

REVIEW ARTICLE



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TRANSFORMATION OF ZIDOVUDINE DURING WATER TREATMENT WITH CHLORINE: A KINETIC STUDY

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ABSTRACT

Recent studies on water quality assessment indicate that antibiotics are emerging pollutants it also very well established that the existing method of practice for waste water treatment are in efficient in warranties these pollutants. The present paper throw light on fate of zidovudine when subjected to chlorination at varying temperature and ionic strength .It was noticed the rate of transform was equally proportional and is due to ΔH^\ddagger and ΔG^\ddagger being favorable for electron transfer and hence accelerated degradation. An increase in ionic strength resulted negative rate of transformation. The effect of temperature on the rate of the reaction was studied at three different temperatures and rate constants were found to increase with increase in temperature and the thermodynamic activation parameters E_a , ΔH^\ddagger , ΔS^\ddagger and ΔG^\ddagger were evaluated and discussed.

Keywords: Kinetics, Chlorination, Zidovudine, Emerging Contaminant, Pathways

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INTRODUCTION

Zidovudine (INN) or azidothymidine (AZT) is a nucleoside analog reverse transcriptase inhibitor (NRTI), a type of antiretroviral drug . It is a synthetic drug with pyrimidine nucleoside analogue active against HIV-1, AIDS and pre- AIDS. The chemical name of Zidovudine is 1- (3- azide-2, 3-di deoxy- β -D-ribofuranosyl)-5-methyl Pyrimidin-2, 4(1H, 3H) – dione. Zidovudine, also has been referred to as 3'azido-3'-deoxythymidine. It has a molecular formula of $C_{10}H_{13}N_5O_4$ and a molecular weight of 267.24 g/mol. It has the structural formula as shown in fig:1. Zidovudine is a white to light brown, odorless, crystalline solid and it is soluble in ethanol (95%), watchfully soluble in water. The drug is authoritatively listed in United States of Pharmacopiea. Zidovudine can be biological fluids / pharmaceutical waste was evaluated by UV.vis,HPLC and HPTLC techniques as reported in several systematic models.

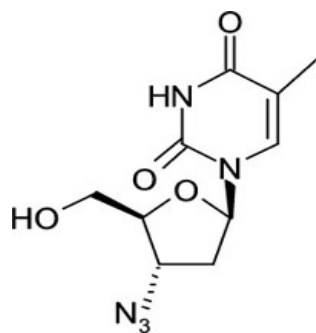


Fig :1 Structure of Zidovudine

Materials and Methodology

Efforts were made for conduction of experiments with standard procedures as per standard literature referred.

A stock solution of zidovudine was arranged by dissolving suitable amount of sample in distilled water. A stock solution of HOCl was set by taking an suitable volume of 5% NaOCl in deionised water. The stock solution was then uniformed by iodometry and DPD (N, N-Diethyl-P-Phenylenediamine)-FAS (Ferrous Ammonium Sulfate) titrimetry respectively. 0.02M acetate (pH 4 – 5), phosphate (pH 6 – 8.5), and borate (pH 9) buffers were used to uphold constant pH through experiments conducted in reagent water .

- All reagents were of analytical grade.
- The Rate of Degradation was assessed i.e (Kinetic Rates) by; a CARY 50 Bio UV-Vis Spectrophotometer (Varian BV, Netherlands) with temperature controller was instrumental.
- For pH analysis, an Elico pH meter model LI 120 was used .

Kinetic Measurements

The kinetic measurements were performed under pseudo first order condition with HOCl. HOCl was at least ten fold of molar excess over ZDV at an invariable ionic strength using 0.02 mol dm⁻³ buffers. The reaction was initiated by mixing thermostatted solutions of HOCl and ZDV which also contains the essential volume of buffers. The temperature was consistently maintained at (25 ± 0.2) °C. The reason of the reaction was followed by monitoring lessen in the absorbance of ZDV as a role of time in a 1 cm path length quartz cell of Carry 50 Bio UV-Visible spectrophotometer. The purpose of Beer's law of ZDV at λ_{max} 266 nm had been confirmed giving $\epsilon = 10116 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ Pseudo first-order rate constants, k'_{obs} , were evaluated from the plots of $\log (A_t - A_\infty)$ versus time, where 'A' refers to absorbance at any time t and t_∞ is at infinite time which excludes the absorbance of any products of ZDV during the reaction. The first-order plots in approximately all the cases were linear up to 80% conclusion of the reaction and k'_{obs} .

RESULT AND DISCUSSION

Effect of Temperature

The rate of the reaction was measured at three different temperatures with varying 10: 1 to 40: 1 [HOCl]⁰ to [ZDV]⁰ ratios by keeping other conditions constant; the rate was found to increase with increase in temperature. The second order rate constants k''_{app} at three different temperatures 10, 25 and 35 °C were obtained. The energy of activation, E_a (51247.3kJ mol⁻¹) corresponding to these rate constants was evaluated the plot of $\log k''_{app}$ versus $1/T$ ($r^2 > 0.873$) and other activation parameters ΔH^\ddagger (enthalpy of activation) (-16874.9kJ mol⁻¹), ΔS^\ddagger (entropy of activation) (-365.3J K⁻¹ mol⁻¹), ΔG^\ddagger (Gibbs energy of activation) (92013.3 kJ mol⁻¹) were calculated. The negative value of ΔS^\ddagger indicates the activated complex is higher ordered. The effect of temperature is shown in Fig:2, Fig :3, Fig:4 and calculated results are tabulated in table 1.

Effect of temperature on the rate of reaction						
T	K	1/T	Logk	k/T	log(k/T)	logT
283	8.08	0.003534	0.907411	0.028551	-1.54438	2.451786
298	2.47	0.003356	0.392697	0.008289	-2.08152	2.474216
308	2.47	0.003247	0.392697	0.008019	-2.09585	2.488551

Table 1: Effect of temperature on the rate of reaction

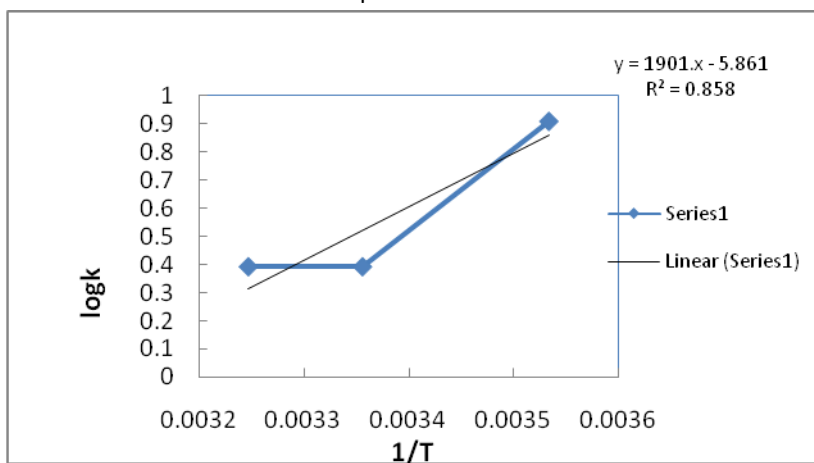


Fig 2: Effect of temperature on the chlorination of zidovudine at 25°C at pH =3

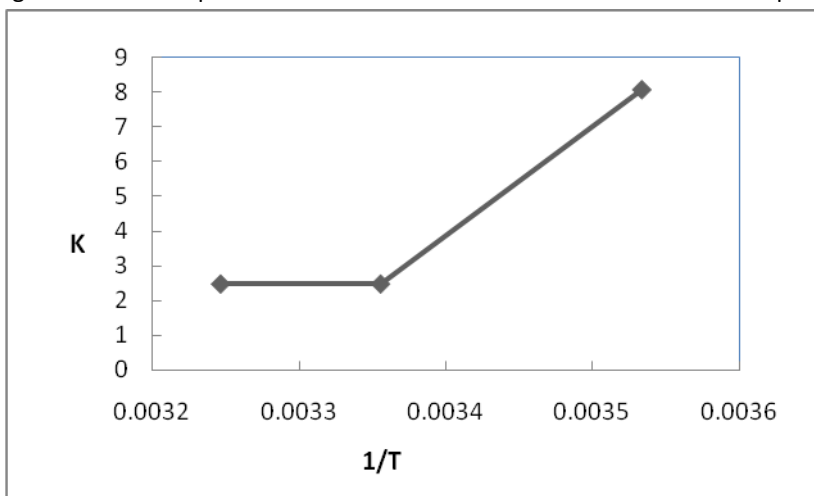


Fig 3: Effect of temperature on the chlorination of zidovudine at 25°C at pH =3 K versus 1 / T

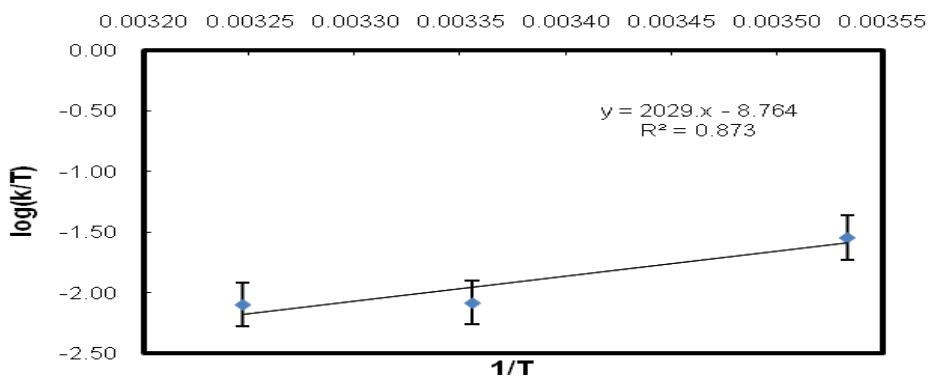


Fig 4: Effect of temperature on the chlorination of zidovudine at 25°C at pH =3 log(/K/T) versus 1/T.

REACTION ORDER

The concentration of ZDV was varied in the range 1×10^{-5} mol dm⁻³ to 2×10^{-5} mol dm⁻³ and linearity of plots of $\log [A_T - A_\infty]$ Vs time ($r \geq 0.9994$) and indicated a reaction order of unity in ZDV. A plot of $\log k'_{\text{obs}}$ versus $\log [\text{HOCl}]^0$ with 5 points was linear with a slope of 0.968 and $r^2 = 0.992$, indicating that this reaction can be treated as first order with respect to ZDV. The concentration of HOCl was varied in the range 2.25×10^{-3} mol dm⁻³ to 3.22×10^{-4} mol dm⁻³ and the plot of $\log k_{\text{obs}}$ Vs $\log [\text{ZDV}]$ was found to be linear with a slope close to unity indicating unit order in HOCl. The reaction of ZDV with HOCl can be described as a bimolecular, second order reaction.

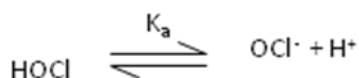


Kinetic Modelling

The reaction of ZDV with HOCl is first order with respect to each reactant and so can be described by a second order rate expansion.

$$\frac{d [\text{ZDV}]_T}{dt} = -k'_{\text{obs.ZDV}} [\text{ZDV}]_T = -k''_{\text{app.ZDV}} [\text{HOCl}]_T [\text{ZDV}]_T \quad \text{----- (1)}$$

Where $k'_{\text{obs.ZDV}}$ is the observed pseudo-first order rate constant, T represents the sum of all acid base species for a given reactant and $k''_{\text{app.ZDV}}$ [in M⁻¹ S⁻¹] is the pH dependent apparent second order rate constant for the overall reaction, which can be calculated from $k''_{\text{app.ZDV}} = (k'_{\text{obs.ZDV}} / [\text{HOCl}]_T)$, kinetic experiments demonstrated a marked dependence of $k''_{\text{app.ZDV}}$ on pH. The variation in $k''_{\text{app.ZDV}}$ from pH 3 can be attributed to the varying importance of specific reaction amongst the individual acid base speciation of ZDV and HOCl. The acid base speciation of HOCl and ZDV can be modeled by



$$[\text{HOCl}]_T = [\text{HOCl}] + [\text{OCl}^-] = \sum_{i=1,2} \alpha_i [\text{HOCl}]_T \quad \text{----- (2)}$$

$$[\text{ZDV}]_T = [\text{ZDV}]^{+} + [\text{ZDV}] + [\text{ZDV}]^{-} = \sum_{j=1,2,3} \beta_j [\text{ZDV}]_T \quad \text{----- (3)}$$

Where $\alpha_1 = \frac{[\text{H}^+]}{([\text{H}^+] + K_{a \text{HOCl}})}$ for HOCl

$\beta_1 = \frac{[\text{H}^+]^2}{([\text{H}^+]^2 + K_{a1}[\text{H}^+] + K_{a1}K_{a2})}$ for [ZDV]⁺

$\alpha_2 = \frac{K_{a \text{HOCl}}}{([\text{H}^+] + K_{a \text{HOCl}})}$ for OCl⁻ (with $K_{a \text{HOCl}} = 10^{-7.5}$)

$$\beta_2 = \frac{K_{a1} [H^+]}{([H^+]^2 + K_{a1} [H^+] + K_{a1} K_{a2})} \quad \text{for [ZDV]}$$

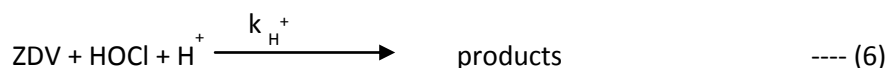
Incorporating Eq. (2) and (3) into Eq. (1) yields

$$\beta_3 = \frac{K_{a1} K_{a2}}{([H^+]^2 + K_{a1} [H^+] + K_{a1} K_{a2})} \quad \text{for [ZDV]}$$

$$\frac{d[ZDV]_T}{dt} = - \sum_{i=1,2} k_{ij} \alpha_i [ZDV]_T \beta_j [ZDV]_T \quad \text{----(4)}$$

$$k''_{app,ZDV} = - \sum_{i=1,2} \sum_{j=1,2,3} k_{ij} \alpha_i \beta_j \quad \text{----(5)}$$

Where, k_{ij} represents specific second order rate constants for the reactions of each oxidant species i with each substrate species j . The decrease in the magnitude of $k''_{app,ZDV}$ above pH3 can be attributed to deprotonation of HOCl to yield OCl⁻, which is generally a much weaker electrophile than HOCl, while the proportion of neutral ZDV remains relatively constant. The latter trend also indicates that kinetics of reaction amongst OCl⁻ and various.



Where k_H^+ represents the third order rate constant for such a reaction in $M^{-2} S^{-1}$.

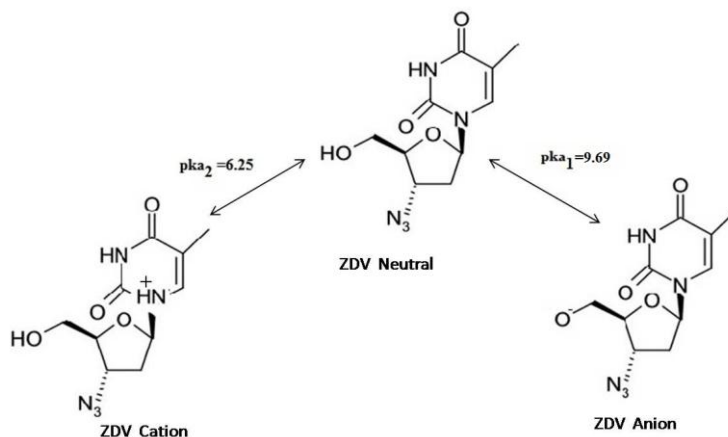


Fig 5: Zidovudine speciation pattern

In the above figure the structure of zidovudine shows that the breaking of hydrogen bond from main structure making it to neutral state and forming positive charge Zidovudine cation and also hydrogen ion released from hydrogen bond forming zidovudine anion as shown in the above figure its pathway. ZDV an amphoteric compound that exhibit the acid base speciation ($pK_{a1} = 9.69$ and $pK_{a2} = 6.25$) A second order kinetic reaction model that accounts for these speciation patterns was used to identify zidovudine's most reactive

species and to achieve preliminary identification of the individual functional moieties participating in reactions with HOCl.

CONCLUSIONS

Zidovudine reacts slowly with HOCl at oxidant concentration and pH conditions, which are similar to those likely to be observed in conventional water chlorination processes. The rate of degradation of Zidovudine decreases rapidly above pH 3. Hence conventional Chlorination cannot be applied for the removal of Zidovudine. Effect of Dielectric Constants on the rate constants of Zidovudine and HOCl reaction indicates the reaction involves dipoles and charged species. Effect of variation of ionic strength on the rate of reaction indicates the reaction is either between two neutral species or neutral and a charged species. The moderate value of ΔH^\ddagger (enthalpy of activation) and ΔG^\ddagger (Gibbs energy of activation) are both favorable for electron-transfer processes.

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