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Uncatalysed kinetic and mechanistic investigation of oxidative degradation of antibacterial drug linezolid by heptavalent manganese at environmentally relevant pH

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ABSTRACT

There is huge increase in the consumption of pharmaceutical drugs by human beings to treat various kinds of diseases due mammoth increase in population across the world. Many analytical techniques have discovered the occurrence of pharmaceutical drugs in environmental waters which shows detrimental effect on human health. Uncatalysed kinetic and mechanistic investigation of oxidative degradation of antibacterial drug linezolid by strong oxidant heptavalent manganese at environmentally relevant pH was studied. Different factors such as [heptavalent manganese], [substrate], variation in pH, variation in solvent polarity, variation in ionic strength, variation in temperature on the rate of degradation reaction were investigated and discussed. The apparent second order rate constants were found higher in acidic and neutral media than in alkaline medium. High Resolution Mass Spectrometry was used to analyze the four degraded products formed during the degradation of antibacterial drug linezolid. Based on experimental results, a suitable mechanism is proposed which involves the formation of complex between permanganate and substrate linezolid which then breaks down to form oxidized compounds of linezolid. Experimental results indicate that the rate of elimination of antibacterial drug linezolid by heptavalent manganese increases with increase in temperature. Activation parameters were determined from the effect of temperature and discussed.

Keywords: Degradation, emerging contaminants, kinetics, oxidation, water treatment

I. INTRODUCTION

There is huge increase in the consumption of pharmaceutical drugs by human beings to treat various kinds of diseases due mammoth increase in population across the world. The occurrence of pharmaceutical drugs in environmental waters has become a serious concern all the water research community and public [1-3].These drugs are not completely metabolized in the human bodies. Many analytical techniques have discovered the occurrence of pharmaceutical drugs in environmental waters which shows detrimental effect on human health. These drugs are discharged improperly into the environmental waters without any treatment [4-6].

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Literature survey reveals that conventional methods such as coagulation, sedimentation, and filtration are not efficient to eliminate toxic micro-contaminants completely during the water treatment processes [7, 8]. Chlorine and ozone are also used for the treatment of water but these oxidants give halogenated side products which show detrimental effect on health of human beings [9, 10]. Hence, strong green oxidant Heptavalent manganese (HVMG) was preferred for the water treatment process due its special features such as broad pH range (acidic, neutral and alkaline), low cost and formation of harmless by-products [11].

Linezolid (LZD) is a synthetic antibacterial drug of oxazolidinone class and taken as a model compound for this investigation. It is antibacterial drug which is generally to treat the infectious diseases [12]. The presence of different antibacterials in environmental waters is reported by previous investigations [13]. It shows slight solubility in the water with pH varies from 5.0 to 9.0. It exhibit weak basic properties [14, 15].

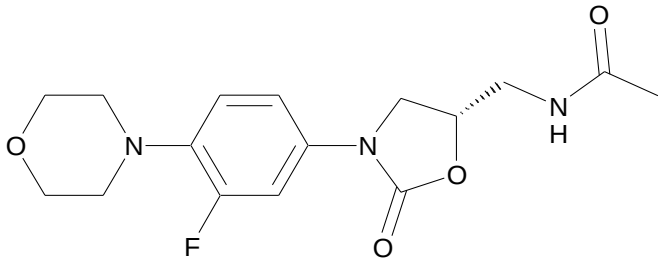

Fig. 1. Structure of antibactrial drug LZD

The prime objectives of this uncatalysed oxidation kinetics of antibacterial drug LZD by strong oxidant HVM at environmentally relevant pH were to find out oxidation degraded products of LZD by using High Resolution Mass Spectrometry, to propose mechanism, to study influences of different parameters on oxidation kinetics at environmentally relevant pH, to deduce the rate law from experimental results and to determine Ea, $\Delta H^{\#}$, $\Delta S^{\#}$ and $\Delta G^{\#}$) from the effect of temperature.

II. EXPERIMENTAL

2.1. Chemicals Analysis

High-resolution mass spectrophotometer (HR-MS) system (Thermo Scientific Q Exactive) along with a column Thermo Scientific Hypersil Gold C18 and temperature controller was used for the analysis of oxidation byproducts of LZD formed during the reaction. High performance calibrated Elico pH meter (Model Li 120) was employed to measure the pH of the reaction mixtures. A CARY 50 Bio UV-vis spectrophotometer (Varian BV, The Netherlands) was employed to record the kinetic data spectrophotometrically.

2.2. Materials

LZD was obtained from Dr. Reddy Laboratories and its stock solution of required concentration 1 x 10^{-2} mol dm^{-3} was prepared in double-distilled water. HVMG was procured from MERCK Specialties Pvt. Ltd. and used without further purification. The stock solution of concentration 1 x 10^{-3} mol dm^{-3} of HVMG was prepared and titrated against suitable concentration of $H_2C_2O_4$ solution to ascertain the accurate concentration of HVMG for oxidation kinetics of LZD by HVMG [16]. Acetate, phosphate and borate buffers solutions of concentration 2 x

10^{-2} mol dm^{-3} were prepared in double-distilled water for oxidation kinetics of LZD by HVMG.

2.3 Kinetic Spectroscopic Measurements

In order to study oxidation kinetics of LZD by HVMG, solution A and solution B were mixed into each other at the same temperature. Solution A is a mixture of [LZD], [H^+] ion while solution B contained a suitable [HVMG]. Phosphate buffer of concentration 6 x 10^{-3} mol dm^{-3} was used to maintain the environmentally relevant pH 6.0 and ionic strength (I) = 2 x 10^{-2} mol dm^{-3}. The progress of the oxidation kinetics of LZD by HVMG was monitored at λ_{max} 526 nm which is the highest absorption wavelength of HVMG. By verifying the Beer's law for oxidation kinetics of LZD by HVMG at environmentally relevant pH, the value of an extinction coefficient (ε) was evaluated (2084 ± 20 dm^3 mol^{-1} cm^{-1}) and found to be in good agreement with literature value (ε =2200 ± 20 dm^3 mol^{-1} cm^{-1}) [17]. During the kinetic spectroscopic measurement, there was no hindrance of any other species found at λ_{max} 526 nm of HVMG [18]. UV-vis spectral changes give spectroscopic evidence for decrease in the absorbance or concentration of HVMG as shown in Fig. 2. The kinetic data shows that the oxidation kinetics of LZD by HVMG at environmentally relevant pH (6.0) was completed more than 83 %. Pseudo first-order- rate constant values were determined from the plots of log (absorbance) versus time (t) in min as shown in Fig. 4. The experimental data shows that the values of rate constants k_U were found to be very close and indicates that order with respect to [HVMG] is unity at 298 K.

2.4 Analysis and identification of degraded products

LZD was added to phosphate buffer having concentration, 2 x 10^{-2} mol dm^{-3} to preserve environmentally relevant pH 6.0 so as to get an initial concentration of 400 mg dm^{-3}. The HVMG solution was added to instigate the reaction at oxidant: substrate molar ratio 4:1. This reaction mixture was allowed to accomplish the oxidation kinetics of LZD by HVMG at environmentally relevant pH 6.0 for the period of 16 hrs in a closed container at 298 K. After completion of reaction, a small amount of reaction mixture was taken out and filtered. In order to carry reaction mixture, the mobile phase of acetonitrile: water ratio 50:50 was used with the flow rate (500 µL/min) and pressure (33.2 bar) throughout the analysis of components of reaction mixture. With the help of HR-MS system, mass spectrum (Fig. 3) of the reaction mixture was recorded over the mass scan range of 100-800 m/z. All the identified oxidative degraded products of LZD are presented in TABLE 1.

TABLE 1 Analysis of the degraded products of LZD by HVMG at environmentally relevant pH

LZD Products	Retention time in minute	Measured molecular ion peak ($M+H^+$)	Theoretical Mass of products (Da)	(Molecular Formulae of the products)	(Measured mass - Theoretical mass)	Degradation site moiety
LZD_P1	3.29	159.07	158(Major Product)	$C_6H_{10}O_3N_2$	+1.07	Morpholine
LZD_P2	3.29	181.05	180	$C_{10}H_{11}NOF$	+1.05	Oxazolidinone
LZD_P3	3.29	197.03	196	$C_9H_5O_2NF$	+1.03	Oxazolidinone & Phenyl
LZD_P4	3.73	352.12	351	$C_{16}H_{18}O_5N_3F$	+1.12	Morpholine

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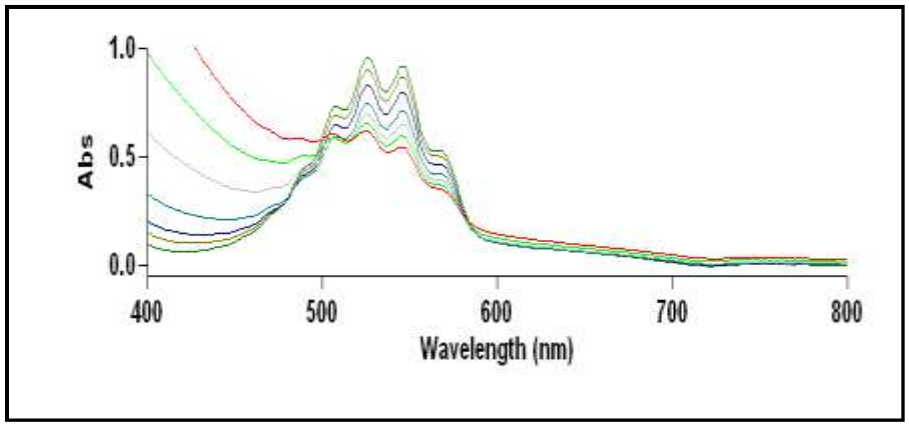
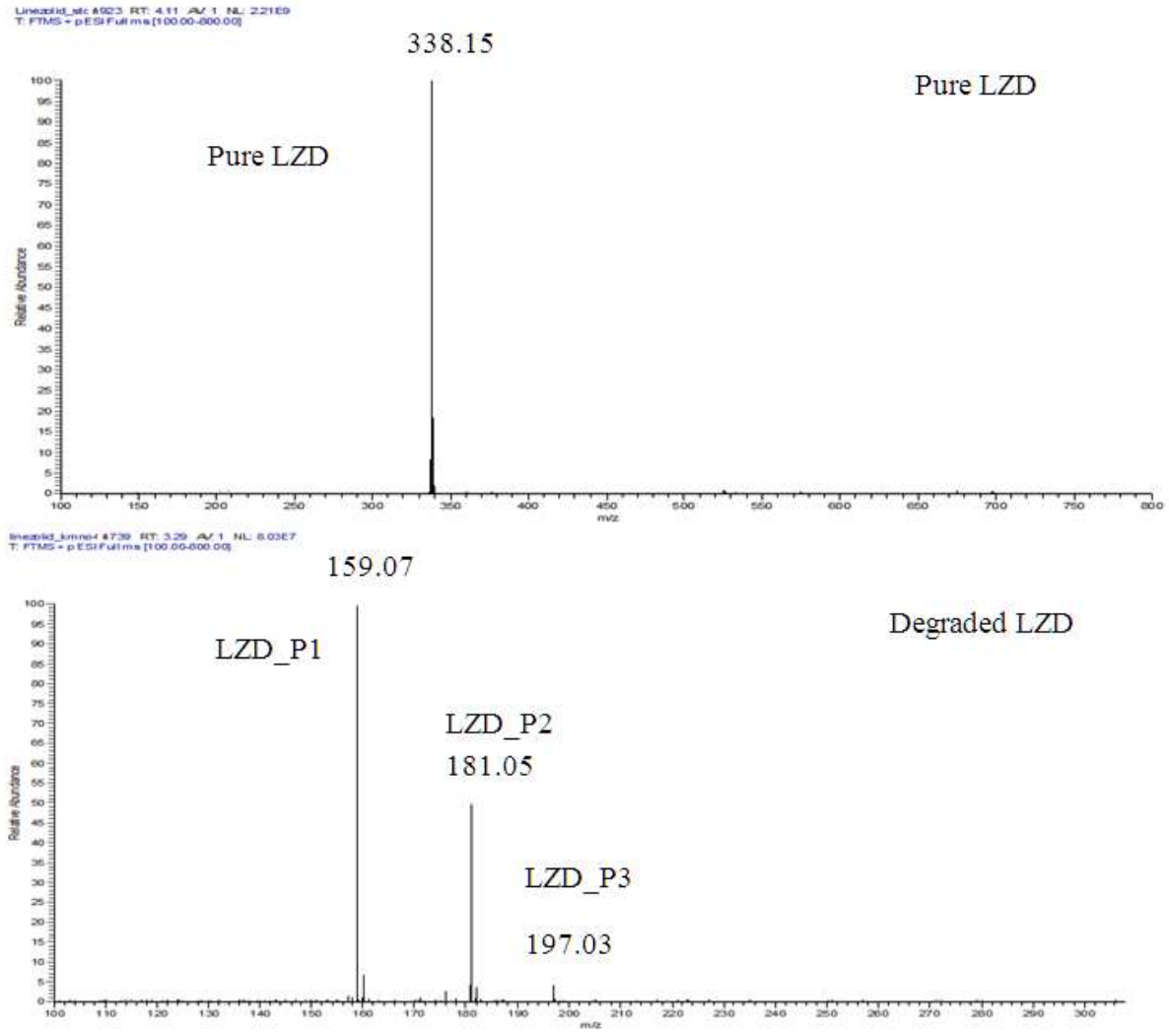


Fig. 2. UV-Vis spectral changes for the oxidation kinetics of LZD by HVMG at environmentally relevant pH 6.0 and scanning times: (1) 0.5 (2) 1.0 (3) 1.5 (4) 2.0 (5) 2.5 (6) 3.0 (7) 3.5 min



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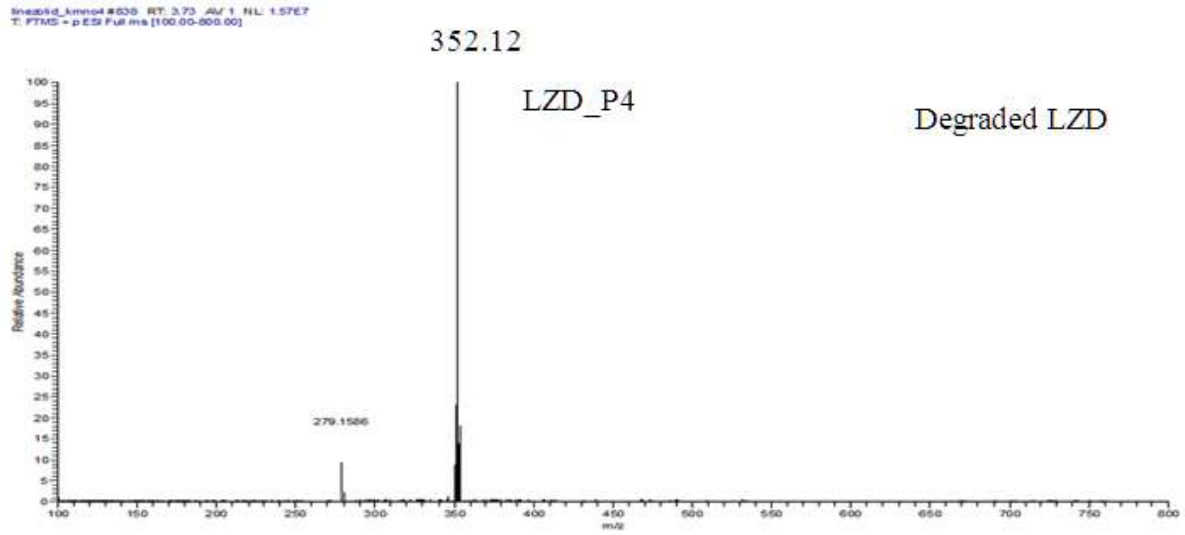

Fig.3. HR-MS spectra of pure LZD and degraded products of LZD by HVMG at environmentally relevant pH 6.0 with its molecular ion peak $(M+H)^+$ m/z

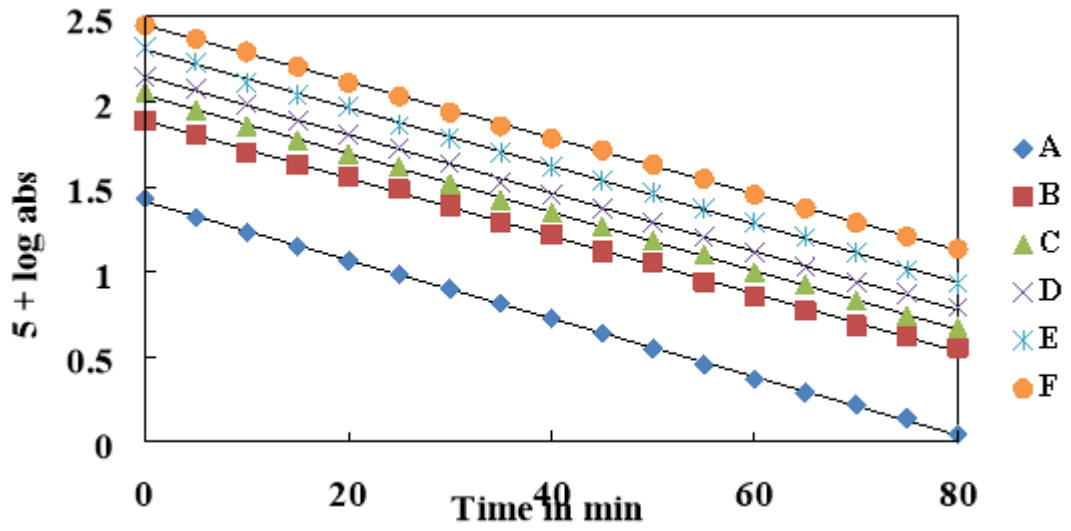

Fig. 4. First order plots of the oxidation kinetics of LZD by HVMG at environmentally relevant pH 6.0 and temperature 298K.

III. RESULTS AND DISCUSSION

3.1 Evaluation of pseudo-first-order rate constants

The pseudo-first-order rate constants (k_{obs}) were evaluated by varying [HVMG] in the range of $2.5x10^{-5}$ mol dm^{-3} to $2.5x10^{-4}$ mol dm^{-3} at fixed [LZD] $=1x10^{-3}$ mol dm^{-3}, [Buffer] = $6\ x10^{-3}$ mol dm^{-3} to maintain environmentally relevant constant pH 6.0 and constant ionic strength (I) $=2\ x\ 10^{-2}$ mol dm^{-3} at temperature 298 K. Using the recorded values of absorbance of non-reacted HVMG spectrophotometrically, the plots of log

(absorbance) versus time (min) were plotted (Fig. 4) and indicated that the order with respect to [HVMG] was unity which was also confirmed from the fairly constant values of k_{obs} at temperature 298 K.

3.2 Influence of variation in [LZD] on oxidation kinetics of LZD by HVMG

The experimental order with respect to [LZD] was evaluated by changing [LZD] from 5×10^{-4} mol dm^{-3} to 3.0×10^{-3} mol dm^{-3} at fixed [HVMG] $=1x10^{-4}$ mol dm^{-3}, [Buffer] $= 6\ x10^{-3}$ mol dm^{-3} to maintain environmentally relevant constant pH 6.0 and constant ionic strength (I) $=2 \times 10^{-2}$ mol dm^{-3} at 298 K. The values of velocity constants k_{obs} are found to be increased with increase in [LZD] at 298 K. The graph of log k_{obs} versus log [LZD] was plotted to evaluate the order for [LZD] as shown in Fig. 5 (fractional order 0.61).

3.3 Influence of variation in ionic strength on oxidation kinetics of LZD by HVMG

In order to investigate the effect of ionic strength (I) on oxidation kinetics of LZD by HVMG at 298 K, the concentration of phosphate buffer having environmentally relevant pH 6.0 was changed in the range of 0.002 mol dm^{-3} to 0.012 mol dm^{-3} at fixed [LZD] $=1x10^{-3}$ mol dm^{-3} and [HVMG] $=1x10^{-4}$ mol dm^{-3}. The experimental data shows that the values of velocity constants k_{obs} were found fairly constant. This insignificant effect of ionic strength (I) on the values of velocity constants k_{obs} indicate that there is no reaction took place between solvent and the oxidant HVMG [19].

3.4 Influence of variation in dielectric constant on oxidation kinetics of LZD by HVMG

In order to study the influence of variation in dielectric constant on oxidation kinetics of LZD by HVMG, the percentage of tertiary butanol-water mixture was changed at fixed concentration of other reaction conditions of mixture. The experimental values indicate that the values of velocity constant k_{obs} were found decreased at the higher concentration of volume of tertiary butanol. This shows that velocity constants values were found to be decreased with increase in solvent polarity or decrease in dielectric constant. Using these k_{obs} values, the plot of logk_{obs} versus 1/D was plotted and found to be linear with negative slope as shown in Fig. 6 [20].

3.5 Polymerization study for free radical intervention

The study was significant to propose the plausible mechanism of oxidation kinetics of LZD by HVMG at environmentally relevant pH 6.0. The required amount of monomer acrylonitrile was added into the reaction mixture and placed for 13 hours. Dilution of this reaction mixture was done by using suitable amount of solvent methyl alcohol. This study revealed that there was not any formation of precipitate in the reaction mixture which confirmed no intervention of free radical in the reaction mixture [21].

3.6 Influence of pH on oxidation kinetics of LZD by HVMG

In order to investigate the crucial role of medium on oxidation kinetics of LZD by HVMG at 298 K, the pH was varied in the range of 3.0 to 6.0 using phosphate (pH 6.0 - 7.0) and acetate (pH 3.0 - 5.0) buffers of concentrations 2×10^{-2} mol dm^{-3} at fixed [HVMG] $= 1x10^{-4}$ mol dm^{-3}, [LZD] $= 1x10^{-3}$ mol dm^{-3}, [buffer] $= 6 \times 10^{-3}$ mol dm^{-3} and Ionic strength (I) $= 2 \times 10^{-2}$ mol dm^{-3}. The values of k_{obs} were obtained from the slopes of plots log (absorbance) versus time (min). The kinetic data shows that the values of velocity constants k_{obs} were found to be decreased with decrease in the concentration of H^+ ions 298 K.

The concentration of substrate LZD was varied in the range of 5×10^{-4} mol dm^{-3} to 3.0×10^{-3} mol dm^{-3} for different pH 3.0 to 6.0 to evaluate pH-dependent apparent second-order constants at 298 K while keeping other

reaction conditions fixed i.e. [HVMG] = $1x10^{-4}$ mol dm^{-3}, [buffer] =6×10^{-3} mol dm^{-3} and Ionic strength (I) = 2×10^{-2} mol dm^{-3}. The slopes of k_{obs} versus [LZD] were used to obtain the pH-dependent second-order rate constants k_{apps} and presented in Table 2. The values of pH-dependent second-order rate constants k_{apps} indicates that the values are found to be decreased with increase in the pH range 3.0 to 9.0. This shows that the rate of oxidative degradation of LZD by HVMG is faster at environmentally relevant pH 6.0 and lower at basic medium 9.0.

3.7. Influence of temperature on oxidation kinetics of LZD by HVMG

In order to evaluate the values of velocity constants k at four different temperatures (283 K, 288 K, 293 K and 298 K) for the slow step as proposed in a mechanism, the concentration of LZD was changed starting from 5×10^{-4} mol dm^{-3} to 3.0×10^{-3} mol dm^{-3} at fixed [HVMG] = 1×10^{-4} mol dm^{-3}, [buffer] = $6 x10^{-3}$ mol dm^{-3} and Ionic strength (I) = 2×10^{-2} mol dm^{-3}. The intercepts of plots $1/k_{obs}$ versus 1/ [LZD] were used to obtain the values of k. These values of velocity constants k were found to be increased with increase in temperature of the reaction mixture from 283K to 299 K at environmentally relevant pH 6.0 as presented in TABLE 3(a). By using these values of velocity constants k for the rate determining step, Arrhenius plots (log k versus 1/T) as shown in Fig. 8 were used to evaluate the activation parameters and thermodynamic quantities as presented in TABLE 3(b).

The effect of various parameters on oxidation kinetics of LZD by HVMG shows that the order with respect to [HVMG] is unity while fractional order with respect to [LZD] and $[H^+]$ ion.

$$\textbf{Rate} = \frac{-d[MnO_4^-]}{dt} = k\,K_1\,K_2\,[MnO_4^-]^1\,[LNZ]^{0.61}[H^+]^{0.1} \qquad \text{---- (1)}$$

The order which is found to be fractional for $[H^+]$ ion indicates that HVMG ions forms permanganic acid ($HMnO_4$). The permanganic acid is a strong oxidizing agent than HVMG ions [22] at environmentally relevant pH 6.0. It is observed that the velocity constants attain a limiting value at the higher concentration of H^+ ions after the initial increase in the values of velocity constants. This confirms that protonation of HVMG ions is completed at environmentally relevant pH 6.0. This indicates that the permanganic acid is only active species which are present in reaction mixture at the lower pH. The chemical equilibrium which is formed between HVMG ions and $HMnO_4$ is shown as

$$H^+ + MnO_4^- \underset{}{\overset{K_1}{\rightleftharpoons}} HMnO_4 \qquad \text{----(2)}$$

$$K_1 = \frac{[HMnO_4]}{[H^+]\,[MnO_4^-]} \qquad \text{--- (3)}$$

The evaluated value of K_1 (first equilibrium constant) is found to be $3.09 x10^2$ dm^3 mol^{-1}. This evaluated value of K_1 is also in agreement with pKa value of permanganic acid as recorded in earlier investigations.

This present investigations shows that the stoichiometry ratio between oxidant HVMG and substrate LZD was found to be 1:1 with unit order dependence on oxidant HVMG and fractional orders dependence on substrate [LZD] and $[H^+]$ ion. Based on experimental results of oxidation kinetics of LZD by HVMG at environmentally

relevant pH 6.0, a plausible mechanism scheme 1 was projected accommodating the observed experimental orders for [HVMG], [LZD] and [H^+]. As per scheme 1, K_1 is the first equilibrium constant which was established between HVMG and H^+ ion. The formation of strong oxidizing species permanganic acid was also reported in the earlier studies [20]. The stable complex C was formed between the substrate LZD and the strong oxidizing species $HMnO_4$ in the second equilibrium step. K_2 is the equilibrium constant for the second step of formation of complex C. In the next step, this complex C forms a protonated unstable intermediate compound in the rate determining step (RDS) as per scheme 1. The velocity constant for the rate determining step (RDS) is k. Subsequently, the protonated unstable intermediate compound break into the major product LZD_P1while Mn^{7+} is converted into Mn^{6+} in the next fast step. Mn^{6+} reacts with an unstable intermediate compound in the fast step and it forms another oxidative degraded products LZD_P2 while Mn^{6+} reduced to MnO_4^{-3} (Mn^{5+}). Then, MnO_4^{3-} (Mn^{5+}) further reacts with LZD_P2 to form LZD_P3 and MnO_2 (Mn^{4+}). This MnO_2 reduces to MnO (Mn^{2+}) and oxidizes protonated unstable intermediate compound into LZD_P4. These four oxidative degraded products (LZD_P1, LZD_P2, LZD_P3 and LZD_P4) of oxidation kinetics of LZD by HVMG at environmentally relevant pH 6.0 are presented in TABLE 1. The results of oxidation kinetics of LZD by HVMG at environmentally relevant pH 6.0 may be interpreted as per the scheme 1. Literature survey reveals that there are many investigations which support the projected plausible mechanism as per scheme 1[23, 24].

UV-vis spectra were recorded of the substrate LZD (1×10^{-3} mol dm^{-3}), oxidant HVMG (1×10^{-4} mol dm^{-3}) and a mixture of substrate-oxidant (LZD- HVMG) at environmentally relevant pH 6.0 spectrophotometrically in each case using A CARY 50 Bio UV-vis spectrophotometer. The UV-vis spectral data gives the spectroscopic confirmation for the formation of complex C between the substrate LZD and $HMnO_4$ at environmentally relevant pH 6.0. The positive intercept obtained in Michaelis–Menton plot $1/k_{obs}$ vs. 1/ [LZD] proves that complex C is formed between the substrate LZD and $HMnO_4$ at environmentally relevant pH 6.0. The formation of complex C between substrate LZD and $HMnO_4$ was also observed in the previous studies. The order which was found less than unity in $1/k_{obs}$ vs. 1/ [ZDV] plot also confirms the complex C formation between the substrate LZD and $HMnO_4$ at environmentally relevant pH 6.0 [25].

The rate of the reaction for rate-determining step as per the proposed mechanism can be expressed as follows:

$$\textbf{Rate} = \frac{-d[MnO_4^-]}{dt} = k\,[\text{Complex C}]\quad [HMnO_4] \qquad \text{---(4)}$$

By rearranging the above mentioned equation 3, we get

$$[HMnO_4] = K_1\ [H^+]\ [MnO_4^-] \qquad \text{--- (5)}$$

According to scheme 1,the equilibrium constant (K_2) can be written as follows:

$$K_2 = \frac{[\text{Complex C}]}{[\text{LZD}]\ [H^+]} \qquad \text{---(6)}$$

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$$[\text{Complex C}] = K_2\,[\text{LZD}]\,[H^+] \quad \text{---(7)}$$

Using equation (5) and equation (7), the equation (4) becomes

$$\text{Rate} = \frac{-d[MnO_4^-]}{dt} = k\,K_1\,K_2\,[\text{LZD}]_f\,[MnO_4^-]_f\,[H^+]_f \quad \text{---(8)}$$

In the above equation (8), the letter f denotes free concentrations of substrate LZD, oxidant MnO_4^- and H^+ ion. In order to substitute for these terms $[LZD]_f$, $[MnO_4^-]_f$ and $[H^+]_f$ as mentioned in the above equation (8), the total concentrations of these terms $[LZD]_T$, $[Mn^{7+}]_T$, and $[H^+]_T$ can be expressed as follows:

$$[MnO_4^-]_T = [MnO_4^-]_f + [HMnO_4] + [\text{Complex C}]$$

$$[MnO_4^-]_T = [MnO_4^-]_f + K_1\,[H^+]\,[MnO_4^-]_f + K_1\,K_2\,[\text{LZD}]\,[H^+]\,[MnO_4^-]_f$$

$$[MnO_4^-]_T = [MnO_4^-]_f\,\{1 + K_1\,[H^+] + K_1\,K_2\,[H^+]\,[\text{LZD}]\}$$

Rearrangement of the above equation gives the value of $[MnO_4^-]_f$ which is shown below

$$[MnO_4^-]_f = \frac{[MnO_4^-]_T}{1 + K_1\,[H^+] + K_1\,K_2\,[H^+]\,[\text{LZD}]} \quad \text{----(9)}$$

$[H^+]_T$ ion can be expressed in a similar way as shown below,

$$[H^+]_T = [H^+]_f + [HMnO_4]$$

$$[H^+]_T = [H^+]_f + K_1\,[H^+]\,[MnO_4^-]$$

Experimental values of $[H^+]$ indicates that its value is very small. As a result of this, the term $K_1\,[H^+]\,[MnO_4^-]$ becomes extremely small. Therefore, the term $K_1\,[H^+]\,[MnO_4^-]$ can be ignored in the above mentioned equation. Hence, we get

$$[H^+]_T = [H^+]_f \quad \text{----(10)}$$

In the similar way, $[LZD]_T$ can be expressed as,

$$[\text{LZD}]_T = [\text{LZD}]_f \quad \text{----(11)}$$

These above expressed values of free concentrations of different terms $[MnO_4^-]_f$, $[LZD]_f$, and $[H^+]_f$ with omitting the subscripts were put in the equation (8), so the rate law equation for the projected mechanism (scheme 1) can be written as follows:

$$\text{Rate} = \frac{-d[MnO_4^-]}{dt} = \frac{k\,K_1K_2\,[MnO_4^-]\,[\text{LZD}]\,[H^+]}{1 + K_1[H^+] + K_1\,K_2\,[H^+]\,[\text{LZD}]} \quad \text{-----(12)}$$

$$\frac{\text{Rate}}{[MnO_4^-]} = k_{obs} = \frac{k\,K_1K_2[MnO_4^-]\,[\text{LZD}]\,[H^+]}{1 + K_1[H^+] + K_1\,K_2\,[H^+]\,[\text{LZD}]} \quad \text{-----(13)}$$

After rearranging the equation of rate law (13), we get

$$\frac{1}{k_{obs}} = \frac{1}{k\,K_1K_2\,[\text{LZD}]\,[H^+]} + \frac{1}{k\,K_2\,[\text{LZD}]} + \frac{1}{k} \quad \text{-----(14)}$$

Using the above mentioned equation 14, plots $1/k_{obs}$ versus 1/[LZD] and $1/k_{obs}$ versus $1/[H^+]$ give a straight lines having a positive intercepts. The values of k, K_1 and K_2 as mentioned in mechanism (scheme 1) are evaluated from the slopes and intercepts of these plots. The evaluated values of k, K_1 and K_2 are 4.153×10^{-2} dm^3 mol^{-1} s^{-1}, 39 dm^3 mol^{-1} and 2.912×10^3 dm^3 mol^{-1} respectively at temperature 298 K. The evaluated value K_1 is found to be very close with the reported value in previous investigations [20]. By using these evaluated values (k, K_1 and K_2), the rate constants were determined at different reaction conditions which are then compared with experimental values. These calculated and experimental values were found to be very close which provides support to the projected plausible mechanism as per scheme 1 as shown in Fig. 5.9.

The energy of activation (Ea) was evaluated from log kobs versus 1/T (Arrhenius plot). The evaluated value of Ea was then used further to determine other activation parameters which are listed in TABLE 3(b). The calculated value of entropy of activation was found to be negative and indicates the formation of more activated complex between active species $HMnO_4$ and the substrate LZD. The determined values of free energy of the activation $\Delta G^{\neq}$ and enthalpy of activation $\Delta H^{\neq}$ were found to be positive which implies the more solvation of transition state between the substrate LZD and permanganic acid. The evaluated values of activation energy, free energy of activation and entropy of activation for the oxidation kinetics of LZD by HVMG at environmentally relevant pH suggest that the strongly active species $HMnO_4$ forms the activated complex as per mechanism more readily in comparison to the other oxidants. The values of free energy of reaction $\Delta G^{\neq}$, enthalpy of reaction $\Delta H^{\neq}$ and entropy of reaction $\Delta S^{\neq}$ were calculated for the first and second equilibrium steps. A comparison of the later values (from K_2) with those obtained for the slow step of the reaction shows that these values mainly refer to the rate-limiting step, supporting the fact that the reaction before rate determining step is fairly fast and involves low activation energy. The various activation parameters were also determined for first two the equilibrium steps involved in the proposed mechanism (scheme 1). The comparison of these values with the values of activation parameters which were determined for the rate-determining step indicates that both the first and second equilibrium reactions are faster due to low activation energy than the rate determining step [26, 27].The fairly constant values of velocity constants of variation in ionic strength (I) for oxidation kinetics of LZD by HVMG at environmentally relevant pH 6.0 indicates that there is no reaction between oxidizing agent and solvent. This insignificant effect on ionic strength (I) confirms that the reaction is between two neutral species or a neutral and charged species [28]. The experimental data of the influence of dielectric constant indicates the reaction is between two dipoles as explained by Amis [29].

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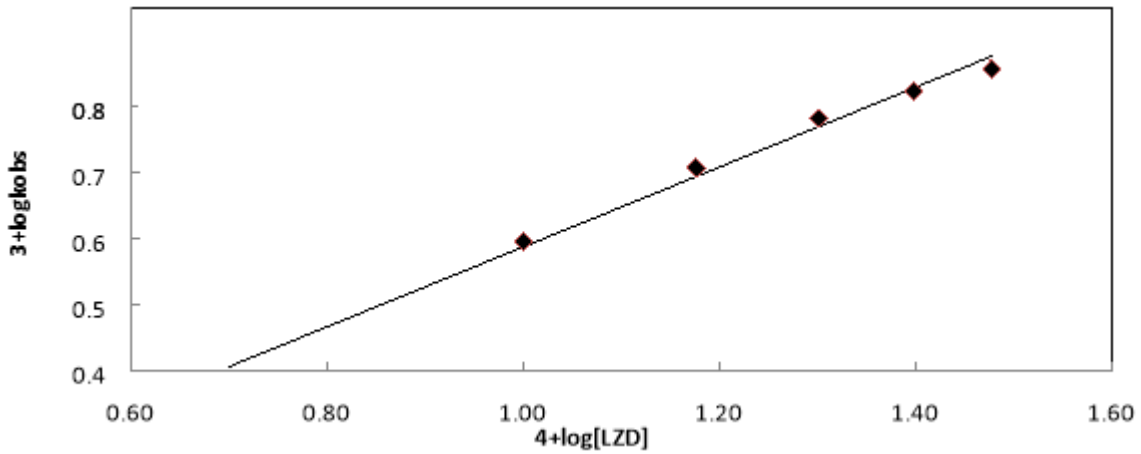

Fig. 5. Effect of variation in [LZD] for the oxidation kinetics of LZD by HVMG in uncatalyzed reaction at environmentally relevant pH 6.0

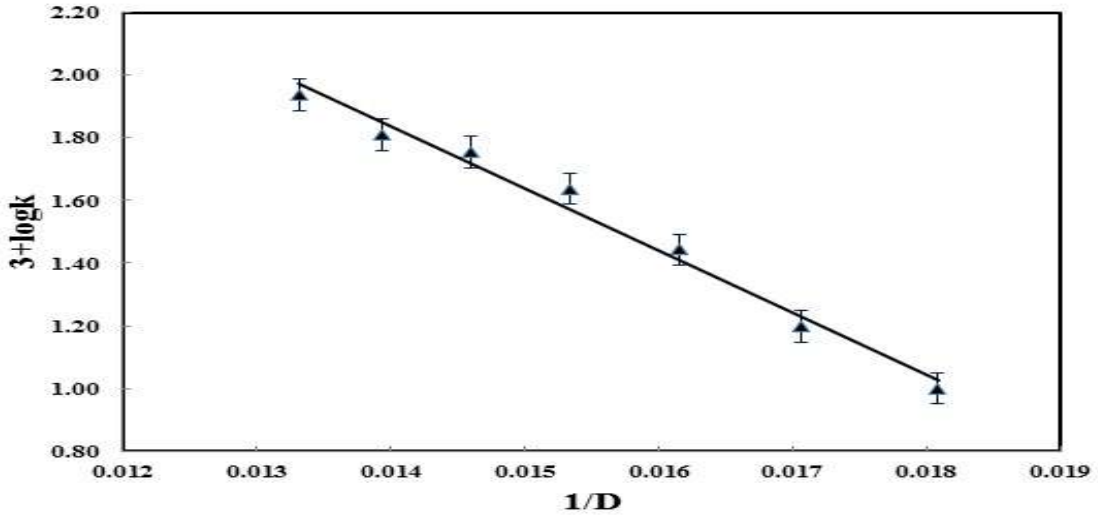

Fig. 6. Influence of dielectric constant on the oxidation of LZD by HVMG in uncatalyzed reaction at environmentally relevant pH 6.0.

TABLE 2 pH dependent second order rate constants for the variation in pH for the uncatalysed oxidation kinetics of LZD by HVMG at environmnetally relevant pH

pH	kus
3.0	6.32
4.0	5.18
5.0	4.73
6.0	3.73
7.0	2.83
8.0	2.62
9.0	1.56

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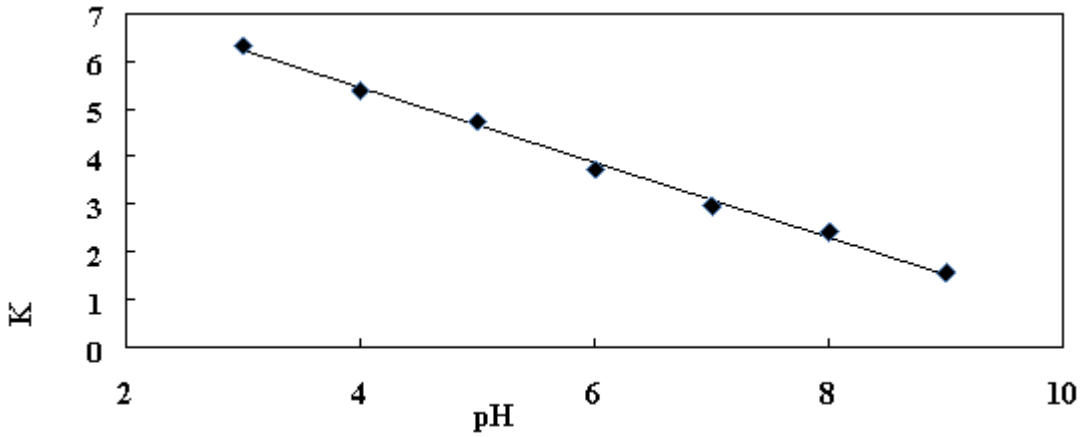

Fig. 7. Second order rate constants for uncatalysed LZD oxidative degradation by HVMG at different pH from 3.0 to 9.0

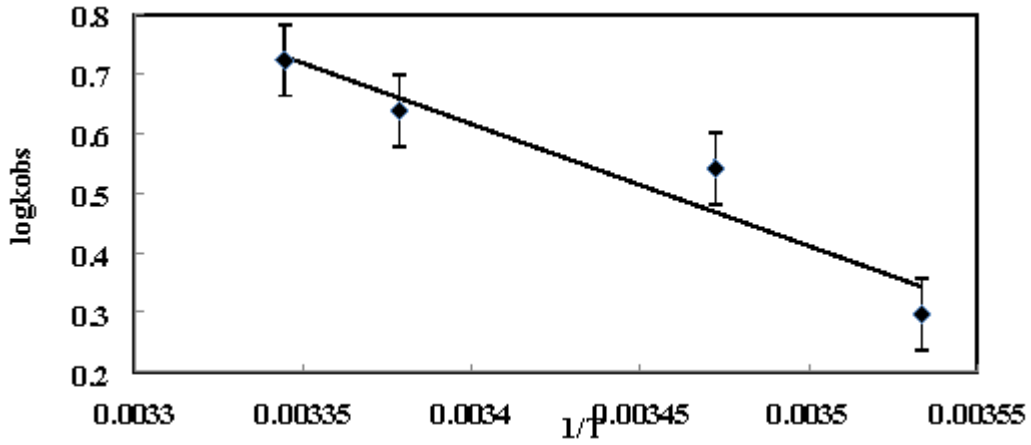

Fig. 8. Influence of variation in temperature on the oxidation kinetics of LZD by HVMG

Table 3 Calculation of activation parameters and thermodynamic quantities at different temperatures 283K, 288K, 296K and 299K

(a)Influence of temperature:

Temperature(Kelvin)	10^3 k_U s^{-1}
283	3.96
288	6.96
296	8.68
299	10.56

(b)Activation parameters:

Activation parameters	Values for Uncatalyzed reaction
Ea (kJ mol^{-1})	39.08 ± 1.99

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$\Delta H^{\#}$ (kJ mol^{-1})	36.66 ± 2.13
$\Delta S^{\#}$ (Jk^{-1} mol^{-1})	-160.06 ± 13.98
$\Delta G^{\#}$ (kJ mol^{-1})	83.32 ± 6.35

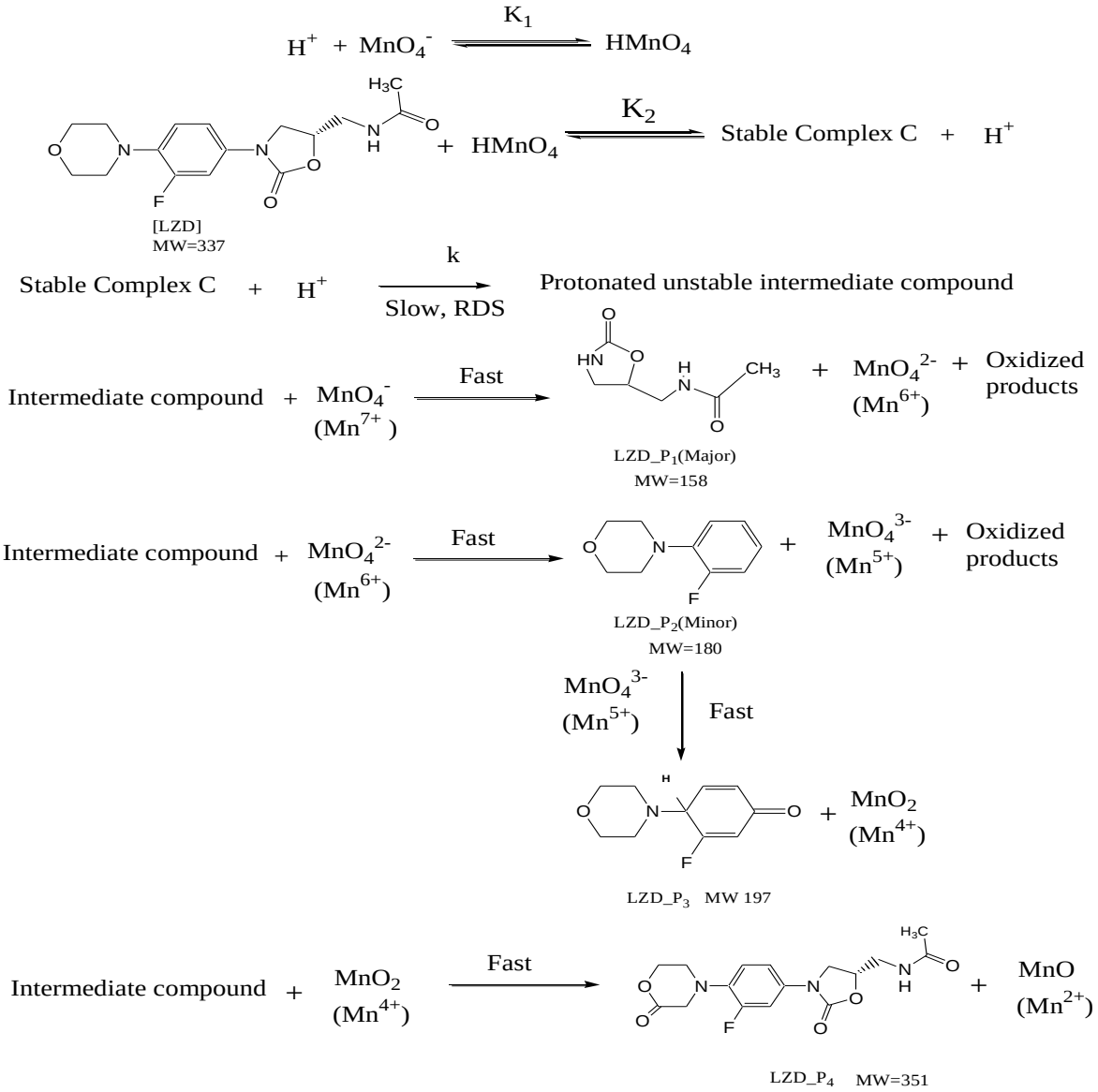

Fig. 9 Plausible mechanism for the uncatalysed oxidative degrdation of LZDby HVMG at environmnetally relevant pH 6.0 and temperature 298 K.

V. CONCLUSION

Permanganic acid is found to be a better oxidizing species than oxidant HVMG and oxidizes the antibacterial drug LZD easily at environmentally relevant pH 6.0. The oxidative degradation of LZD by HVMG at environmentally relevant pH 6.0 forms four degraded byproducts. The values of k, K_1 and K_2 are evaluated as

per the scheme 1 of the proposed plausible mechanism. The spectroscopic data shows that orders of [LZD] and [H^+] ion are fractional while order with respect to [HVMG] is unity. The fractional order with respect to [LZD] and Michaelis-Menton indicates the formation of complex between LZD and permanganic acid. The effect of ionic strength concludes that the oxidation kinetics of LZD by HVMG is between neutral and charged species or two neutral species. The effect of dielectric constant concludes that the reaction is between two dipoles. Activation energy and other activation parameters were evaluated from the effect of variation in temperature on oxidation kinetics of LZD by HVMG at environmentally relevant pH 6.0. The experimental results indicate the formation of more activated complex due to higher negative value entropy of activation ($\Delta S^{\neq}$). Higher positive values of enthalpy of activation ($\Delta H^{\neq}$) and free energy of the activation ($\Delta G^{\neq}$) suggests that the more solvation of transition state. This current investigation shows that HVMG acts as an efficient and strong oxidant in the oxidative degradation of substrate LZD at environmentally relevant pH 6.0 during water treatment process.

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