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Kinetic Studies of Charge Transfer Formation of Erythromycin and 2, 3 Dichloro-5, 6-Dicyano -1,4-Benzoquinone

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Abstract

The kinetics of erythromycin with 2, 3 dichloro-5,6-dicyano -1,4- benzoquinone [DDQ] is described for the determination of erythromycin. It was carried in aqueous $HClO_4$ (2M) medium at ionic strength of 0.01moldm^{-3}, Kinetics of the reactions infer that the rate of formation of the charge transfer complex did not vary significantly with increase in concentration of erythromycin indicating likely zeroth order dependence of the rate with respect to concentration of the drug. However, the linearity of the pseudo-first order plot points to first order dependence of rate on [DDQ].The overall rate equation for the reactions can be given as

$$-\frac{d[DDQ]}{dt} = k_{obs}[DDQ]$$

Keywords: Kinetic studies; Erythromycin; Charge transfer; DDQ

Introduction

The kinetic methods of analysis are highly sensitive, selective, simple, accurate and less expensive [1]. Erythromycin, 3R, 45 55, 6R, 7R, 9R, 11R, 12R, 13R, 14R – 4-[(2,6-didiocy -3-c-methy 1-3-0-methy 1 –a-l-ribo –hexopy- ransyi) oxy]- 14 ethy 1-7, 12,13-trihydroxy- 3, 5,7,9,11,13-hexamethy 1-6-[(3,4,6-trideoxy -3-dimethy kmiro – P-D-xylo-hexopy ransoyl) –oxy] oxa – cydofetradecare -2, 10-dione is a macrolide antibiotic used for the treatment of urinary tract infection. It targets at the ribosome and inhibits the protein synthesis of gram positive bacteria such as mycoplasma and Chlamydia [2]. In recent years, several kinetic catalytic techniques have been reported for the detection of biomolecules [3,4]. Literature revealed different techniques for the analysis of erythromycin as follows: spectrofluorimetry [5]. Capillary electrophoresis [6], HPLC [7], microbiological method [8] spectrophotometry [9,10]. Therefore, the aim of this research is to determine a kinetic method based on formation of charge transfer complex between erythromycin and DDQ that is simple, fast, economical and less laborious.

Materials and Methods

Equipment

All kinetic measurements were carried out using a UV-1800 Shidmazu and 752w UV – Vis grating with a silica glass cell of l cm thickness. All chemicals were of analytical grade and were used as such. Erythromycin powder was supplied by AC pharmaceutical limited, Enugu, Nigeria. The commercial erythromycin tablet (500mg per tablet) was purchased from the local market (Syncom formulations limited, India) 2,3 dichloro – 5, 6- dicyano-1,4-benzoquinone (98% purity) was supplied by sigma Aldrich, Germany.

Kinetic Measurements

Kinetics of the reactions of DDQ with erythromycin was followed spectrophotometrically under pseudo-first order condition with one of the reactants (donor) in at least 10 fold in excess over the reactant (acceptor) at 29^{0}C. The pseudo-first order rate constants were determined by using various concentrations of erythromycin (0.001 M to 0.0035 M) with fixed concentration of acceptor (2.5 x10-4 M). Effects of ionic strength, pH and hydrogen ion on the rates of reaction were also determined.

The pseudo-first order rates constant were obtained from a plot of log versus time following equation 1.

$$(A_\alpha - A_t) = (A_\alpha - A_0)e^{obs^{-kt}} \quad (1)$$

where A_α and A_0 are the final and initial absorbencies respectively, At is absorbance at time t and K_{obs} is pseudo-first order rate constant.

Effect of Hydrogen Ion Concentration on the Rate of Erythromycin and DDQ Reaction

Within the hydrogen ion concentration range 1.0 $x10^{-2}$ to 1.0mol dm^{-3}, kinetic runs were carried out keeping the concentrations of the drug and reagent constant at I =1.02mol dm^{-3} and T= 30.0 ± 0.2^0C.

Effect of Ionic Strength on the Rate of Erythromycin-DDQ Reaction

Within the range of ionic strength of the media 0.001-0.03mol dm-3, the variation of rate of reaction with ionic strength was investigated for the reaction of erythromycin and DDQ, At T = 28^0C and keeping the concentrations of drug and reagent constant, the ionic strength was varied and the rate of plot is represented in Figure 1.

reaction monitored.

Results and Discussion

Reaction of Erythromycin with DDQ

The wavelength of maximum absorption spectrum was found to be 464nm with a stoiochiometric ratio of 1:1 of erythromycin – DDQ complex [11].

Kinetic Studies

The rate of the charge transfer reaction of erythromycin and DDQ was followed spectrophotometrically under pseudo - first order conditions by monitoring the rate of consumption of DDQ at 464nm. Erythromycin was at least 10 fold in excess of DDQ and the reaction was carried out at pH 8.Kinetic decays were exponential and pseudo first rate constants were determined from the plots of log versus time according to equation 1. The plots were linear for more than 90 % extent of reaction. Typical

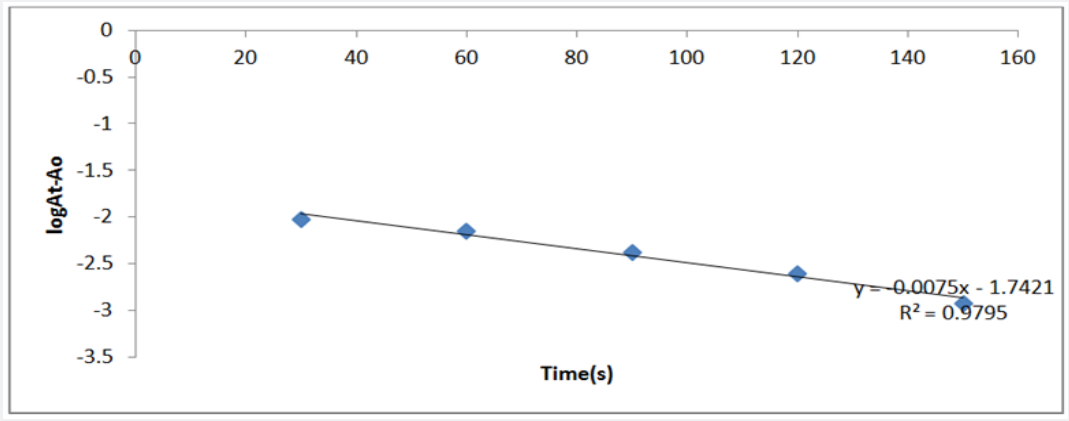

Figure 1

Table 1: Values of pseudo-first order and second order rate constants for the formation of erythromycin-DDQ reaction, [DDQ] =10^{-3}M at 30°C.

Vol of Erythromycin (10^{-2}M)	Vol of Methanol (cm^3)	k_{obs} (s^{-1})	k_2 ($dm^3mol^{-1}s^{-1}$)
0.4	1.2	0.016	0.2
0.6	1.0	0.016	3.33
0.8	0.8	0.0138	1.0
1.0	0.6	0.0138	2.0
1.2	0.4	0.0115	0.67
1.4	0.2	0.0115	0.57

$NaClO_4$ = 1.02M, [Erythromycin] = $2.0x10^{-5}$ M, [DDQ] = 1 x 10^{-6} M

The second order rate constants were determined by dividing K_{obs} with [erythromycin]. The values of K_{obs} and k_2 are represented in Table 1. The result from table 1 shows that as concentration of erythromycin increased from 0.001M to 0.0035M, the Kobs values did not vary significantly indicating a zero order dependence on reaction rate with respect to the concentration of erythromycin. However, the linearity of the pseudo – first order plot points to first – order dependence of rate with respect to [DDQ].

Effect of Hydrogen Ion Concentration on Erythromycin – DDQ Complex

The H+ concentration was varied from 0.08M to 1M while keeping other variables constant. Table 2 shows that Kobs increase from 0.08M to 1M. This infers that within this acid concentration range, protonation of the reactants played significant role in the charge transfer reaction. The Second order rate constants were determined by dividing Kobs with[erythromycin]. Table 2 is a display of pseudo-first order and second order rate constants.

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Table 2: Acid values for the pseudo-first order and second order rate constant of erythromycin-DDQ complex at λ_{max} = 464 nm, T = 30 °C $NaClO_4$ = 1.02M, [Erythromycin]=2.0x10-5 M,[DDQ]=1 x 10^{-6} M

I (mold m^{-3})	k_{obs} (s^{-1})	k_2 x10^2 ($dm^3mol^{-1}s^{-1}$)
0.001	0.005	2.5
0.005	0.005	2.5
0.01	0.005	2.5
0.015	0.002	1.0
0.02	0.009	4.5
0.025	0.009	4.5
0.03	0.002	1.0

Effect of Ionic Strength on Erythromycin – DDQ Complex

In addition, ionic strength medium was varied from 0.001M to 0.03M. Table 3 shows that K_{obs} did not vary significantly at 0.001M-0.01M but increased from 0.015M to 0.025M of the varied ionic strength which indicates primary salt effect and likely involvement of charged partners at the rate determining step.

Table 3: Effect of ionic strength on the rate of erythromycin-DDQ reaction at λmax = 464 nm, T = 30°C, $NaClO_4$ = 0.1M, [Erythromycin] =2.0x10^{-5} M, [DDQ] =1 x 10^{-6} M.

I (mold m^{-3})	k_{obs} (s^{-1})	k_2 x10^2 ($dm^3mol^{-1}s^{-1}$)
0.001	0.005	2.5
0.005	0.005	2.5
0.01	0.005	2.5
0.015	0.002	1.0
0.02	0.009	4.5
0.025	0.009	4.5
0.03	0.002	1.0

Effect of Temperature on Erythromycin – DDQ Complex

Effect of temperature was studied between 303k- 333k. Result in (Table 4) shows a drop in K_{obs} from 313k to 333k, this shows that as the temperature increases, the rate of reaction decreased. Also, Table 4 reveals a negative entropy, negative enthalpy change and positive Gibb's free energy change which means that the reaction does not occur spontaneously.

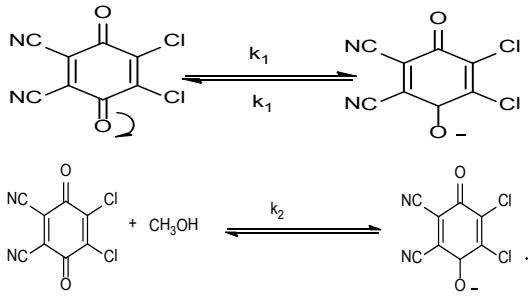
Least square fit of log K_{obs}/T vs $1/T$ based on the Eyring – Polanyi [12] (equation 2) is represented in Figure 2.

$$k_r\left(\frac{KT}{h}\right)\exp\left(\frac{\Delta S^{\#}}{R}\right)\exp\left(\frac{-\Delta H^{\#}}{RT}\right) \quad (2)$$

Where, kr = rate constant, k = Boltzmann's constant, h = Planck's constant, ΔS# = entropy of activation ΔH# = enthalpy of activation, T = absolute temperature, R = gas constant.

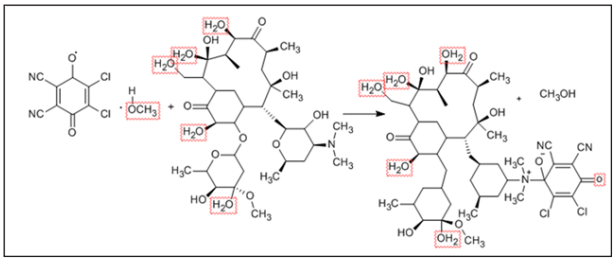
The rate determining steps of erythromycin-DDQ complex are as follows:

$$-\frac{d[DDQ]}{dt} = k_{obs}[DDQ] \quad (3)$$



(4)

(5)



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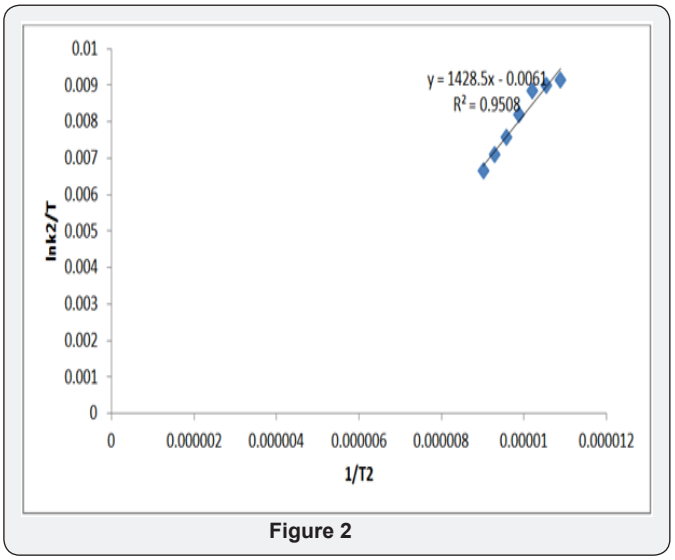

Figure 2

Table 4: Effect of temperature on the pseudo-first order rate constant and activation parameters for the formation of erythromycin-DDQ complex at λ_{max} = 464 nm, [Erythromycin] = 10^{-2} M, [DDQ] = 10^{-3} M.

Temperature (°C)	ΔG° x 10^5 (kJ mol^{-1})	k_{obs} (s^{-1})	k^2 ($dm^3mol^{-1}s^{-1}$)
30	7.25	0.016	16
35	7.37	0.016	16
40	7.49	0.016	16
45	7.61	0.01375	13.75
50	7.73	0.0115	11.5
55	7.84	0.01035	10.35
60	7.96	0.0092	9.2

ΔS# (kJk^{-1}/mol) = -2391; ΔH# (kJ mol^{-1}) = -11

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Conclusion

The proposed kinetic method infer that the rate of formation of charge transfer complexes did not vary significantly with increase in concentration of erythromycin indicating a likely zeroth order dependence of the rate with respect to the concentration of erythromycin. However, the linearity of the pseudo – first order plot points to first order dependence of rate on [DDQ].

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