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Original Research Article

Oxidative degradation of some antibiotics by permanganate ion in alkaline medium: A kinetic and mechanistic approach

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Abstract

Purpose: *To investigate the kinetics of oxidative removal of two β-lactam antibiotics (A), namely, ampicillin and flucloxacillin.*
Methods: *In this study, permanganate ion (MnO_4^-) was used as an oxidant in an alkaline medium at fixed ionic strength of 0.1 mol dm^{-3} and a temperature of 298 K utilizing a spectrophotometric technique. The obtained oxidation products were characterized using spot tests and FT-IR spectra.*
Results: *The stoichiometry of the reactions was 1:4 (A : MnO_4^-). The reactions were a first order credence in [MnO_4^-] and fractional-first order kinetics in antibiotic and hydroxyl ion. Influence of ionic strength was successfully explored. Dependence of reaction rates on temperature was studied and the activation parameters were computed and discussed. A plausible mechanism for the oxidation reactions has been elucidated. A consistent rate-law expression was also derived.*
Conclusion: *This study introduces a significant treatment method for antibiotic removal, thus helping to protect the environment and human health.*

Keywords: *Permanganate, Antibiotics, Oxidative degradation, Kinetics, Mechanism*

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INTRODUCTION

Antibiotics are amongst the most noteworthy group of pharmaceutical drugs utilized in curing human and animals from fungal and bacterial inflammations [1]. These antibiotics are used also in food manufacturing [2]. Although, antibiotics are presumed to be drugs for human and animals, they are foreign matter to the body and must be eliminated from the body after their medical action via drug metabolism process. Through drug metabolism, antibiotics undergo oxidation, reduction and hydrolysis, resulting in biotransformation of antibiotics in the body so that they can be eliminated more easily.

This process may lead to an active, inactive or pharmacological metabolite entering the environment and water cycle, and this can have a negative and harmful impact, disturbing the ecological balance [3,4]. Therefore, it is of utmost importance to find green, safe and powerful

treatment methods to eliminate antibiotic residues present in the contaminated environment and water to protect the environment and human health [5,6]. Bio-techniques are still limited and are not effective because of the complicated chemical structures of antibiotics [7]. It is very important to use improved treatments, or combine several biological, chemical and physical methods [8].

Antibiotics are susceptible to oxidation, leading to their degradation, termination of their action and/or their elimination from the body [9-12]. Although, oxidation is a relatively common method for drug decomposition, it has not been studied extensively because oxidative degradation can often be reduced to reasonable levels through various ways. One of the most presumed techniques for the removal of antibiotics is chemical oxidation, which is a widespread path for their decomposition, and they have a principal role in water treatment operations and in understanding the metabolism of such medications. The role of oxidizing agents during the oxidation process is the conversion of the poisonous substances into less harmful compounds in order to make them safe when they are discharged into the environment [11,12].

A review of literature revealed little reported investigations into the kinetics of oxidative degradation of antibiotic drugs in aqueous acidic or alkaline media [10-13]. In view of the previously mentioned aspects, the existing investigation is concerned with the kinetic mechanism of oxidative removal of two *β*-lactam antibiotics, viz, ampicillin and flucloxacillin (their structures shown in Figure 1) using permanganate ion (MnO_4^-), which is a significant, powerful and inexpensive oxidant [14-16] in aqueous alkaline medium. This study aims to find out the reactive species of antibiotic bioreductants, as well as permanganate ion oxidant in alkaline medium, in order to to discover the selectivity of antibiotics towards MnO_4^- in such medium. This study is also extended to delineating a mechanistic picture of the existing redox reactions and to derive the rate-law expression consistent with the acquired investigational kinetic outcomes.

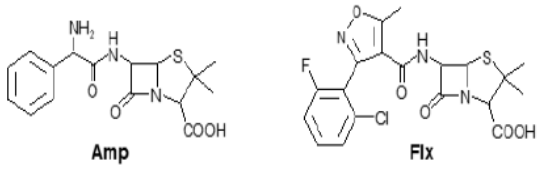


Figure 1: Structures of ampicillin (Amp) and flucloxacillin (Flx) antibiotics

EXPERIMENTAL

Materials

Ampicillin and flucloxacillin antibiotics were purchased from Glentham Life Sciences. All other chemicals were purchased from Merck or Sigma in spectroscopic grade and were utilized as supplied. Antibiotic solutions were freshly prepared by dissolving their weighted samples (ampicillin, flucloxacillin sodium) in double-distilled water. Potassium permanganate solutions have been prepared and consolidated as mentioned earlier [14]. NaOH solutions were employed to supply the necessary alkalinity. Sodium perchlorate solution was used to fix and explore the influence of the ionic strength (*I*). The temperature of all reactions were under control to within ± 0.1 ^oC.

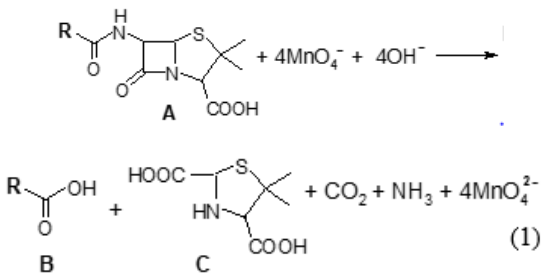
Kinetic measurements

Kinetic measurements were ascertained in fractional-first order circumstances, where the antibiotics existed in significant excess, higher than that of [MnO_4^-] at a fixed *I* and T. The measured UV-Vis absorption readings were done on a Shimadzu UV-1800 PC double-beam spectrophotometer. The reactions were tracked by recording the reduction of the absorbance of MnO_4^- (at λ = 526 nm) with time. All experiments were performed three times and the rate constants were found to be reproducible in the range of ± 3 %.

RESULTS

Reactions stoichiometry and products identification

It is important to determine the stoichiometries of the overall reactions before considering the acquired kinetic data in more details, because of the complexity of the kinetics of these reactions due to construction of transient species of manganate (VI) and/or manganate (V) intermediate complexes [15]. Stoichiometric measurements were performed at [OH^-] = $5.0x10^{-3}$ mol dm^{-3} with slightly excess permanganate concentration. The reaction mixtures were left in a dark place for 1 day. Unreacted [MnO_4^-] was estimated by the conventional spectrophotometric technique until the completion of the reactions. The obtained results indicated that the stoichiometric ratios ([MnO_4^-]$_{consumed}$: [A]$_0$), where [A] is the antibiotic concentration, were found to be 4.0 ± 0.2 mol, i.e., each mole of antibiotic was reacted with four moles of permanganate ion as illustrated by the following equation:



(1)

where, **A** refers to ampicillin and flucloxacillin (Figure 1), and **B** and **C** are their identified oxidation products; the corresponding carboxylic acids and 5,5-dimethyl-thiazolidine-2,4-dicarboxlic acid, respectively. Such oxidation products were identified employed spot tests and FT-IR spectra. The FT-IR spectra showed appearance of sharp band at around 1660 cm^{-1} which is characteristic for carboxylic C=O stretch in the product **B**.

Also, appearance of new broad band at around 3370 cm^{-1} which is due to carboxylic OH with N-H stretching confirming the product **C**. Ammonia and CO_2 byproducts were identified by spot tests [36]. The same oxidation products were identified earlier for ampicillin [11,12] and flucloxacillin [13].

Spectroscopic changes

Initial experiments showed that the existing oxidation reactions were of such rates that can be monitored using the traditional spectrophotometer. Spectroscopic changes (200 - 700 nm) during the oxidation of ampicillin (Amp) and flucloxacillin (Flx) by permanganate ion are shown in Figure 2 (a,b).

As manifested in these graphs, there is a progressive decay of MnO_4^- ion band at λ = 526 nm with a concurrent appearance of new bands at about 606 and 435 nm especially in case of ampicillin.

Dependence of oxidation rate on permanganate concentration

The pseudo-first order plots (ln Abs. vs. time) in the oxidation of ampicillin and flucloxacillin by permanganate ion in alkaline medium was examined at various $[MnO_4^-]_0$, ranging between 1.0 x 10^{-4} and 8.0 x 10^{-4} mol dm^{-3} while other constituents were kept constant. The results indicated that the obtained pseudo-first order rate constant plots are straight lines for about 80% of the reactions accomplishment as illustrated in Figure 3. Also, changing the initial concentration of the oxidant didn't affect much on the observed rate constant values (k_{obs}) as included in Table 1. These results indicated that the reactions were first order in $[MnO_4^-]$.

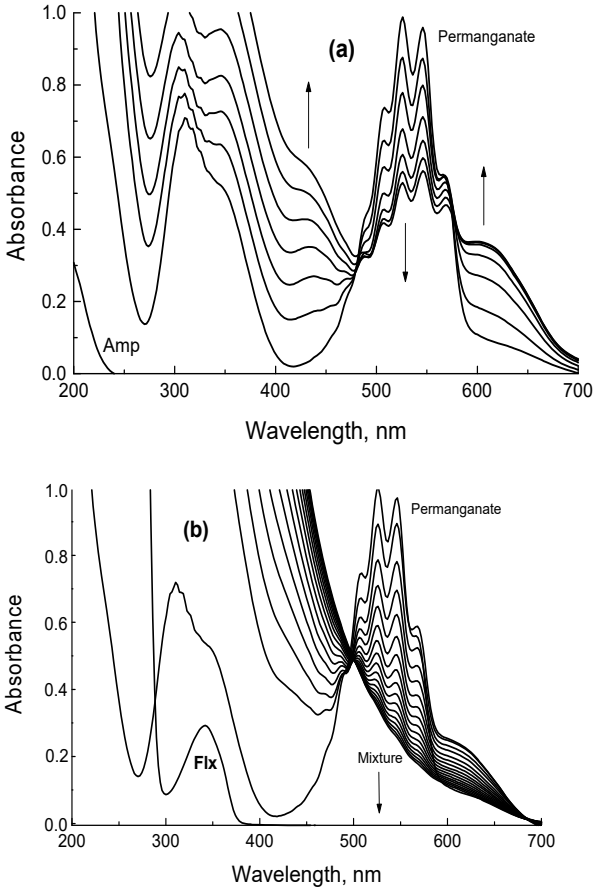


Figure 2: Spectroscopic changes during oxidation of: (a) ampicillin (Amp) and (b) flucloxacillin (Flx), by alkaline permanganate. $[MnO_4^-]$ = 4.0 x 10^{-4}, [A] = 5.0 x 10^{-3}, $[OH^-]$ = 5.0 x 10^{-3} and I = 0.1 mol dm^{-3} at 298 K

Dependence of oxidation rates on antibiotic concentration

In another set of experiments, the values of k_{obs} were calculated at various concentrations of the examined antibiotics, [A], but at fixed $[MnO_4^-]$, $[OH^-]$, I and T. The first order rate constant graphs, as well as the corresponding values of k_{obs} summarized in Table 1 indicated that the rates of oxidation reactions augmented gradually with rising concentrations of antibiotics. On the other hand, the plots of k_{obs} against [A] gave good straight lines with significant positive intercepts on the k_{obs} axes as illustrated in Figure 4(a). Furthermore, when the values of log [A] were plotted against those of log k_{obs}, straight lines with slopes of 0.59 and 0.52 were obtained, Figure 4(b), confirming that such reactions were fractional-first orders in [A].

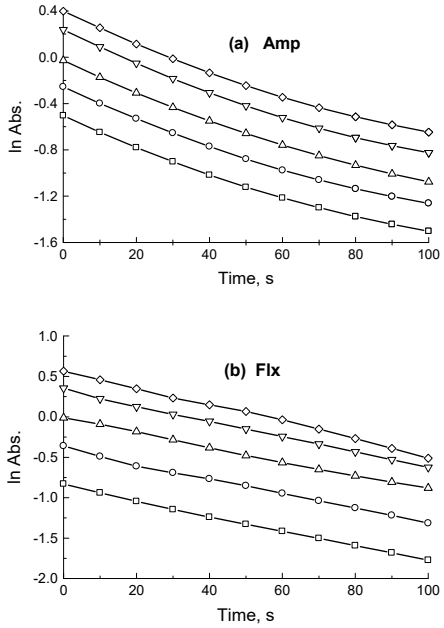


Figure 3: Effect of [MnO_4^-] on the first order plots in the alkaline permanganate oxidation of: **(a)** ampicillin (Amp) and **(b)** flucloxacillin (Flx) at [A] = 5.0 x 10^{-3}, [OH^-] = 5.0 x 10^{-3}, *I* = 0.1 mol dm^{-3} and T = 298 K. (□) 1.0 x 10^{-4}, (o) 2.0 x 10^{-4}, (Δ) 4.0 x 10^{-4}, ( ) 6.0 x 10^{-4}, (◊) 8.0 x 10^{-4}

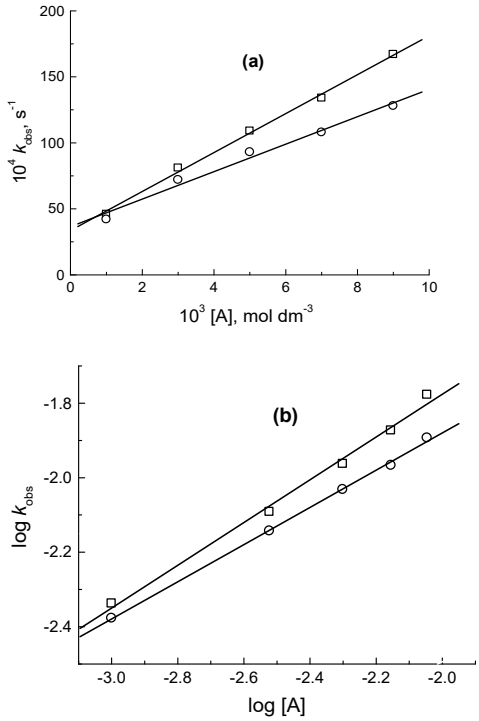


Figure 4: Plots of: **(a)** k_{obs} vs. [A], and **(b)** log k_{obs} vs. log [A], in the alkaline permanganate oxidation of: (□) ampicillin (Amp) and (o) flucloxacillin (Flx) at [MnO_4^-] = 4.0 x 10^{-4}, [OH^-] = 5.0 x 10^{-3}, *I* = 0.1 mol dm^{-3} and T = 298 K

Dependence of oxidation rates on [OH^-]

The rates of oxidation of the investigated antibiotics by alkaline permanganate was determined at different pH values in order to clarify the reactions mechanism. The experimental observation indicated that the rates of oxidation reactions were increased with rising [OH^-] as indicated from the k_{obs} values included in Table 1. The plots of k_{obs} versus [OH^-] gave good straight lines with positive intercepts on the k_{obs} axes, Figure 5(a). Also, the plots of log k_{obs} vs. log [OH^-] yielded straight lines with slopes of 0.894 and 0.883 as illustrated in Figure 5(b), indicating that such reactions were fractional-first orders in [OH^-].

Dependence of oxidation rates on ionic strength (*I*) of reactions medium

In order to show the nature of the interactive species in the rate-determining step of the redox reactions and the suggested mechanism of the oxidation reactions, kinetic experiments were accomplished at fixed alkali and antibiotic concentrations, while the concentration of

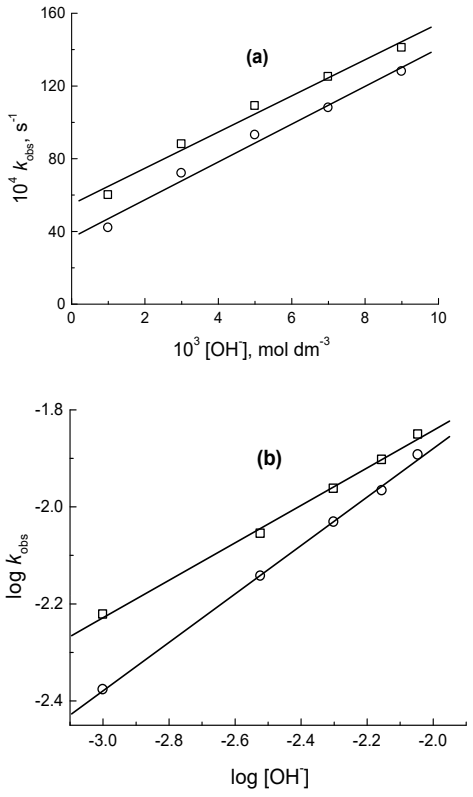


Figure 5: Plots of: **(a)** k_{obs} vs. [OH^-], and **(b)** log k_{obs} vs. log [OH^-], in the alkaline permanganate oxidation of: (□) ampicillin (Amp) and (o) flucloxacillin (Flx) at [A] = 5.0 x 10^{-4}, [MnO_4^-] = 4.0 x 10^{-4}, *I* = 0.1 mol dm^{-3} and T = 298 K

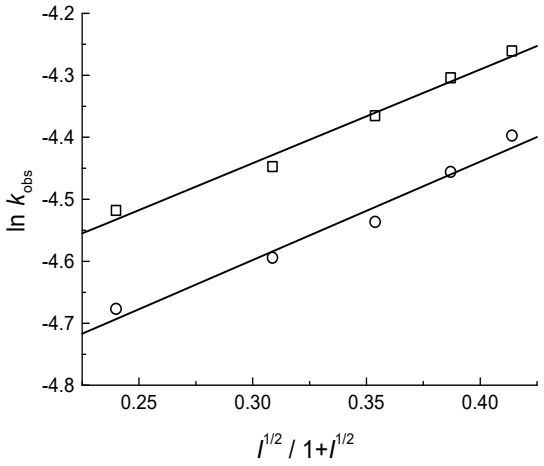


Figure 6: Debye-Hückel plots in the alkaline permanganate oxidation of: (□) ampicillin (Amp) and (o) flucloxacillin at [A] = 5.0 x 10^{-3}, [MnO_4^-] = 4.0 x 10^{-4}, [OH^-] = 5.0 x 10^{-3} mol dm^{-3} and T = 298 K

sodium perchlorate was increased. The obtained results indicated that the rates of the oxidation reactions were increased as *I* increased, as noticed from the values of k_{obs} listed in Table 1. The Debye-Hückel plots were set to be linear with positive slopes as illustrated in Figure 6.

Dependence of oxidation rates on temperature

To determine activation parameters, the reactions were conveyed at a variety of temperatures, as well as at a fixed concentration of the other reaction ingredients. The experimental results showed that the rates of the oxidation reactions were found to increase by raising the temperature as listed in Table 2. On the other hand, Eyring and Arrhenius plots of the second order rate constant values (k_2) were set to be linear as illustrated in Figure 7 (a) and (b), correspondingly. The activation parameters were assessed from the slopes and intercepts of these plots and are introduced in Table 3.

Table 1: Influence of [MnO_4^-], [OH^-], [A] and (*I*) on the values of k_{obs} in the alkaline permanganate oxidation of ampicillin (Amp) and flucloxacillin (Flx) at T = 298 K

10^4 [MnO_4^-] (mol dm^{-3})	10^3 [A] (mol dm^{-3})	10^3 [OH^-] (mol dm^{-3})	*I* (mol dm^{-3})	k_{obs} (s^{-1}) 10^4	
				Amp	Flx
1.0	5.0	5.0	0.1	107.09	84.90
2.0	5.0	5.0	0.1	104.72	85.76
4.0	5.0	5.0	0.1	109.10	85.05
6.0	5.0	5.0	0.1	106.21	86.04
8.0	5.0	5.0	0.1	105.83	85.49
4.0	**1.0**	5.0	0.1	46.07	41.89
4.0	**3.0**	5.0	0.1	81.37	72.17
4.0	**5.0**	5.0	0.1	109.10	85.05
4.0	**7.0**	5.0	0.1	134.14	108.11
4.0	**9.0**	5.0	0.1	166.98	128.07
4.0	5.0	**1.0**	0.1	60.61	41.98
4.0	5.0	**3.0**	0.1	88.04	72.17
4.0	5.0	**5.0**	0.1	109.10	85.05
4.0	5.0	**7.0**	0.1	125.61	108.03
4.0	5.0	**9.0**	0.1	141.13	128.00
4.0	5.0	5.0	**0.1**	109.10	85.05
4.0	5.0	5.0	**0.2**	116.88	101.17
4.0	5.0	5.0	**0.3**	127.04	106.99
4.0	5.0	5.0	**0.4**	135.22	115.87
4.0	5.0	5.0	**0.5**	141.31	123.23

Table 2: Effect of temperature on the values of k_{obs} in alkaline permanganate oxidation of ampicillin (Amp) and flucloxacillin (Flx) at [A] = 5.0 x 10^{-3}, [MnO_4^-] = 4.0 x 10^{-4}, [OH^-] = 5.0 x 10^{-3} and *I* = 0.1 mol dm^{-3}

Temp (K)	k_{obs} (s^{-1}) 10^4	
	Amp	Flx
288	83.91	69.95
298	109.10	85.05
308	144.20	125.07
318	203.05	159.87
328	272.41	193.10

Table 3: Activation parameters of k_2 in the alkaline permanganate oxidation of ampicillin (Amp) and flucloxacillin (Flx) at [A] = 5.0 x 10^{-3}, [MnO_4^-] = 4.0 x 10^{-4}, [OH^-] = 5.0 x 10^{-3} and I = 0.1 mol dm^{-3}

Antibiotic	$\Delta S^{\neq}$ (J $mol^{-1}K^{-1}$)	$\Delta H^{\neq}$ (kJ mol^{-1})	$\Delta G^{\neq}_{298}$ (kJ mol^{-1})	$E_a^{\neq}$ (kJ mol^{-1})
Amp	-166.28	20.70	70.25	22.35
Flx	-180.98	17.63	71.56	20.23

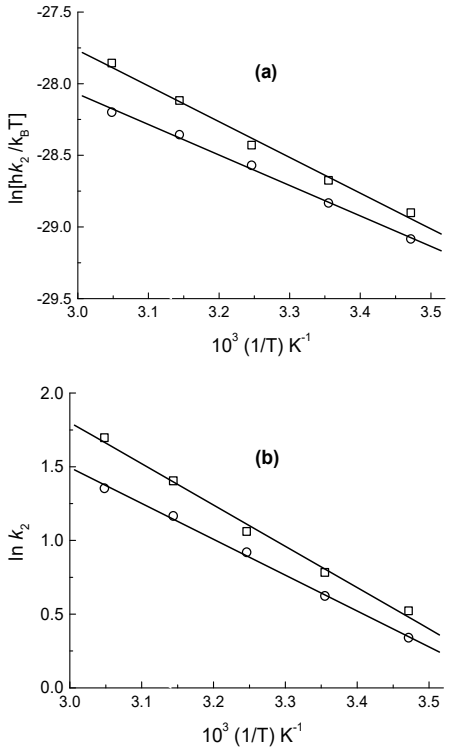


Figure 7: (a) Eyring plots, and **(b)** Arrhenius plots k_2 in the alkaline permanganate oxidation of: (□) ampicillin (Amp) and (o) flucloxacillin (Flx) at [A] = 5.0 x 10^{-3}, [MnO_4^-] = 4.0 x 10^{-4}, [OH^-] = 5.0 x 10^{-3} and I = 0.1 mol dm^{-3}

Polymerization

The eventual formation of free radicals in the oxidation reactions between the examined antibiotics and permanganate ion in an alkaline medium, was examined by conducting a polymerization test. This test was carried out by the addition of a definite acrylonitrile quantity to the reaction mixture for about 4 h. No polymerization appeared in all reaction mixtures (there were no white precipitates formed), implying that the existing oxidation reactions did not proceed via formation of the free radicals mechanism.

Suggested reaction mechanism

The obtained increase in the oxidation rates as a result of increasing alkali concentration, as well as the structures of the examined antibiotics [18], suggested a deprotonation of antibiotic molecules (AH) according to the following equation:

$$AH + OH^- \overset{K_1}{\rightleftharpoons} A^- + H_2O \quad \cdots\cdots\cdots\cdots (3)$$

The deprotonated form (A^-) appears to be the reactive species in the rate-controlling stage of the proposed reactions mechanism.

It is well known [19] that permanganate ion in strong alkaline solutions is reduced by either one-electron change to give manganate (VI) ion, or by simultaneous two-electron changes to form hypomanganate (V). But it is difficult to decide whether permanganate is reduced by one- or by two-electron transfer mechanism owing to the following fast reactions (Eqs 4 and 5).

$$MnO_4^- + Mn^{V}O_4^{3-} = 2\ Mn^{VI}O_4^{2-} \quad \ldots\ldots\ldots\ldots (4)$$

$$2\ Mn^{V}O_4^{3-} = Mn^{VI}O_4^{2-} + Mn^{IV} \quad \ldots\ldots\ldots\ldots (5)$$

A further reaction of $Mn^{V}O_4^{3-}$ will proceed at a much lower rate owing to its lower reactivity [20]. This fact may be considered as good evidence against the assumption of accumulation of Mn^{V} transient species, since its formation is followed by one of the fast reactions 4 and 5.

Many investigators [21,22] proposed that supreme oxidation reactions by MnO_4^- in alkaline and neutral media occurred via construction of complexes between reductant and oxidant. In the present study, complex construction was indicated spectrophotometrically by the achieved UV–Vis spectra as shown in Figure 1, as well as kinetically, as the graphs of $1/k_{obs}$ vs. 1/[A] were linear with positive slopes [23] as shown in Figure 8 (a). Increasing rates of oxidation with increasing ionic strength suggests that oxidation reactions occurred between ions of similar charges [24,25].

In the light of the experimental observations, the most acceptable suggested mechanism for the present oxidation reactions, includes a rapid deprotonation of the antibiotic (Eq. 3), followed by the attack of MnO_4^- on the deprotonated antibiotic to construct a complex, [A - $Mn^{VI}O_4^{2-}$] (C), Eq. (6):

$A^- + MnO_4^- \underset{}{\overset{K_2}{\rightleftharpoons}} [A - Mn^{VI}O_4^{2-}]$ (C)…. (6)

Then, the formed transient complex decays in the rate-controlling stage to yield the preliminary oxidation products as follows:

$[A - Mn^{VI}O_4^{2-}] \xrightarrow{k_1}$ Preliminary oxidation products ….. (7)

The latter interacts with three moles of MnO_4^- ions in subsequent fast steps to yield the final oxidation products of the antibiotic.

The rate of decay of MnO_4^- could be expressed by the rate-law (8):

$$\text{Rate} = -\frac{d[MnO_4^-]_o}{dt} = k_1[C] \text{ …….. (8)}$$

The change in the reaction rate with the antibiotic, OH^- and oxidant concentrations can be written as follows:

$$\text{Rate} = \frac{k_1K_1K_2[A][OH^-][MnO_4^-]}{1+K_1[OH^-]+K_1K_2[OH^-][A]} \text{ ……. (9)}$$

When the antibiotic exists in a high excess over that of $[MnO_4^-]$, the rate-law could be written as:

Rate = $k_{obs}[MnO_4^-]$ ……. (10)

Comparing Eqs. (9) and (10), Eq. (11) was obtained:

$$k_{obs} = \frac{k_1K_1K_2[A][OH^-]}{1+K_1[OH^-]+K_1K_2[OH^-][A]} \text{ …… (11)}$$

Rearranging Eq. (11) led to the following two equations:

$$\frac{1}{k_{obs}} = \left(\frac{1+K_1[OH^-]}{k_1K_1K_2[OH^-]}\right)\frac{1}{[A]} + \frac{1}{k_1} \text{ ……. (12)}$$

$$\frac{1}{k_{obs}} = \left(\frac{1}{k_1K_1K_2[A]}\right)\frac{1}{[OH^-]} + \left(\frac{1}{k_1K_2[A]} + \frac{1}{k_1}\right) \text{ …… (13)}$$

With regards to Eqs. 12 and 13, the plots of $1/k_{obs}$ versus 1/[A] at fixed $[OH^-]$ and $1/k_{obs}$ versus $1/[OH^-]$ at fixed [A] must be linear with positive intercepts on the $1/k_{obs}$ axes. The investigational outcomes met this prerequisite as presented in Figure 8 (a) and (b). Values of the rate constant of slow step of the proposed reactions mechanism (k_1) and the equilibrium constants (K_1 and K_2) could be computed from the slopes and intercepts of these plots and are inserted in Table 4.

Activation parameters

Table 3 includes the computed activation parameters which were in accordance with the suggested oxidation mechanism. The obtained higher negative values of $\Delta S^{\neq}$ reaffirms construction of complexes amongst the reacting species [24]. The positive values of $\Delta H^{\neq}$ and $\Delta G^{\neq}$ signifies that the complexes formation was endothermic and non-spontaneous [25]. The higher values of $E_a^{\neq}$ indicated that the rate-controlling stage was the decay of the constructed complexes.

Table 4: Values of k_1, K_1 and K_2 in the alkaline permanganate oxidation of ampicillin (Amp) and flucloxacillin (Flx). [A] = 5.0 x 10^{-3}, $[MnO_4^-]$ = 4.0 x 10^{-4}, $[OH^-]$ = 5.0 x 10^{-3}, I = 0.1 mol dm^{-3} at T = 298 K.

Antibiotic	Constant		
	$10^2 k_1$, s^{-1}	K_1, dm^3 mol^{-1}	$10^{-2} K_2$, dm^3 mol^{-1}
Amp	1.88	149.05	7.07
Flx	1.49	17.99	44.68

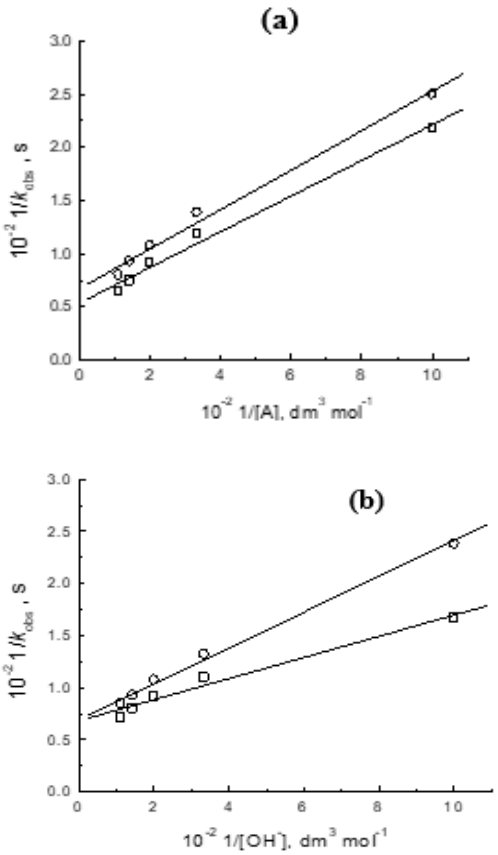


Figure 8: Plots of: **(a)** $1/k_{obs}$ vs. 1/[A], and **(b)** $1/k_{obs}$ vs. $1/[OH^-]$, in the alkaline permanganate oxidation of: (□) ampicillin (Amp) and (o) flucloxacillin (Flx) at $[MnO_4^-]$ = 4.0 x 10^{-4}, I = 0.1 mol dm^{-3} and T = 298 K

CONCLUSION

The kinetics of oxidative removal of ampicillin and flucloxacillin by permanganate ion in alkaline medium were investigated using a spectrophotometer. Stoichiometry of the reactions is 4.0 ± 0.2. A conceivable oxidation reactions mechanism was elucidated. The derived rate-law expression was fully consistent with the obtained results. The existing investigation may be considered a significant treatment method for antibiotic removal, helping to protect the environment and human health.

DECLARATIONS

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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REFERENCES

1. *Schatz A, Bugie E, Waksman SA. Streptomycin, a substance exhibiting antibiotic activity against gram-positive and gram-negative bacteria 1944. Exp Biol Med 2005; 437: 3-6.*
2. *Ann-Marie D. Pharmaceuticals in industrial wastewater and their removal using photo-Fenton's oxidation Ph.D. Research Thesis. School of Biotechnology Dublin City University Dublin 9 Ireland 2011.*
3. *Carvalho IT, Santos L. Antibiotics in the aquatic environments: A review of the European scenario. Environ Int 2016; 94: 736-757.*
4. *Brausch JM, Connors KA, Brooks BW, Rand GM. Human pharmaceuticals in the aquatic environment: A review of recent toxicological studies and considerations for toxicity testing. Rev Environ Contam Toxicol 2012; 218: 1-99.*
5. *AL-Othman ZA, Ali R, Naushad M. Hexavalent chromium removal from aqueous medium by activated carbon prepared from peanut shell: Adsorption kinetics, equilibrium and thermodynamic studies. Chem Eng J 2012; 184: 238-247.*
6. *Alqadami AA, Naushad M, Abdalla MA, Ahamad T, Ghfar AA. Efficient removal of toxic metal ions from wastewater using a recyclable nanocomposite: A study of adsorption parameters and interaction mechanism. J Clean Prod 2017; 156: 426-436.*
7. *Trovó AG, Nogueira RFP, Agüera A, Fernandez-Alba AR, Sirtori C, Malato S. Degradation of sulfamethoxazole in water by solar photo-Fenton. Chemical and toxicological evaluation. Water Res 2009; 43: 3922–3931.*
8. *Oppenlander T. "Photochemical Purification of Water and Air" (Weinheim, Germany: Wiley-VCH Verlag 2003; Ozkala CB, Koruyucub A, Merica S. Heterogeneous photocatalytic degradation, mineralization and detoxification of ampicillin under varying pH and incident photon flux conditions. Desalin Water Treat 2016; 57: 18391–18397; Garcıa AM, Navarro PG, Martınez PJ. de las Parras. Degradation of ampicillin in the presence of cadmium(II) ions. Talanta 1998; 46: 101–109.*
9. *Keen OS, Linden KG. Degradation of antibiotic activity during UV/H_2O_2 advanced oxidation and photolysis in wastewater effluent. Environ. Sci Technol 2013; 47: 13020–13030.*
10. *Rajesh NPS, Nandibewoor ST. Structure reactivity and thermodynamic analysis on the oxidation of ampicillin drug by copper(III) complex in aqueous alkaline medium (stopped-flow technique). J Mol Str 2009; 930: 180-186.*
11. *Singh AK, Yadav R, Srivastava J, Bala RS, Pradhan R, Rahmani S. Kinetics of Ir(III)-catalysed oxidation of ampicillin by Cu(Bip)22+ in alkaline medium: a spectrophotometric study. Int J Chem Tech Res 2017; 10: 514-524.*
12. *Hosamani RR, Shetti NP, Nandibewoor ST. Mechanistic investigation on the oxidation of ampicillin drug by diperiodatoargentate (III) in aqueous alkaline medium. J Org Phys Chem 2009; 22: 234-240.*
13. *Fawzy A. Removal of toxic tellurium (IV) compounds via bioreduction using flucloxacillin in aqueous acidic medium: A kinetic and mechanistic approach. J Mol Liq 2019; 111436.*
14. *Vogel IA. A Text book of quantitative inorganic analysis. 4th edn. ELBS and Longman, New York. 1978; p 352.*
15. *Wei MM, Stewart R. The Mechanisms of permanganate oxidation. VIII. Substituted benzylamines. J Am Chem Soc 1966; 88: 1974-1979.*
16. *Stewart R. In "Oxidation in organic chemistry. Wiberg KB. ed. Part A, Academic Press, New York. 1965; p 48.*
17. *Cotton FA, Wilkinson G. "Advanced Inorganic Chemistry". 4th ed. John Wiley and Sons, New York, NY, 1980; p 747.*
18. *Chemie VF. Ph D Thesis, Duisburg University, Germany. 2005.*

19. Szimmer J, Jacky M, Gerasimov OV. Oxidation by permanganate in strong alkaline medium. Oxidation of ethane-1,2-diol, glycol aldehyde, glycollic acid, and glyoxylic acid. Int J Chem Kinet 1992; 24: 145-154.
20. Carrington A, Symons MCR. Structure and reactivity of the oxyanions of transition metals. Chem Rev 1963; 63: 443-460.
21. Kini AK, Farokhi SA, Nandibewoor ST. A comparative study of ruthenium(III) catalyzed oxidation of L-leucine and L-isoleucine by alkaline permanganate. A kinetic and mechanistic approach. Transition Met Chem 2002; 27: 532–540.
22. Halligudi LL, Desai SM, Mavalangi AK, Nandibewoor ST. Free radical intervention, deamination and decarboxylation in the ruthenium(III)-catalysed oxidation of L-arginine by alkaline permanganate—a kinetic study. Transition Met Chem 2000; 26: 28–35.
23. Michaelis L, Menten ML. The kinetics of invertase action. Biochem Z 1913; 49: 333–369.
24. Stewart R, Moden RV. The mechanism of the permanganate oxidation of fluoro alcohols in aqueous solution. Disc Faraday Soc 1960; 29: 211–218.
25. Laider KJ. "Chemical Kinetics". McGraw-Hill, New York, 1965.