Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research

J. Chem. Pharm. Res., 2011, 3(6):899-904

ISSN No: 0975-7384
CODEN(USA): JCPRC5

Kinetic method for estimation of Atenolol

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ABSTRACT

Kinetic methods are now accepted as standard analytical procedure for various types of samples. A simple, rapid and sensitive kinetic method has been proposed for estimation of antihypertensive drug Atenolol in sulphuric acid medium by cerium(IV).The kinetics of the indicator reaction was monitored spectrophotometrically by measuring the decrease in absorbance of cerium(IV) at 360nm.Oxidation of atenolol by Cerium(IV) has been found to follow pseudo first order kinetics. The oxidation rate increases with the increase in acid concentration and decrease with complexing bisulphate ions. The fixed time and fixed absorbance methods have been utilized for constructing calibration graphs to determine the concentration of drug in simulated samples the method has been successfully applied for the determination of atenolol in pharmaceutical formulations.

Key words: Kinetic Determination, Atenolol, spectrophotometrically, estimation and pharmaceutical formulations.

INTRODUCTION

Atenolol, chemically known as 4-(2-hydroxy-3-isopropylaminopropoxy)Phenyl-acetamide, is preferred as potent drug for regulating blood pressure because of its cardio-selectivity action as a betablocker[1].Cerium (IV) has been used as an oxidizing agent and an analytical reagent, especially in acid media[2].Kinetic method of analysis have been widely developed and accepted in chemical analysis of different samples[3-7] including kinetic cerimetric estimations of various aldosugars[8].The present study decribes preliminary procedure for estimation of atenolol with Ce(IV) in sulphuric acid medium.

EXPERIMENTAL SECTION

Material:

Commercially available chemicals of pure quality were used without further purification .A stock solution of atenolol(IPCA Laboratories Ltd. Ratlam) was prepared by dissolving appropriate amount of sample in double distilled water Ce(IV) stock solution was prepared by dissolving ceric sulphate(99.9%Loba chem.) in aqueous sulphuric acid.

Kinetic method:

The kinetic runs were performed in stoppered glass vessel in a controlled temperature (±0.1ºC) water bath. The kinetics of redox reaction between atenolol and cerium (IV) in sulphuric acid medium was followed under pseudo first order condition in presence of excess concentrations of atenolol and sulphuric acid by measuring the absorbance at 360nm for Ce(IV)-Visible spectrophotometer Systronics-104.The unknown is calculated in simulated sample by fixed time method and fixed absorbance method from the regression equations and from the graphs.

RESULTS AND DISCUSSION

Indicator reaction:

The value of k_{obs} calculated from the rate data shows that the indicator reaction between the cerium (IV) and atenolol in aqueous sulphuric acid medium follows the first order kinetics uniformly. The pseudo first order observed rate constants k_{obs} showed proportionate increase with atenolol and sulphuric acid concentrations whereas decrease with bisulphate ion concentration.

The stoichiometric equation under present kinetic experimental conditions can be represented as:

$$C_{14}H_{22}N_2O_3 + 2Ce(IV) + 2H_2O = C_{10}H_{10}O_5 + C_4H_{11}N + NH_3 + 2Ce(III) + 2H^+ \quad \text{———} \quad (1)$$

Kinetic Estimation:

The rate of these indicator reactions[11] under the present kinetic conditions in terms of disappearance of metal ion concentration with time at constant temperature and sulphuric acid concentration can be given by

$$\frac{-d[Ce^{IV}]}{dt} = k_0[\text{Cerium(IV)}]_0\,[\text{atenolol}]_0 == k_{obs}[Ce^{IV}]_0 \quad \text{---------} \quad (2)$$

Thus when $[\text{atenolol}]_0 \gg [Ce^{IV}]_0$ then,

$$k_{obs} = k_0\,[\text{atenolol}] \quad \text{----------} \quad (3)$$

Equation (2) alternatively expressed as eq.(4) for the finite change in the initial concentration of cerium(IV) in a given fixed time interval.

$$\frac{-\Delta[Ce^{IV}]}{\Delta t} = k_0[Ce^{IV}]_0\,[\text{atenolol}]_0 \quad \text{----------} \quad (4)$$

The initial concentration of cerium(IV) i.e. $[Ce^{IV}]_0$ is kept constant in each kinetic run varying initial concentration of atenolol i.e. $[\text{atenolol}]_0$ therefore,

$$\frac{-\Delta[Ce^{IV}]}{\Delta t} = k_0\,[\text{atenolol}]_0 \quad \text{----------} \quad (5)$$

Eq.(3) and(5) have been used to obtain three different calibration plots to determine the concentration of simulated samples of atenolol.

- k_{obs} and[atenolol].
- Absorbance i.e. $[Ce^{IV}]_0$ and $[atenolol]_0$ at fixed time intervals.
- Time in seconds and $[atenolol]_0$ at fixed absorbance i.e. at fixed concentration of $[Ce^{IV}]_0$.

The kinetic data of variation of k_{obs} [Fig.1], absorbance at fixed time interval[Fig.2] and time at fixed absorbance with initial concentration of atenolol [Fig.3]in different kinetic runs are given graphically for atenolol.

Table -1 : variation of k_{obs} absorbance at fixed time and time at fixed absorbance with initial concentration of atenolol

$10^4[Ce(IV)]=2.5moldm^{-3}$, $[H_2SO_4]=0.7moldm^{-3}$,Temperature=296±0.1K, λ =360nm

10^3[Atenolol]moldm^{-3} (Sec)at fixed Absorbance	Absorbance at fixed 10^{-2}time (Sec)			10^{-2}time		
	2.4	**4.8**	**7.2**	**0.7**	**0.5**	**0.3**
2.5	0.822	0.649	0.512	4	7.2	12
3.125	0.781	0.574	0.415	3.2	5.7	9.7
4.375	0.679	0.447	0.289	2.2	4.2	7
5	0.635	0.397	0.236	2	3.6	6.2
5.625	0.597	0.342	0.196	1.7	3.2	5.4
6.875	0.532	0.231	0.134	1.4	2.5	4.3
7.5	0.488	0.231	0.106	1.2	2.3	3.9
Unknown-1	**0.732**	**0.518**	**0.368**	**2.8**	**4.7**	**8.4**
10^3[Unknown-1]moldm^{-3}	**3.75**	**3.77**	**3.75**	**3.81**	**3.8**	**3.8**
Unknown-2	**0.566**	**0.311**	**0.169**	**1.6**	**2.6**	**5**
10^3[Unknown-2]moldm^{-3}	**6.27**	**6.27**	**6.2**	**6.2**	**6.19**	**6.23**

IILUSTRATIONS:

Fixed Time Method:
10^3[Unknown-1]moldm^{-3} = 3.75(calculated): 3.75(actual)
10^3[Unknown-2]moldm^{-3} = 6.26 ± 0.01(calculated): 6.25(actual)

Fixed Absorbance Method:
10^3[Unknown-1]moldm^{-3} = 3.8 ± 0.05 (calculated): 3.75(actual)
10^3[Unknown-1]moldm^{-3} = 6.22 ± 0.03 (calculated): 6.25(actual)

The data of table-1 has been used to obtain the following regression equations(6,7&8) for the three linear calibration plots .

10^4 k_{obs} = 4.312[atenolol] – 1.504 Corr.Coeff.= 0.999 ---------(6)
A_{240} = -0.66 [atenolol] + 0.980 Corr.Coeff.= 0.993 ---------(7a)
A_{480} = -0.83 [atenolol] + 0.831 Corr.Coeff.= 0.983 ---------(7b)
A_{240} = -0.79 [atenolol] + 0.665 Corr.Coeff.= 0.957 ---------(7c)
$t_{0.7}$ = -0.526[atenolol] + 4.859 Corr.Coeff.= 0.904 ---------(8a)
$t_{0.5}$ = -0.92[atenolol] + 8.214 Corr.Coeff.= 0.918 ---------(8b)
$t_{0.3}$ = -1.544[atenolol] + 14.63 Corr.Coeff.= 0.922 ---------(8c)

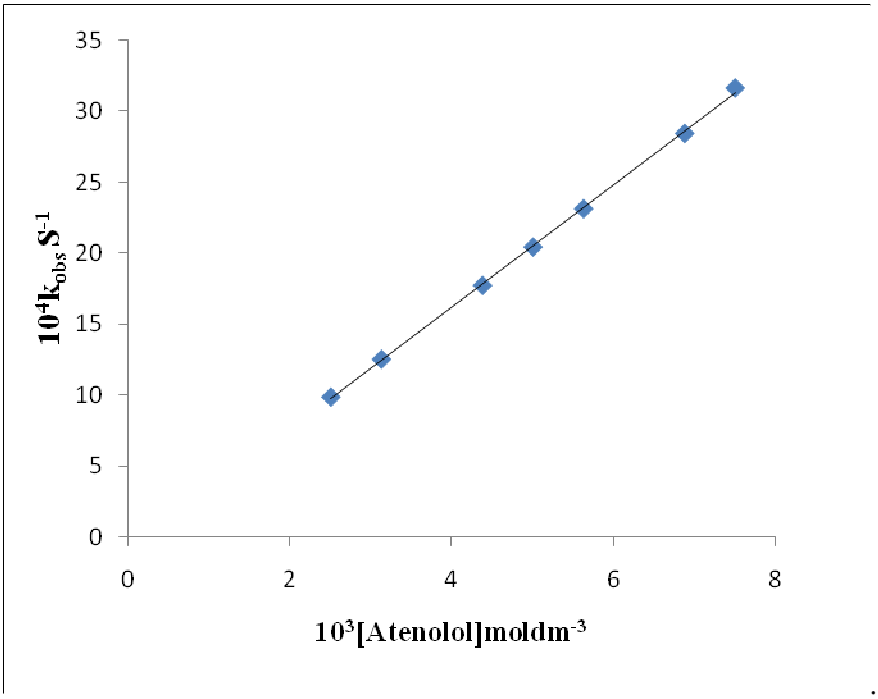

Fig1: Estimation of atenolol by variation of kobs with [atenolol]. 104[CeIV] = 2.5moldm-3; [H2SO4]= 0.7moldm-3; Temp=296K; λ=360nm.

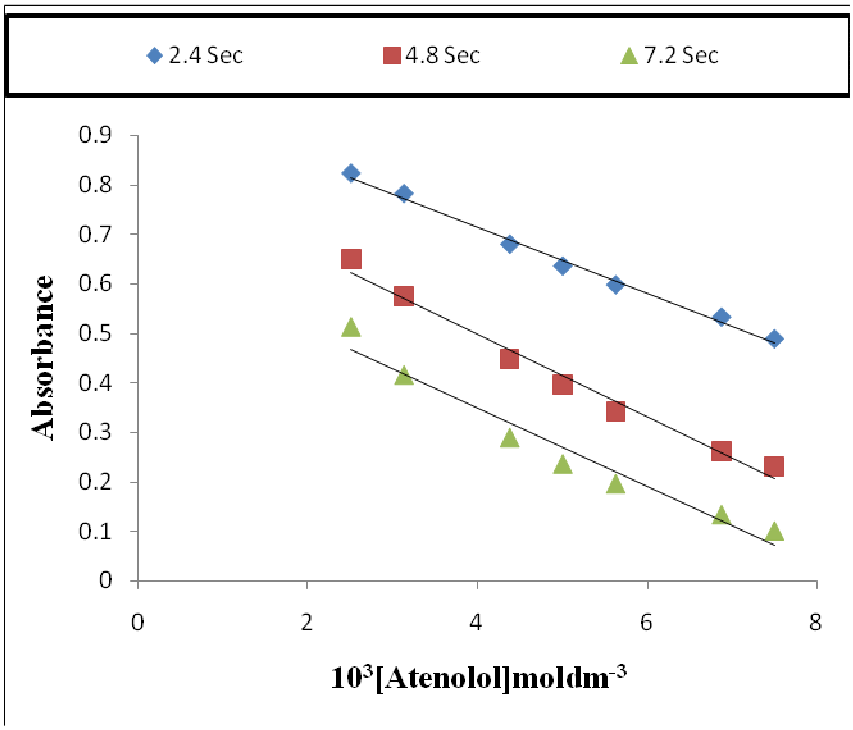

Fig.2: Estimation of atenolol by variation of absorbance at fixed time. 104[CeIV] = 2.5moldm-3; [H2SO4]= 0.7moldm-3; Temp=296K; λ=360nm.

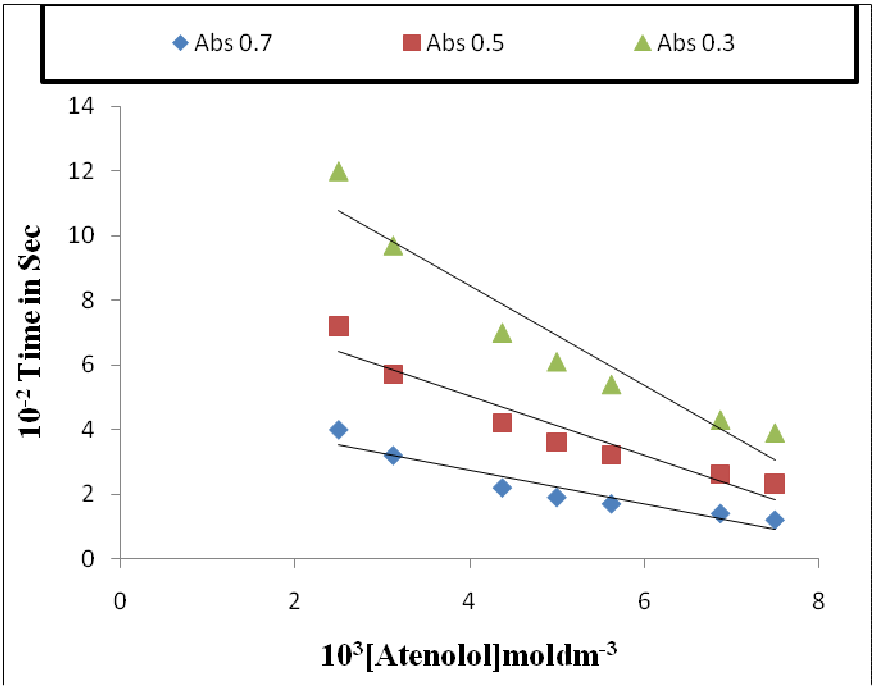

Fig.3: Estimation of atenolol by variation of time at fixed absorbance. 104[CeIV] = 2.5moldm-3; [H2SO4]= 0.7moldm-3; Temp=296K; λ=360nm.

The graphical data has been used to obtain unknown concentration of simulated samples of atenolol using regression equation in respective graphs. The results of the estimations with actual theoretical values are given with table-1.

CONCLUSION

The spectrophotometric method for the determination of atenolol is also easier and cheaper to perform than many currently available methods[12-13] and is 10 to 100-fold more sensitive than the existing spectrophotometric methods. Even the kinetic method is much more sensitive than most of the procedures known, but is not very precise. The procedures are suitable for the analysis of atenolol in pharmaceuticals, as there are no interferences from the excipients normally found in commercial formulations [14-15].

Acknowledgement
Sincere thanks to IPCA Laboratories Ltd.(Ratlam) for providing gift samples of Atenolol. We are also grateful to Prof. and Head Chemistry Department and Pharmaceuticals department, Govt. Holkar Science College Indore for permitting to undertake the present work and for their valuable guidance.

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