



Experimental and theoretical studies on the oxidation of lomefloxacin by alkaline permanganate

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ABSTRACT

The kinetic and mechanistic investigation of oxidation of emerging contaminant lomefloxacin (LMF) by alkaline permanganate was carried out spectrophotometrically. The oxidation product 7-amino-1-ethyl-6, 8-difluoro-4-oxo-quinoline-3-carboxylic acid was identified by Agilent 6130 Series Quadrupole LC/MS. The stoichiometry was found to be 1:2, that is, 1 mol of lomefloxacin reacted with 2 mol Mn(VII). Orders with respect to [LMF] and [OH⁻] were found to be fractional and less than one. The oxidation reaction proceeds via an alkali permanganate species that forms a complex with lomefloxacin and the complex then decomposes to give the product. The rate of reaction was found to decrease with decrease in the dielectric constant. The effects of initially added products and ionic strength have also been investigated. The kinetics of the reaction was also studied at four different temperatures, and the thermodynamic activation parameters for the reaction were evaluated and discussed. The geometry optimization of reactants and activated complex were carried out using density functional theory (DFT). The DFT calculations were accomplished with the TURBOMOLE program package (Version-6.4). The activation energy was found to be ~21 kJ/mol at RI-BP86.def 2-TZVPP level of theory.

Keywords: Lomefloxacin; Fluoroquinolone; Permanganate; Oxidation; Kinetics

1. Introduction

In synthetic organic chemistry (in acidic, alkaline, or neutral medium), permanganate has been extensively employed as an oxidizing agent [1,2]. The mechanism of oxidation depends not only on

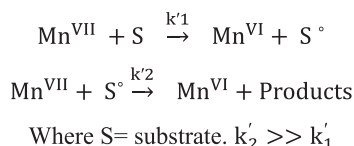
permanganate but also on substrate and pH of the medium [3]. Oxidation by permanganate ion gained importance in synthetic organic chemistry after the discovery of phase transfer catalysis [4–7]. Potassium permanganate is also used as a disinfectant in water and wastewater treatment, since its oxidation

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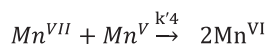
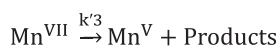
properties enable to oxidize the organic matter [8,9]. Permanganate is the strongest oxidizing species in acidic, alkaline, and neutral media among all the oxidation states of manganese [10,11]. The mechanistic information is missing in the literature to differentiate between a direct reduction of Mn(VII) to Mn(VI) (Scheme 1) and a pathway involving Mn(V) formation by two-electron reduction, subsequent rapid reoxidation to Mn(VI) (Scheme 2) [12–14]. In this connection, Bohm et al. [15] have proposed the process described in Scheme 3. According to the values of the reduction potentials for these chemical species, an alternative process in which Mn(V) in the presence of Mn(VII) gives rise to Mn(VI) and Mn(IV) (Scheme 3) is also feasible.

The products of this latter reaction are Mn(IV) and Mn(VI), may be relatively stable oxidation states of manganese in alkali solution. The reaction is thermodynamically very favored as revealed by the positive value of the reaction potential.

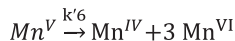
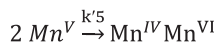
Fluoroquinolones are broad-spectrum antibacterial agents used to treat the bacterial infections in human beings. Though, antibiotics have been used in large extent for few decades, the presence of these molecules in the environment has attracted little



Scheme 1. Direct reduction of Mn(VII) to Mn(VI).



Scheme 2. Mn(V) formation by two-electron reduction, subsequent rapid reoxidation to Mn(VI).



Scheme 3. Mn(V) disproportionate in the presence of Mn(VII) to give Mn(VI) and Mn(IV).

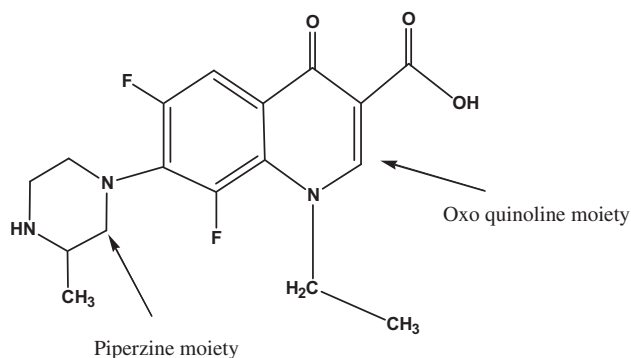
attention till today. Pharmaceuticals, of which antibacterial groups are important, have been identified as emerging environmental contaminants [16]. These pharmaceuticals have emerged as a novel class of pollutants because of their potential adverse effects on human health and the environment [17–19]. A major fraction of the prescribed dosage of fluoroquinolones enters into the domestic sewage due to partial metabolism in the human body. This represents the main route for entry of such pharmaceutical compounds into natural aquatic environment. Micrograms to nanogram per liter of fluoroquinolones have been detected in municipal wastewater and effluents from sewage treatment plants. The transformations of fluoroquinolone antibacterial agents in suitable water treatment process definitely play a major role in this context [20].

Lomefloxacin (LMF) (Scheme 4) belongs to the fluoroquinolone class of antibacterial agent, which is used to treat various bacterial infections, such as bronchitis and urinary tract infections. Permanganate has been extensively applied for the water and wastewater treatment from last five decades [21]. The oxidation of lomefloxacin by permanganate was studied to investigate the kinetics, mechanism, and transformation of lomefloxacin during wastewater treatment by permanganate.

2. Experimental

2.1. Materials and methods

To prepare the stock solution of substrate, an appropriate amount of LMF (Dr Reddy's Laboratory) was dissolved in double-distilled water. The stock solution of potassium permanganate (MERCK) was prepared in double-distilled water and standardized by titrating against standard oxalic acid [22]. NaOH (Sd Fine) was used to maintain the pH > 12 and



Scheme 4. Chemical structure of lomefloxacin.

NaClO₄ (RANKEM) was used to maintain constant ionic strength. All the chemicals and reagents were used of analytical grade.

2.1.1. Instruments used

- (1) UV–vis Spectrophotometer (CARY 50 Bio, Varian BV, the Netherlands) with a temperature controller and HPLC system (Agilent 1100 series, USA) were used for kinetic studies.
- (2) For product analysis, Agilent 6130 Series Quadrupole LC/MS. Column-Atlantis C18 (50 mm × 4.6 mm, 5 μm) dual mode was used.
- (3) pH meter (Elico model LI 120) was used for pH measurements.

2.2. Kinetic procedure

Lomefloxacin oxidation by permanganate was carried out under pseudo-first-order conditions, where LMF was taken in greater concentration than permanganate at 25 ± 0.2 °C. The reaction was initiated by mixing thermostatted solutions of permanganate and LMF with required quantity of alkali and ionic strength. The decrease in the concentration of permanganate with time at 526 nm was followed using a UV–vis Spectrophotometer to monitor the progress of the reaction. The application of Beer's law for permanganate was followed at 526 nm and the molar absorptivity was found to be $\epsilon = 2,283 \pm 20 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ which is in agreement with literature [23]. It was observed that there is no significant interference from other compounds at this wavelength. UV–visible Spectral changes during permanganate oxidation of LMF at 25 °C are shown in Fig. 1 and log (abs) vs. time plots were used to evaluate the pseudo-first-order rate constants (k'_{obs}). The plots were found to be linear, up to 90% conclusion of the reaction. The obtained k'_{obs} values were reproducible within an error margin of ±8% (Table 1) and are the mean of three separate runs. The product analysis was done by Agilent 6130 Series Quadrupole LC/MS. Column-Atlantis C18 (50 mm × 4.6 mm, 5 μm) dual mode.

3. Results and discussion

3.1. Stoichiometry and product identification method

The reaction mixtures containing an excess permanganate concentration over lomefloxacin, NaOH of 0.10 mol dm⁻³, and an adjusted ionic strength of 0.50 mol dm⁻³ has allowed for reaction to 12 h at

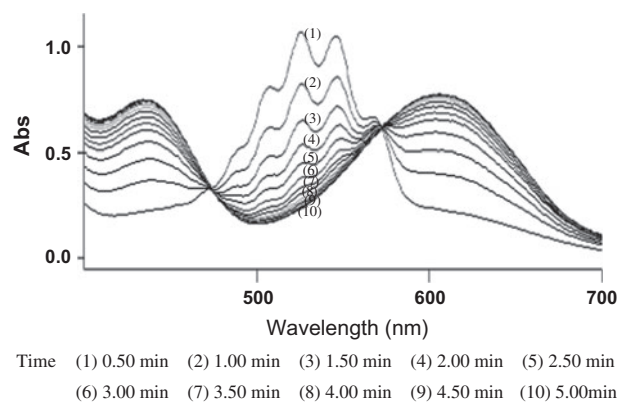


Fig. 1. UV–visible spectral changes during the permanganate oxidation of LMF at 25 °C.

25 ± 0.2 °C. The concentration of the unreacted permanganate was analyzed after the conclusion of the reaction. The results indicated that two mol of permanganate were consumed by one mol of lomefloxacin (Scheme 5).

The reactions by products were detected as ammonia by Nessler's test [24], Mn(VI) by visible spectrum and CO₂ by lime water test [25]. The reaction mixture containing lomefloxacin and excess concentration of MnO₄⁻ with constant OH⁻ were taken in a reaction cell. The reaction mixture was kept for 24 h and the products of LMF were investigated by Agilent quadrupole 6130 series HPLC system. For the HPLC analysis 0.1% HCOOH, acetonitrile was used as a solvent and flow rate 1.2 cm³ min⁻¹ was maintained using Column-Atlantis C18 (50 mm × 4.6 mm, 5 μm) dual mode (Fig. 2). LC/MS product analysis also shows that permanganate attacks the piperazinyl moiety of LMF and degrades completely and forms the final product 7-Amino-1-ethyl-6, 8-difluoro-4-oxo-quinoline-3-carboxylic acid, Mn(VI), loss of H₂O, CO₂, and NH₃ from the piperazine group in the LMF molecule.

3.2. Reaction order

Reaction orders were experimentally determined by graphical method. Reaction orders were obtained from slopes of log k'_{obs} vs. log (concentration) plots by changing the concentrations of permanganate, LMF and alkali, while maintaining all other experimental conditions constant.

3.3. Influence of permanganate

The permanganate concentration was changed in the range of 5.00 × 10⁻⁵ mol dm⁻³ to 5.00 × 10⁻⁴ mol dm⁻³ with constant concentrations of

Table 1

Influence of variation of permanganate, LMF and OH^- on the oxidation of lomefloxacin by permanganate in aqueous alkaline medium at 25°C. And $I = 0.50 \text{ mol dm}^{-3}$

10^4 [Permanganate] (mol dm^{-3})	10^3 [LMF] (mol dm^{-3})	10^1 [OH^-] (mol dm^{-3})	$10^2 k'_{\text{obs}}$ (s^{-1})	$10^2 k'_{\text{cal}}$ (s^{-1})	k'_{app} (Expt.) $\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$
0.50	2.00	1.00	2.02	1.91	
1.00	2.00	1.00	2.03	1.91	
1.50	2.00	1.00	2.01	1.91	
2.00	2.00	1.00	2.00	1.91	
2.50	2.00	1.00	1.96	1.91	
3.00	2.00	1.00	1.92	1.91	
3.50	2.00	1.00	1.90	1.91	
2.50	0.50	1.00	0.49	0.49	
2.50	1.00	1.00	0.96	0.97	
2.50	1.50	1.00	1.50	1.43	
2.50	2.00	1.00	1.96	1.91	9.357
2.50	2.50	1.00	2.47	2.40	
2.50	3.00	1.00	2.98	2.82	
2.50	3.50	1.00	3.24	3.30	
2.50	2.00	0.20	0.52	0.46	
2.50	2.00	0.40	0.96	0.88	
2.50	2.00	0.80	1.71	1.60	
2.50	2.00	1.00	1.96	1.91	0.142
2.50	2.00	1.20	2.35	2.21	
2.50	2.00	1.60	2.74	2.73	
2.50	2.00	2.00	3.06	3.10	

Note: $\pm 8\%$ Error.

LMF, $2.00 \times 10^{-3} \text{ mol dm}^{-3}$, and alkali, 0.10 mol dm^{-3} , NaClO_4 , 0.40 mol dm^{-3} . The plots of \log [absorbance] vs. time, for various initial concentrations of permanganate were found to be linear, with values of $R^2 > 0.988$; k'_{obs} values (Table 1) indicated the unit order dependence of permanganate.

3.4. Influence of [LMF]

To study the influence of LMF concentration on the rate of reaction, the concentration of substrate, LMF was varied within the range of $0.50 \times 10^{-3} \text{ mol dm}^{-3}$ to $3.50 \times 10^{-3} \text{ mol dm}^{-3}$ maintained by keeping reaction conditions constant. The rate constant, k'_{obs} (Table 1), was found to increase with LMF concentration increases. The plot of $\log k'_{\text{obs}}$ vs. \log [LMF] confirms the fractional order (0.810) ($R^2 > 0.971$) dependence on LMF. The order with respect to LMF most probably results from the complex formation between oxidant and LMF.

3.5. Influence of [OH^-]

The influence of alkali concentration on the reaction rate was studied, the concentration of alkali was varied between 0.02 mol dm^{-3} and 0.20 mol dm^{-3}

keeping other reaction conditions constant (Table 1). The rate constant, k'_{obs} , was observed to an instant increase with increase in concentration of OH^- . The plot of $\log k'_{\text{obs}}$ vs. \log [OH^-] confirms fractional order dependence on OH^- ions (0.510) ($R^2 > 0.993$).

3.6. Influence of ionic strength

To study the influence of ionic strength on the rate of reaction, the concentration of sodium perchlorate was varied from 0.10 to 1.00 mol dm^{-3} at constant permanganate, LMF and alkali concentration. It has been observed that increase in ionic strength has negligible influence or no effect on to the rate constant. It was observed that increase in ionic strength had negligible effect or no influence on the rate constant. This points out that insignificant effect of variation of ionic strength on the rate of reaction explains the reaction is between two neutral species or a neutral and a charged species [26].

3.7. Influence of dielectric constant

The influence of dielectric constant (D) was analyzed by changing the tertiary-butanol–water volume in the reaction mixture, while all remaining conditions

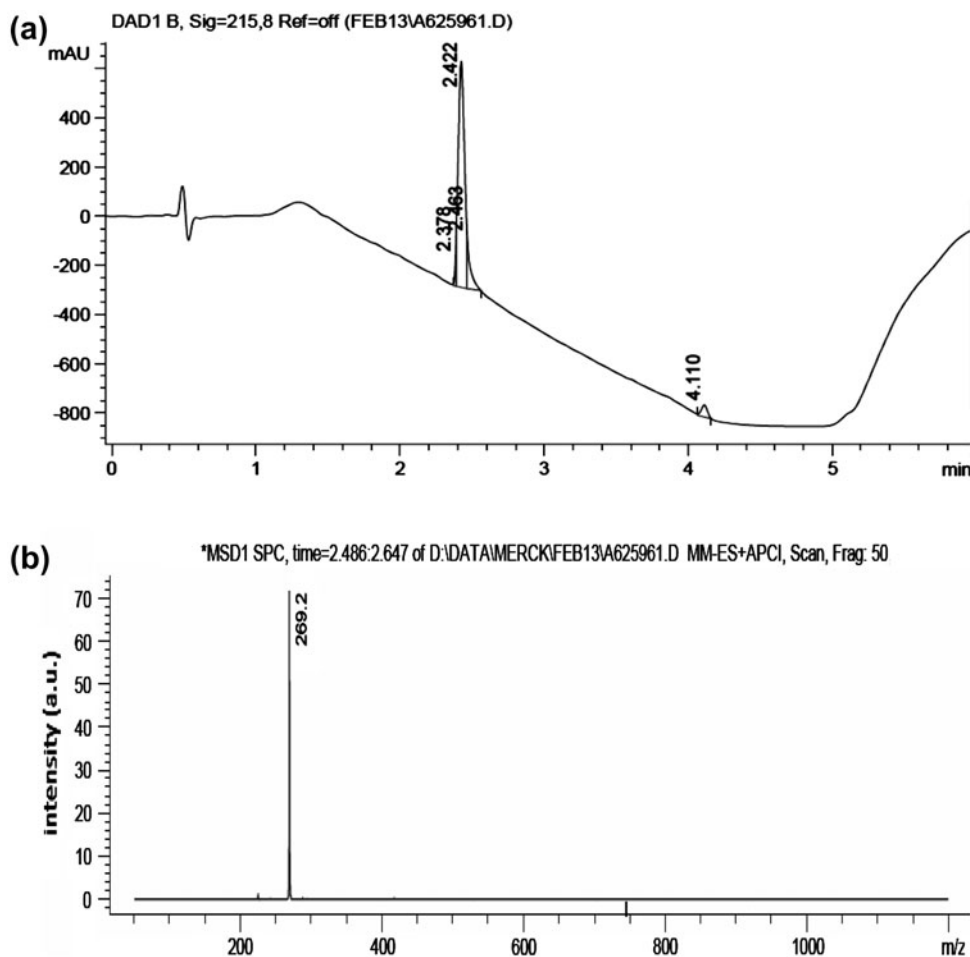


Fig. 2. LC/MS spectra of lomefloxacin oxidation products. (a) Total ion chromatogram (TIC). (b) Mass spectrum of reaction product m/z 269.

are kept unchanged. The rate of reaction decreases with increase in the volume of tertiary-butanol. The plot of $\log k'_{\text{obs}}$ vs. $1/D$ was extending along a straight line having a negative slope of -144.30 and $R^2 \geq 0.974$. The negative slope indicates that the interaction is between negative ions and dipole [27].

3.8. Influence of temperature

The kinetics study was conducted at four distinct temperatures by changing the concentrations of LMF by maintaining other conditions constant. Increase in temperature from 10 to 40°C increased rate constants. Arrhenius equation was made use to evaluate the thermodynamic measurable activation parameters. The energy of activation, E_a , ($27.59 \pm 2.76 \text{ kJ mol}^{-1}$) related to those rate constants were reviewed from plot of $\log k'_{\text{obs}}$ vs. $1/T$ ($R^2 > 0.988$) and other activation parameters ΔH^\ddagger , ΔS^\ddagger , ΔG^\ddagger calculation were made and are specified in Tables 2 and 3.

3.9. Influence of initially added products

Permanganate ion concentration variations carried to change from $0.50 \times 10^{-4} \text{ mol dm}^{-3}$ to $3.5 \times 10^{-4} \text{ mol dm}^{-3}$ at constant lomefloxacin and alkali concentrations and ionic strength. It was observed that initially added permanganate ions have no influence on the rate constant. The rate equation for the experimental results is given as follows. Order with respect to each reactant is given in Eq. (1) with $\pm 8\%$ error.

$$\text{Rate} = \frac{-d[\text{MnO}_4^-]}{dt} = k[\text{MnO}_4^-]^1[\text{LMF}]^{0.81}[\text{OH}^-]^{0.51} \quad (1)$$

3.10. Theoretical calculations

The geometry optimization of reactants and activated complex were carried out using density functional theory (DFT). The reactants are fully optimized,

Table 2
Influence of temperature on kinetics of oxidation of lomefloxacin by alkaline permanganate

Temperature K	k''_{app} (dm ³ mol ⁻¹ s ⁻¹)	$1/T \times 10^3$	$10^2 k$ s ⁻¹	log k	$k/T \times 10^3$	log (k/T)
283	5.16	3.53	1.03	0.71	18.23	-1.74
293	6.85	3.41	1.37	0.84	23.38	-1.63
298	8.90	3.36	1.78	0.95	29.87	-1.52
313	15.55	3.20	3.11	1.19	49.68	-1.30

Table 3
Thermodynamic activation parameters for the oxidation of LMF by alkaline permanganate

Activation parameters	Values
E_a (kJ mol ⁻¹)	27.59 ± 2.76
ΔH (kJ mol ⁻¹)	25.55 ± 2.60
ΔS (JK ⁻¹ mol ⁻¹)	-0.87 ± 0.10
ΔG (kJ mol ⁻¹)	25.80 ± 2.59
log A	5.70 ± 0.28

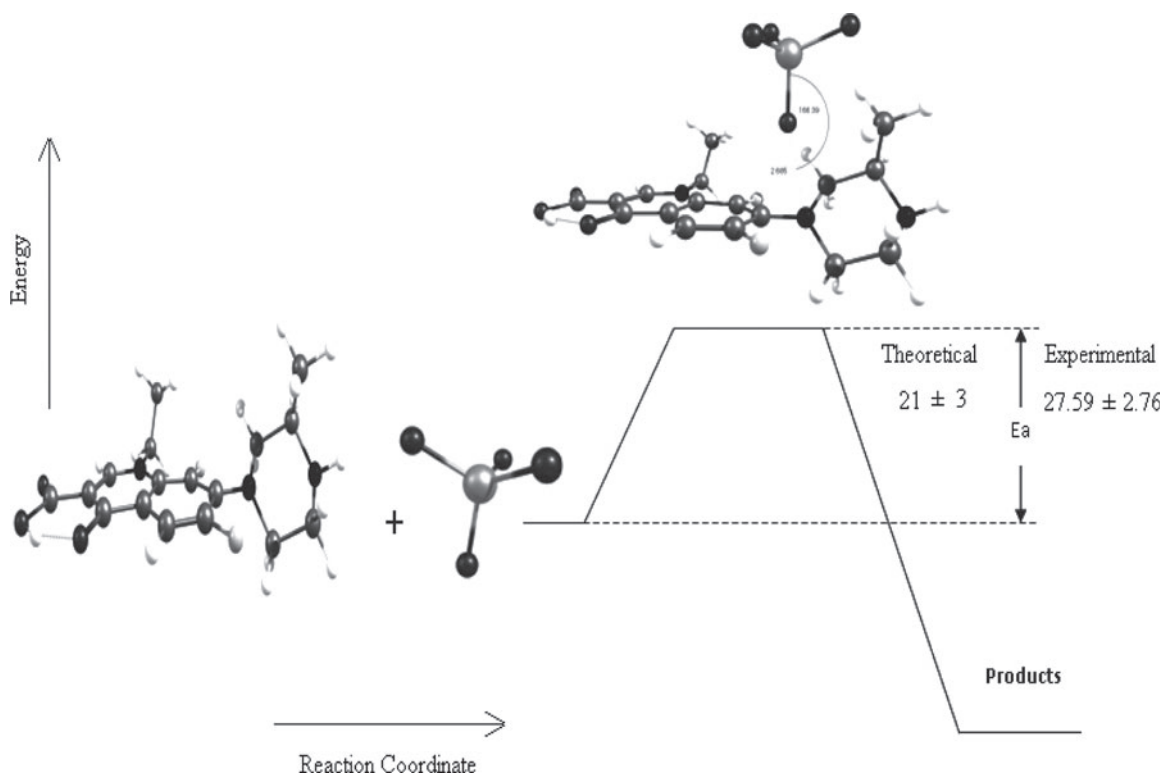
and the activated complex was partially optimized. The BP86 functional and def 2-TZVPP basis set inside the RI (resolution-of-the-identity) approximation [28,29] (RI-BP86/def2-TZVPP in short) was employed for the optimization procedure. Frequency calculations

of the optimized structures were done to ensure that they were true minima not the transition states. The DFT calculations were accomplished with the Turbo mole program package (Version-6.4) [30].

LMF reacts with MnO_4^- giving rise to the formation of the activated complex, so that the formed activated complex decomposes to give the product. The calculated activation energy 21 ± 3.0 kJ mol⁻¹ is in agreement with experimentally determined activation energy 27.59 ± 3.0 kJ mol⁻¹ (Fig. 3).

3.11. Test for free radicals

The participatory study of free radicals in the reaction with addition acrylonitrile in the reaction mixture.



The calculations were done at BP86/def 2-TZVPP level of theory using Turbo mole 6.4 suite software.

Fig. 3. Energy of activation for LMF/ MnO_4^- reaction based on kinetic data and LC-MS spectra.

The reactants were allowed to react in an inert atmosphere for 6 h and addition of methanol to the reaction mixture did not produce any precipitate, which indicates the absence of free radicals [31].

3.12. Proposed reaction pathway

Permanganate ion is a potent oxidant in an aqueous alkaline media. Since it shows various oxidation states, the stoichiometric results and the pH of reaction medium play a significant role. Present experimental conditions above pH 12, the reduced form of manganese (VII) is Mn(VI), which is stable and further reduction of Mn(VI) may be checked as reported by Simandi et al. [13,32]. However, prolong standing, green Mn(VI) is reduced Mn(IV) under experimental conditions. The permanganate shows various oxidation states, such as Mn(VII), Mn(V), and Mn(VI) in the alkaline medium. The color of the reaction mixture turns from violet to blue, and then, it turns to green except the accumulation of hypomanganate (V). The violet color originates from the pink of permanganate, and blue color from hypomanganate (V) was viewed during the progress of the reaction. The change in the color of permanganate solution from violet heptavalent manganese ion to dark green hexavalent manganese ion through blue pentavalent manganese ion has been observed.

It is clear from Fig. 1 that during the course of reaction the absorbance of permanganate decreases at 526 nm and the absorbance of product manganate (VI) increases at 610 and 460 nm. If a longer time is elapsed, the solution becomes colorless and then appears brown precipitate. This proposes that the products formed may be undergoing also oxidation ensuing in lesser oxidation state of manganese, Mn(IV). In fact, a dark-brown precipitate of MnO_2 is observed in many redox reactions involving permanganate when the pH of the medium is not acidic enough to enable further reduction of Mn(IV) to Mn(II). This experimental evidence is in good accordance with the reaction pathway proposed in Scheme 3, where the formation of Mn(IV)

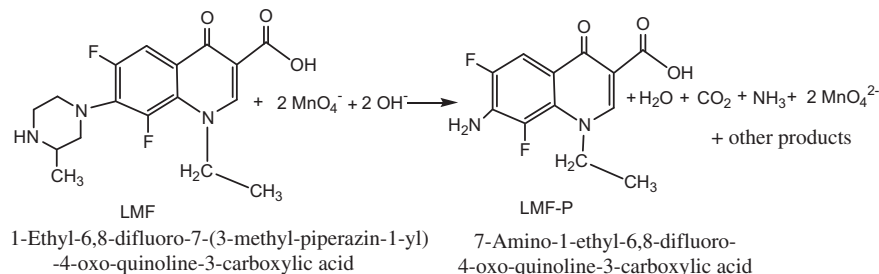
is predicted although kinetically handicapped. The results indicate that OH^- ions first combined with permanganate to form a basic permanganate reactive species $[\text{MnO}_4 \cdot \text{OH}]^{2-}$ in a previous to equilibrium state. Afterward $[\text{MnO}_4 \cdot \text{OH}]^{2-}$ reacts with LMF to form an complex (C) (Intermediate). The less than unit order with respect to LMF may be due to the complex formation between the $[\text{MnO}_4 \cdot \text{OH}]^{2-}$ and LMF before the rate determining step. The major reaction product identified by the analysis LC/MS spectrum was 7-amino-1-ethyl-6, 8-difluoro-4-oxo-quinoline-3-carboxylic acid (LMF-P), which has a lomefloxacin structure, in which the piperazine ring was replaced with $-\text{NH}_2$ group. The loss of piperazine ring results in mass loss 99 daltons and addition of $-\text{NH}_2$ group results in the mass increases with 16 daltons. This would give up a net reduction of 83 daltons comparative to the parent lomefloxacin molecule, corresponding to the mass disparity between LMF (MW = 351) and LMF-P (MW = 268). The same oxidation product was reported for lomefloxacin oxidation by manganese oxide and also by TiO_2 photo catalysis [33,34]. Scheme 6 shows the degradation mechanism of LMF by permanganate manganese in alkaline medium. In this degradation pathway, the complete elimination of piperazynilic ring was observed for LMF. At the same time, nitrogen moieties in LMF were transformed into NH_3 (NH_4^+ ions) by the oxidation. This result is consistent with previously reported literature for ciprofloxacin and norfloxacin [18,35].

As stated in Schemes 5 and 6:

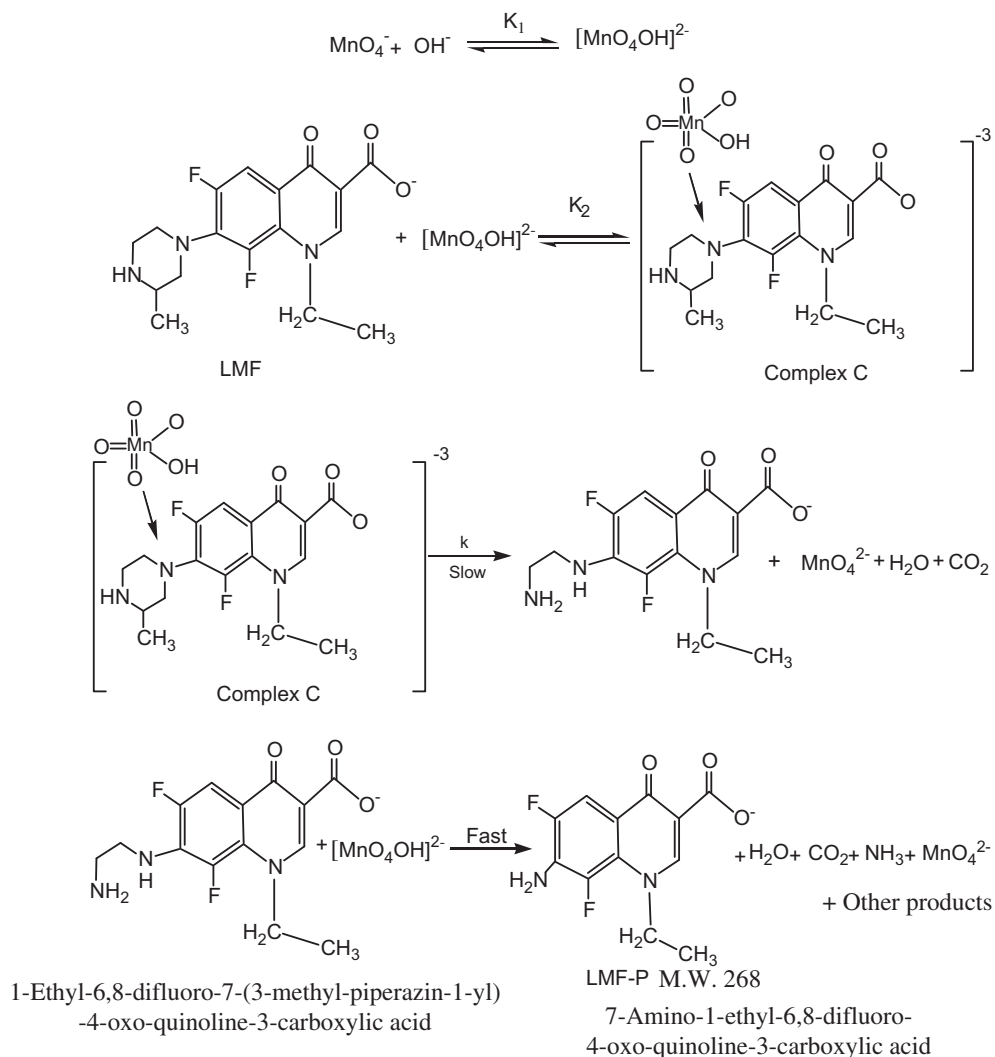
$$\text{Rate} = \frac{-d[\text{MnO}_4^-]}{dt} = kK_1K_2[\text{MnO}_4^-][\text{LMF}]_f[\text{OH}^-]_f \quad (2)$$

The total $[\text{MnO}_4^-]$ can be written as:

$$\begin{aligned} [\text{MnO}_4^-]_T &= [\text{MnO}_4^-]_f + [\text{MnO}_4 \cdot \text{OH}]^{2-} + [\text{Complex}] \\ &= [\text{MnO}_4^-]_f + K_1[\text{MnO}_4^-][\text{OH}^-] \\ &\quad + K_1K_2[\text{MnO}_4^-][\text{OH}^-][\text{LMF}] \\ &= [\text{MnO}_4^-]_f(1 + K_1[\text{OH}^-] + K_1K_2[\text{OH}^-][\text{LMF}]) \end{aligned}$$



Scheme 5. Stoichiometric equation for the oxidation of lomefloxacin by alkaline permanganate.



Scheme 6. Proposed mechanism for the oxidation of lomefloxacin by alkaline permanganate.

where T and f stands for total and free

$$[\text{LMF}]_T = [\text{LMF}]_f \quad (5)$$

$$[\text{MnO}_4^-]_f = \frac{[\text{MnO}_4^-]_T}{1 + K_1[\text{OH}^-] + K_1K_2[\text{OH}^-][\text{LMF}]}$$

(3) Substituting Eqs. (3)–(5) in Eq. (2) we get,

Similarly, total $[\text{OH}^-]$ can be calculated as:

$$\text{Rate} = \frac{kK_1K_2[\text{MnO}_4^-][\text{OH}^-][\text{LMF}]}{1 + K_1[\text{OH}^-] + K_1K_2[\text{OH}^-][\text{LMF}]} \quad (6)$$

$$[\text{OH}^-]_T = [\text{OH}^-]_f + [\text{MnO}_4 \cdot \text{OH}]^{2-} + [\text{Complex}]$$

In view of low concentration of MnO_4^- and lomefloxacin used, above equation can be written as:

$$\frac{\text{Rate}}{[\text{MnO}_4^-]} = k_{\text{obs}} = \frac{kK_1K_2[\text{OH}^-][\text{LMF}]}{1 + K_1[\text{OH}^-] + K_1K_2[\text{OH}^-][\text{LMF}]} \quad (7)$$

$$[\text{OH}^-]_T = [\text{OH}^-]_f \quad (4)$$

Eq. (7) confirms all the observed orders with respect to different species, which can be verified by rearranging it to

Similarly,

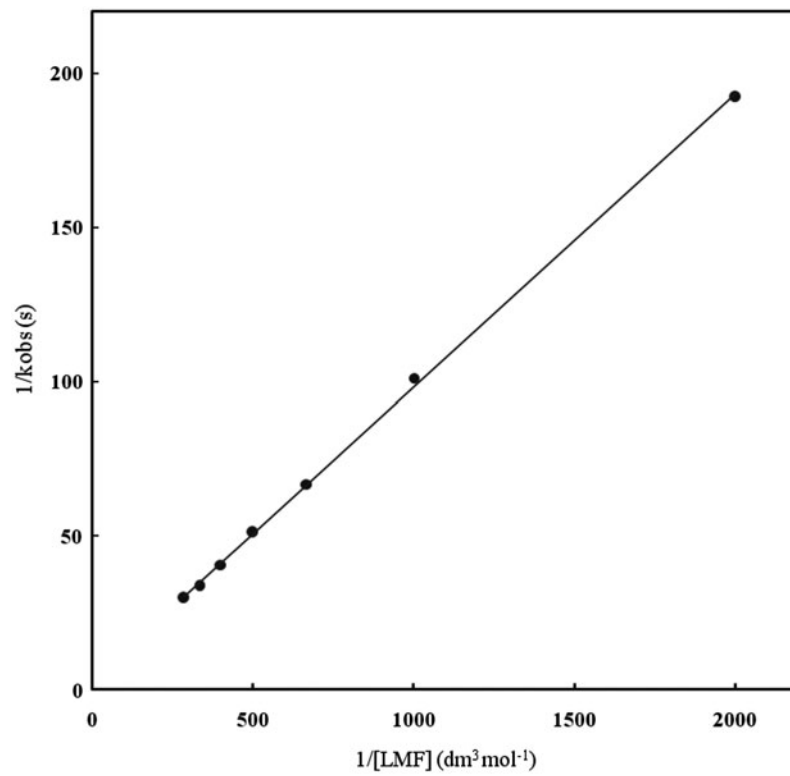


Fig. 4. Plot of $1/k'_{\text{obs}}$ vs. $1/[\text{LMF}]$ for verification of rate equation (law) (7) in the form of (8) on the permanganate oxidation of lomefloxacin in aqueous alkaline medium at 25 °C.

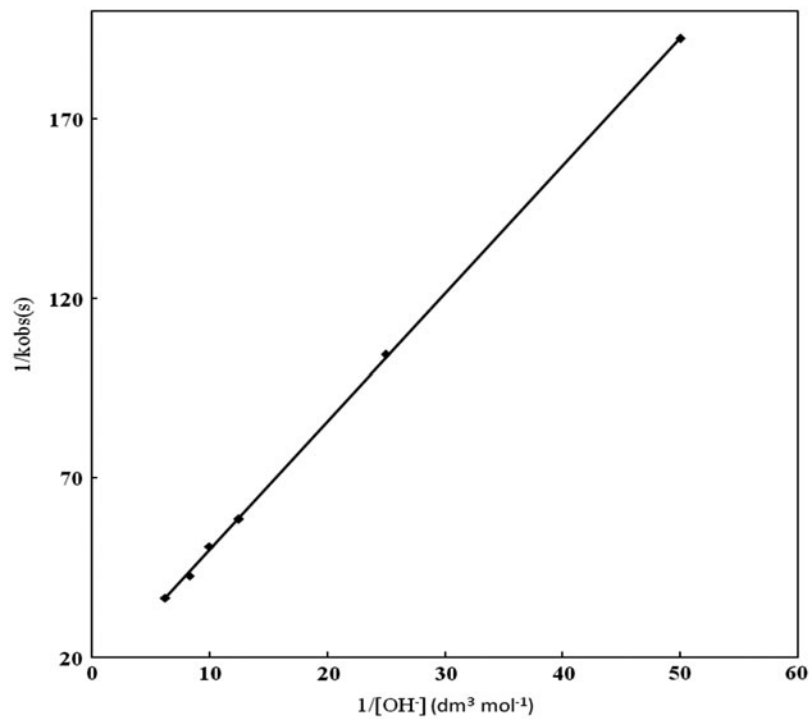


Fig. 5. Plot of $1/k'_{\text{obs}}$ vs. $1/[\text{OH}^-]$ for verification of rate equation (law) (7) in the form of (8) on the permanganate oxidation of lomefloxacin in aqueous alkaline medium at 25 °C.

$$\frac{1}{k_{\text{obs}}} = \frac{1}{kK_1K_2[\text{OH}^-][\text{LMF}]} + \frac{1}{kK_2[\text{LMF}]} + \frac{1}{k} \quad (8)$$

The plots of $1/k'_{\text{obs}}$ vs. $1/[\text{LMF}]$ (Fig. 4) and $1/k'_{\text{obs}}$ vs. $1/[\text{OH}^-]$ (Fig. 5) are drawn, cited for verifying the rate law. A plot of $1/k'_{\text{obs}}$ vs. $1/[\text{LMF}]$ (Michaelis Menten plot) (Fig. 4) shows intercepting, which is in concord with complex being formed [29]. The UV–visible spectra of the reaction mixture are evidence for a hypsochromic shift of 4 nm from 287 to 283 nm and hyperchromicity at 283 nm, which provides spectroscopic evidence in support of complex formation [36]. Two isobestic points were observed for this reaction indicating the presence of two equilibrium steps previous to the slow step of the reaction mechanism [37,38]. The literature review indicates that piperazine ring of lomefloxacin is the tendency of reactivity toward oxidation [39].

The oxidation mechanism of lomefloxacin is quite similar to that of ciprofloxacin. The second-order rate constant of LMF ($9.36 \pm 0.75 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$) is higher than that corresponding to norfloxacin ($1.63 \pm 0.08 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$) [32], and ciprofloxacin ($0.16 \pm 0.01 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$) [18]. The observed higher rate constant of LMF as compared to norfloxacin and ciprofloxacin (Fig. 6) is due to the presence of two highly electronegative fluorine atoms on oxoquinoline moiety. Inductive effect ($-I$) due to the electron retreating of the two fluorine atoms the aromatic ring of oxoquinoline moiety becomes electron deficient, which in turn withdraws electrons from nitrogen atom of piperazine moiety making it electron deficient and also the nitrogen atom of the piperazine moiety releases electrons toward oxoquinoline moiety (Resonance effect) as shown in the resonance structure due to which nitrogen atom becomes electron deficient, susceptible for permanganate ion attack.

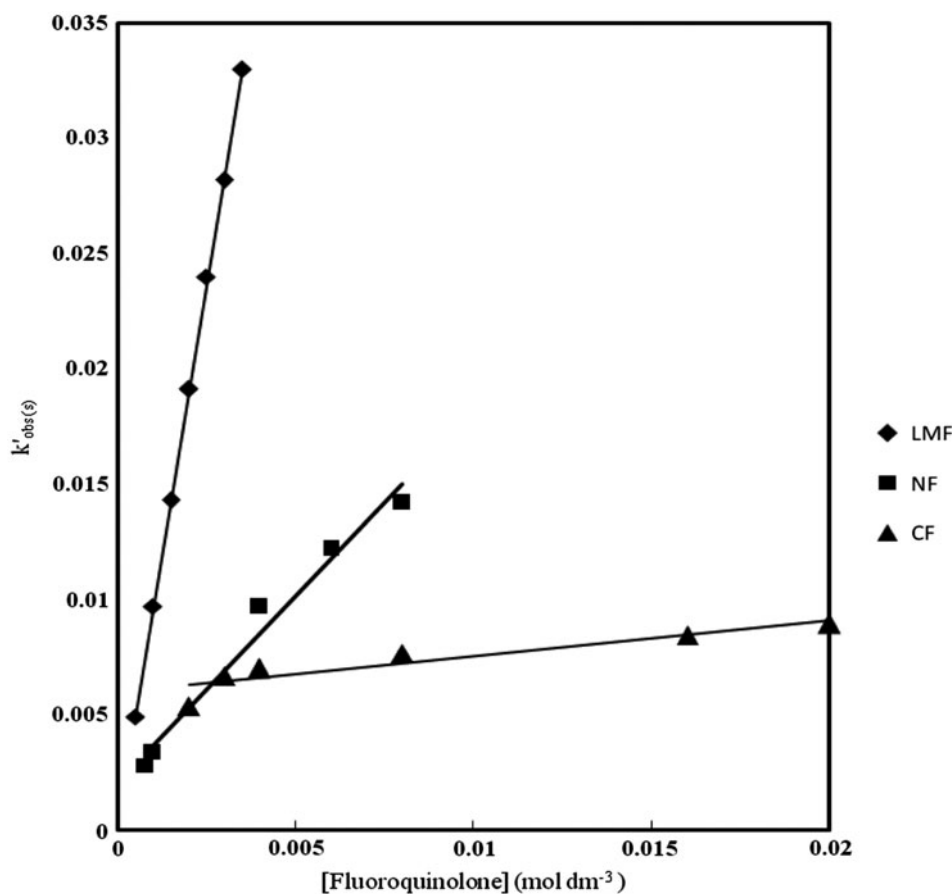
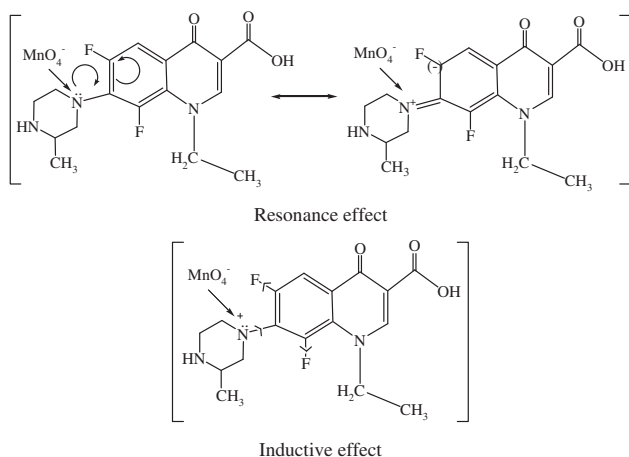


Fig. 6. Second-order plots for oxidation of fluoroquinolones by permanganate in aqueous alkaline media. *LMF: This paper; **CF: Ref. [17]; and ***NF: Ref. [29].



The plots of $1/k'_{\text{obs}}$ vs. $1/[\text{LMF}]$ of ($R^2 > 0.971$, Fig. 4) and $1/k'_{\text{obs}}$ vs. $1/[\text{OH}^-]$ ($R^2 > 0.999$, Fig. 5) give the slopes and intercepts values and help to calculate the values of K_1 , K_2 , and k (i.e. $2.20 \pm 0.15 \text{ mol dm}^{-3}$, $84.78 \pm 6 \text{ mol dm}^{-3}$ and $0.6 \pm 0.03 \text{ s}^{-1}$), respectively, as per the conditions in Table 1. The value of K_1 is in concord with the earlier studies [33]. By using these values, the rate constants were calculated under different experimental conditions, and there is a realistic concurrence between the calculated and experimental data.

The average values of ΔH^\ddagger and ΔS^\ddagger are in favor of electron transfer processes. The values of ΔS^\ddagger in the range for radical reaction has been ascribed to the nature of electron pairing and unpairing process and to the loss of degrees of freedom formerly avail to the reactants upon the formation of rigid transition state [40]. The negative value of ΔS^\ddagger points out that the complex (C) is more sequenced than the reactants [41]. The experiential relatively moderate enthalpy of activation and a comparatively low value of the entropy of activation in addition to a higher rate constant of the slow step point toward that the oxidation apparently taking place via inner-sphere mechanism [42,43].

4. Conclusion

The outcome of this study is to indicate that lomefloxacin is a fluoroquinolone group of antibiotic that is partly reduced chemically under the experimental condition, providing the degraded products. In this reaction, the function of pH is important. It is interesting that the oxidant species permanganate requires $\text{pH} > 12$, below which the system becomes disturbed and the reaction proceeds further to give a reduced oxidation product as manganese (IV), which slowly develops a yellow turbidity. The previous studies

show that de-alkylated products of LMF have reduced antibacterial action [44]. The oxidation–degradation mechanism and pathway proposed for LMF, including the elimination of piperazinyl ring, suggest the effective oxidation by permanganate can be used in the water treatment at the place polluted by fluoroquinolone antibacterial agents. Rate constant with respect to slow step and other equilibrium constants concerned in the mechanism are calculated and activation parameters with reverence to slow step of reaction were calculated. The total mechanism described here is in agreement with mechanism, product, and kinetic studies. These results indicate that attractive treatment technologies for the degradation of fluoroquinolones in aqueous solution are needed because under oxidation–degradation process most of produced intermediates can be finally mineralized into CO_2 , water, and mineral species.

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References

- [1] S. Caron, R.W. Dugger, S.G. Ruggeri, J.A. Ragan, D.H. Brown Ripin, Large-scale oxidations in the pharmaceutical industry, *Chem. Rev.* 106 (2006) 2943–2989.
- [2] A. Shaabani, F. Tavasoli-Rad, D.G. Lee, Potassium permanganate oxidation of organic compounds, *Synth. Commun.* 35 (2005) 571–580.
- [3] D.G. Lee, Phase transfer assisted permanganate oxidations, in: W.S. Trahanovsky (Ed.), *Oxidation in Organic Chemistry, Part D*, Academic Press, New York, NY, 1982, pp. 147–204 (Chapter 11).
- [4] L.I. Simándi, in: S. Patai, Z. Rappoport (Eds.), *The Chemistry of Functional Groups*, Wiley, Chichester, Supplement C., 1983, p. 548 (Chapter 13).
- [5] D.G. Lee, E.J. Lee, K.C. Brown, *Phase Transfer Catalysis, New Chemistry, Catalysis and Applications*, ACS Symposium Series, vol. 326, American Chemical Society, Washington, DC, 1987, pp. 82–95.
- [6] A. Shaabani, F. Tavasoli-Rad, D.G. Lee, Potassium permanganate oxidation of organic compounds, *Synth. Commun.* 35(4) (2005) 571–580.
- [7] R.M. Kulkarni, D.C. Bilehal, S.T. Nandibewoor, Kinetic and mechanistic study of oxidation of sulfamethoxazole by alkaline permanganate, *Inorg. React. Mech.* 3 (4) (2002) 239–247.
- [8] J. Zhang, X. Guan, Ru(III)-catalyzed permanganate oxidation of bisphenol A, *Desalin. Water. Treat.* 52 (2014) 4592–4601.
- [9] T. Lin, S. Pan, W. Chen, C. Yu, Effect of potassium permanganate pre-oxidation on fouling and pore size of ultrafiltration membrane for drinking water treatment, *Desalin. Water Treat.* 50(1–3) (2012) 254–263.

- [10] D.C. Bilehal, R.M. Kulkarni, S.T. Nandibewoor, Comparative study of the chromium(III) catalysed oxidation of l-leucine and l-isoleucine by alkaline permanganate: A kinetic and mechanistic approach, *J. Mol. Catal.* 232 (2005) 21–28.
- [11] R.M. Kulkarni, D.C. Bilehal, S.T. Nandibewoor, Deamination and decarboxylation in the chromium(III)-catalysed oxidation of L-valine by alkaline permanganate and analysis of chromium(III) in microscopic amounts by a kinetic method, *Transition Met. Chem.* 28 (2003) 199–208.
- [12] A.A.P. Khan, A. Khan, A.M. Asiri, N. Azum, M.A. Rub, S.B. Khan, M.M. Rahman, A.O. Al-Youbi, Study of the base-catalysed oxidation of the anti-bacterial and anti-protozoal agent metronidazole by permanganate ion in alkaline medium, *Res. Chem. Intermed.* 40 (2014) 1703–1714.
- [13] L.I. Simandi, M. Jaky, C.R. Savage, Z.A. Schelly, Kinetics and mechanism of the permanganate ion oxidation of sulfite in alkaline solutions. The nature of short-lived intermediates, *J. Am. Chem. Soc.* 107 (1985) 4220–4224.
- [14] D.C. Bilehal, R.M. Kulkarni, S.T. Nandibewoor, Kinetics and mechanistic study of the ruthenium (III) catalyzed oxidative deamination and decarboxylation of L-valine by alkaline permanganate, *Can. J. Chem.* 79(12) (2001) 1926–1933.
- [15] A. Bohm, M. Adam, H. Mauermann, S. Stein, K. Mullen, 2,6-diaza-4,8-dicyanosemibullvalene—a short-lived intermediate, *Tetrahedron Lett.* 33 (1992) 8047–8050.
- [16] M.L. Johnson, L. Berger, L. Philips, R. Speare, Fungicidal effects of chemical disinfectants, UV light, desiccation and heat on the amphibian chytrid *Batrachochytrium dendrobatidis*, *Dis. Aquat. Org.* 57 (2003) 255–260.
- [17] H. Yuan, X. Zhou, Y.L. Zhang, Degradation of acid pharmaceuticals in the UV/H₂O₂ process: Effects of humic acid and inorganic salts, *Clean—Soil, Air, Water* 41 (2013) 43–50.
- [18] R.M. Kulkarni, M.S. Hanagadakar, R.S. Malladi, M.S. Gudaganatti, H.S. Biswal, S.T. Nandibewoor, Transformation of linezolid during water treatment with chlorine: A kinetic study, *Indian J. Chem. Technol.* 21 (2014) 38–43.
- [19] M.S. Gudaganatti, M.S. Hanagadakar, R.M. Kulkarni, R.S. Malladi, R.K. Nagarale, Transformation of levofloxacin during water chlorination process: Kinetics and pathways, *Prog. React. Kinet. Mech.* 37 (2012) 366–382.
- [20] B. Halling-Sørensen, S.N. Nielsen, P.F. Lanzky, F. Ingerslev, H.C. Holten Lützhøft, S.E. Jørgensen, Occurrence, fate and effects of pharmaceutical substances in the environment—A review, *Chemosphere* 36 (1998) 357–393.
- [21] K.A. Thabaj, S.D. Kulkarni, S.A. Chimatadar, S.T. Nandibewoor, Oxidative transformation of ciprofloxacin by alkaline permanganate—A kinetic and mechanistic study, *Polyhedron* 26 (2007) 4877–4885.
- [22] G.H. Jeffery, J. Bassett, J. Mendham, R.C. Denny, *Vogel's Textbook of Quantitative Chemical Analysis*, fifth ed., ELBS, Longman, Essex, 1996, p. 370.
- [23] G.C. Hiremath, R.M. Kulkarni, S.T. Nandibewoor, Kinetics of oxidative degradation and deamination of atenolol by aqueous alkaline permanganate, *Indian J. Chem., Sect. A* 44(2) (2005) 245–250.
- [24] F. Feigl, *Spot Tests in Organic Analysis*, sixth ed., Elsevier, New York, NY, 1960, p. 195.
- [25] A.K. Das, M. Das, Kinetics and mechanism of ruthenium(III) catalysed oxidation of formic acid by cerium (IV) in aqueous sulfuric acid media, *J. Chem. Soc., Dalton Trans.* 4 (1994) 589–593.
- [26] K.J. Laidler, *Chemical Kinetics*, vol. 183, third ed., Pearson Education, Delhi, 2004, p. 198.
- [27] E.S. Amis, *Solvent Effects on Reaction Rates and Mechanisms*, Academic Press, New York, NY, 1966.
- [28] O. Christiansen, H. Koch, P. Jørgensen, The second-order approximate coupled cluster singles and doubles model CC2, *Chem. Phys. Lett.* 243 (1995) 409–418.
- [29] A. Köhn, C. Hättig, Analytic gradients for excited states in the coupled-cluster model CC2 employing the resolution-of-the-identity approximation, *J. Chem. Phys.* 119 (2003) 5021–5036.
- [30] R. Ahlrichs, M. Bär, M. Häser, H. Horn, C. Kölmel, Electronic structure calculations on workstation computers: The program system turbomole, *Chem. Phys. Lett.* 162 (1989) 165–169.
- [31] A.A.P. Khan, A.M. Asiri, N. Azum, M.A. Rub, A. Khan, A.O. Al-Youbi, Kinetics and mechanistic investigation of decarboxylation for the oxidation of levofloxacin by chloroamine-T in acidic medium, *Ind. Eng. Chem. Res.* 51 (2012) 4819–4824.
- [32] P.L. Timmanagoudar, G.A. Hiremath, S.T. Nandibewoor, Permanganate oxidation of chromium (III) in aqueous alkaline-medium—A kinetic study by the stopped-flow technique, *Trans. Met. Chem.* 22 (1997) 193–196.
- [33] H. Zhang, C.H. Huang, Oxidative transformation of fluoroquinolone antibacterial agents and structurally related amines by manganese oxide, *Environ. Sci. Technol.* 39 (2005) 4474–4483.
- [34] A. Taicheng, Y. Hai, S. Weihua, L. Guiying, L. Haiying, W.J. Cooper, Mechanistic considerations for the advanced oxidation treatment of fluoroquinolone pharmaceutical compounds using TiO₂ heterogeneous catalysis, *J. Phys. Chem. A* 114 (2010) 2569–2575.
- [35] P.N. Naik, S.A. Chimatadar, S.T. Nandibewoor, Kinetics and oxidation of fluoroquinoline antibacterial agent, norfloxacin, by alkaline permanganate: A mechanistic study, *Ind. Eng. Chem. Res.* 48 (2009) 2548–2555.
- [36] D.C. Bilehal, R.M. Kulkarni, S.T. Nandibewoor, Kinetics and mechanism of oxidation of Nicotinate ion by alkaline permanganate, *Z. Phys. Chem.* 217 (2003) 1–12.
- [37] A.A.P. Khan, A. Mohd, S. Bano, A. Husain, K.S. Siddiqi, Kinetic and mechanistic investigation of the oxidation of the antibacterial agent levofloxacin by permanganate in alkaline medium, *Trans. Met. Chem.* 35 (2010) 117–123.
- [38] D.N. Sathyanarayana, *Electronic Absorption Spectroscopy and Related Techniques*, Universities Press, Hyderabad, 2001, p. 12.
- [39] M.C. Dodd, A. Shah, U. von Gunten, C.H. Huang, Interactions of fluoroquinolone antibacterial agents with aqueous chlorine: Reaction kinetics, mechanisms, and transformation pathways, *Environ. Sci. Technol.* 39 (2005) 7065–7076.

- [40] R.V. Hosahalli, K.S. Byadagi, S.T. Nandibewoor, S.A. Chimatadar, Kinetics and mechanism of ruthenium (III) catalyzed oxidation of chloromphenicol—An antibiotic drug by diperiodatocuprate(III) in aqueous alkaline medium, *Kinet. Catal.* 53 (2012) 65–74.
- [41] A.M. Asiri, A.A.P. Khan, A. Khan, Spectroscopic investigation on kinetics and mechanistic aspects to electron-transfer process into quinolinium dichromate oxidation of a high blood pressure drug captopril in acidic medium, *J. Mol. Liq.* 203 (2015) 1–6.
- [42] K.W. Hicks, Kinetics of the permanganate ion–potassium octacyanotungstate(IV) reaction, *J. Inorg. Nucl. Chem.* 38 (1976) 1381–1383.
- [43] S.A. Farokhi, S.T. Nandibewoor, Kinetic, mechanistic and spectral studies for the oxidation of sulfanilic acid by alkaline hexacyanoferrate(III), *Tetrahedron* 59 (2003) 7595–7602.
- [44] G. Phillips, B.E. Johnson, J.J. Ferguson, The loss of antibiotic activity of ciprofloxacin by photodegradation, *J. Antimicrob. Chemother.* 26 (1990) 783–789.