4}], NaOH [1X10^{-2}], KCl[1X10^{-1}] on the rate of the reaction at 298K

$[KMnO_4]X10^{-4}$	$[RBZ]X10^{-3}$	$[OH^-]X10^{-2}$	$[KCl]X10^{-1}$	$K_{obs}\ X10^{-3}$	$K_{cal}X10^{-3}$
0.25	1.0	0.025	0.1	7.00	5.68
0.5	1.0	0.025	0.1	6.68	5.68
1.0	**1.0**	0.025	0.1	**6.50**	**5.68**
2.0	1.0	0.025	0.1	6.42	5.68
3.0	1.0	0.025	0.1	6.45	5.68
1.0	**0.25**	0.025	0.1	2.50	1.81
1.0	**0.5**	0.025	0.1	4.35	3.29
1.0	**1.0**	0.025	0.1	**6.50**	**5.68**
1.0	**2.0**	0.025	0.1	9.25	8.87
1.0	**3.0**	0.025	0.1	12.0	10.89
1.0	1.0	**0.012**	0.1	5.50	4.23
1.0	1.0	**0.025**	0.1	**6.50**	**5.68**

1.0	1.0	**0.05**	0.1	7.01	6.77
1.0	1.0	**0.1**	0.1	7.52	7.48
1.0	1.0	**0.2**	0.1	8.20	7.89
1.0	1.0	0.025	**0.05**	6.99	5.68
1.0	1.0	0.025	**0.1**	**6.50**	**5.68**
1.0	1.0	0.025	**0.2**	6.98	5.68
1.0	1.0	0.025	**0.3**	6.97	5.68
1.0	1.0	0.025	**0.4**	7.02	5.68

Discussion

$$\text{Rate} = \frac{-d[MnO_4^-]}{dt} = k[\text{complex-C}]$$

$$\text{Rate} = kK_2[\text{RBZ-Na}][MnO_4.OH]^{2-} \quad (1)$$

$$= k K_1K_2[\text{RBZ-Na}]_f [MnO_4]_f [OH^-]_f$$

$$[\text{RBZ-Na}]_T = [\text{RBZ-Na}]_f \quad (2)$$

$$[MnO_4^-]_T = [MnO_4^-]_f + [MnO_4.OH]^{2-} + [C]$$

$$[MnO_4^-]_T = [MnO_4^-]_f + K_1 [MnO_4^-]_f [OH^-]_f + K_1K_2[\text{RBZ-Na}] [MnO_4^-][OH^-]$$

$$[MnO_4^-]_f = \frac{[MnO_4^-]_T}{1+K_1[OH^-]+K_1K_2[\text{RBZ-Na}] [OH^-]} \quad (3)$$

$$[\text{RBZ-Na}]_T = [\text{RBZ-Na}]_f$$

$$[OH^-]_T = [OH^-]_f$$

$$\text{Rate} = \frac{k K_1K_2 [\text{RBZ-Na}] [MnO_4^-][OH^-]}{1+K_1[OH^-]+K_1K_2[\text{RBZ-Na}][OH^-]} \quad (4)$$

$$K_{obs} = \frac{\text{Rate}}{[MnO_4^-]} = \frac{kK_1K_2[\text{RBZ-Na}][OH^-]}{1+K_1[OH^-]+K_1K_2[\text{RBZ-Na}][OH^-]} \quad (5)$$

Rearranging 5, we get

$$\frac{1}{Kobs} = \frac{1}{kK_1K_2[\text{RBZ-Na}][OH^-]} + \frac{1}{kK_2[\text{RBZ-Na}]} + \frac{1}{k} \quad (6)$$

According to (6) the plots of 1/kobs versus 1/[RBZ-Na] and 1/kobs versus 1/[OH^-] should be linear and are verified in Fig.3 and Fig.4. The slopes and intercepts of such plots lead to the values of k,K_1 ,K_2 were calculated and values are found to be 0.02,50 and 717 respectively.

Using these values, in the rate equation, the rate constants were calculated. Using these constants, the rate constants were calculated over different experimental conditions. The k observed and k calculated values are in good agreement as shown in table III.

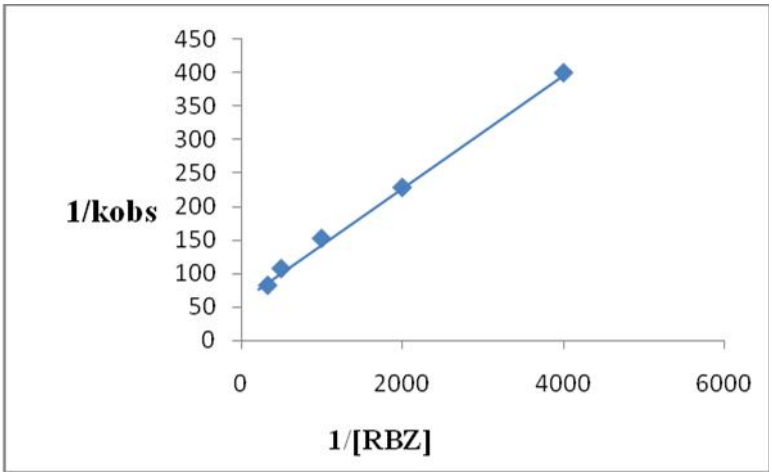


Fig. 3 Plot of 1/Kobs against 1/[RBZ] for the verification of rate law

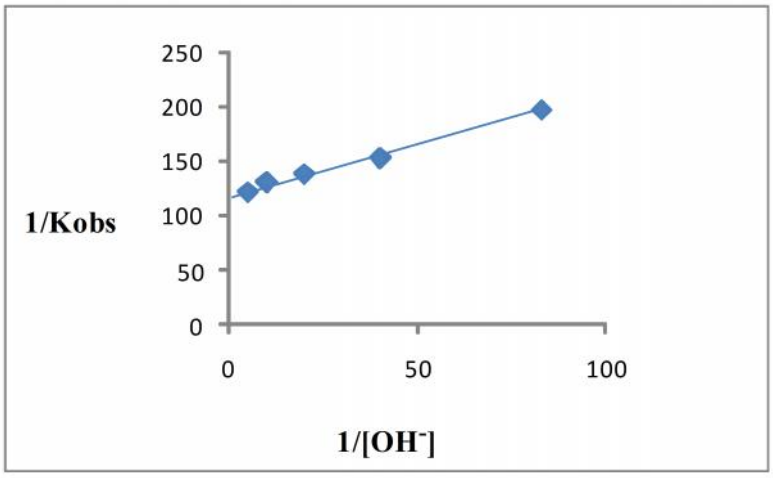


Fig. 4 Plot of 1/kobs against 1/[OH^-] for the verification of rate law

Conclusion

Kinetics and oxidation of Rabeprazole sodium by potassium permanganate in alkaline medium has been studied at 298. The stiochiometry of oxidation Rabeprazole and permanganate is found to be 1:1. The oxidation product was found to be Rabeprazole sulphone. There is no salt effect that means no reaction of the ions and no free radical formation in the reaction. The arrehnius plot shows how activation energy and temperature affect the sensitivity of the reaction rate.

Acknowledgments

We are thankful to SEA College of Engineering and technology, Bangalore for providing the laboratory facilities to bring about this work. And thanks for Everest organics limited, Hyderabad, India for providing drug sample.

References

1.Alok tripathi , B.S. Joshi and Jyothi Joshi ,Polymorphism in Rabeprazole Sodium , (2010) RASĀYAN *J.Chem*.Vol.3,No.4, 736-744

2. Mohammed H. Abdel- Hay [1], Suzy M.Sabry[1] ,Tarek S. Belal[1*] Ahmed A. Mahgoub[2],2013, Spectrophotometric determination of Rabeprazole Sodium using Two Charge Transfer Complexation Reaction . *Journal of applied pharmaceutical science* ,Vol.3 (11),128-133.

3. Yinhe Tan, Xiaoqing Si, Lulu Zhong, Xin Feng, Xinmin Yang. Development and validation of dissolution testings in acidic media for Rabeprazole sodium delayed-released capsules. *Drug Development and Industrial Pharmacy*. Vol.42, 2016-Issue 10.1669-1677.

4. C. V. Garcia , J. Sippel , M. Steppe & E. E. S.Schapoval. 2007,Development and Validation of Derivative Spectrophotometric method for Determination of Rabeprazole Sodium in Pharmaceutical Formulation, Journal of Pharmaceutical and Biomedical Analysis, Vol.46,88-93.

5. C. V. Garcia , J. Sippel , M. Steppe & E. E. S.Schapoval. 2007,Development and Validation of Derivative Spectrophotometric method for Determination of Rabeprazole Sodium in Pharmaceutical Formulation, Journal of Pharmaceutical and Biomedical Analysis, Vol.46,88-93.

6. Rajaa Farhan Hussein,Muhammad M.Hammami,2010, Rabeprazole analysis in human plasma by fully validated HPLC assay, Analytical Chemistry An Indian Journal,Vol 9,309-314.

7. Raviraj M.Kulkarni, Dinesh C .Bilehal & Sharanappa T.Nandibewoor. Kinetics and Mechanistic Study of oxidation of Sulfamethoxazole by Alkaline Permanganate,2002, Inorganic reaction Mechanism ,Vol 3,239-247.

Access this Article in Online	
Quick Response Code	Website: www.ijcrcps.com
	Subject: Chemistry
DOI: 10.22192/ijcrcps.2020.07.01.001	

How to cite this article:
Ramyashree H, Vidyavati Shastry. (2020). Kinetics and mechanism of oxidation of Rabeprazole sodium by potassium permanganate in alkaline medium. Int. J. Curr. Res. Chem. Pharm. Sci. 7(1): 1-8.
DOI: http://dx.doi.org/10.22192/ijcrcps.2020.07.01.001