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Kinetics and mechanism of electron transfer reactions: Oxidative degradation of fluoroquinolone drugs in aqueous acidic/alkaline medium†

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Pharmaceuticals, especially antibiotics, have received increasing global concern, due to their intensive use in the environment and potential harm to ecological system as well as human health. Among various antibiotics, fluoroquinolones are of extreme interest, since they are broad-spectrum antibacterials with agrowing demand in hospitals, households, and veterinary applications. Wastewater discharge from conventional wastewater treatment plants isthe main source of fluoroquinolone in the aquatic environment. Removal of fluoroquinolone residue from aquatic environment is, therefore, considered as a priority and serves as an important study. For the degradation of FQs in aqueous solution, interesting remedy processes are required such as oxidation-degradation process in which formed intermediates mineralized into CO_2, water, and mineral species. The electron transfer reactions and their mechanisms are of much importance in understanding various types of biochemical, pharmaceutical and industrial reactions. Kinetics has played a significant role in understanding the intricacies' of such reactions. Nanosized colloidal manganese dioxide, hexacyanoferrate(III), diperiodatocuprate(III), potassium permanganate etc. used as effective oxidants for oxidative degradation of different fluoroquinolone antibacterial agents in aqueous acidic/alkaline system. In this regard, we investigated a kinetic study of oxidation of moxifloxacin (MF) by diperiodatocuprate(III) (DPC) in aqueous alkaline medium. The reaction was first order with respect to [DPC] and less than unity order with [MF]. The pseudo-first order rate constant (k_{obs}) changes differently under different concentration of alkali. The results indicates at higher hydroxyl ion concentration DPC complex exist in CuL whereas at lower hydroxyl ion concentration in form of $Cu(HL)_2$. The thermodynamic parameters associated with the oxidation reaction have been evaluated and discussed.

Keywords: Fluoroquinolone, aqueous alkaline medium, thermodynamic parameters, kinetics, oxidation.

Introduction

Fluoroquinolones are a family of synthetic antibacterial agents with a rising popularity. These antibiotics display a broad spectrum of antibacterial activity including strong effects on Gram-negative aerobic and anaerobic organisms as well as on Gram-positive and a typical pathogens[1,2]. Moxifloxacin (MF), 1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-[(4*as*,7*as*)-octa-hydro-6*H*-pyrrolo[3,4-*b*]pyridine-6-yl]-4-oxo-3-quinolone carboxylic acid monohydrochloride, is an antibacterial synthetic drug that belongs to the fourth generation of fluoroquinolones[3-5]. As a new generation of antibacterial fluoroquinolone, MF has strong antibacterial activity, good clinical effects with little toxicity. The use of this newer generation fluoroquinolone is increasing due to expand antibacterial spectrum which makes them useful in a broader range of applications[6]. But these are not fully metabolized in the body and are partially excreted in its pharmaceutically active form[7,8]. As a result of their excessive usage, antibacterial may enter into the environment through waste water and manure from animal husbandry etc.[9,10]. The presence of antibacterial drugs in the aquatic environment that will become the source of potable supply, merits particular concern because of health recites. Effective removal of antibacterial drugs by water treatment process is important to minimize the potential health risks. For the removal of these fluoroquinolone many studies are used, in which oxidation process is mostly used and degrade them from the environment[11,12]. Recently, transition metals in their higher oxidation states can be stabilized by chelation with metal chelate such as diperiodatocuprate(III), diperiodatoargenate(III) and

†**Invited Lecture.**

diperiodatonickelate(IV)[13–15]. These metal chelates exhibits good oxidize properties with an appropriate pH value. Diperiodatocuprate(III) (DPC) is one-electron transfer oxidant for the substrate[16] and kinetic study of DPC are scanty because of its low solubility and stability in aqueous medium[17–25]. A literature survey revealed that the kinetics and mechanism of oxidation of MF by different oxidants such as potassium permanganate and TiO_2 using various processes like electro-Fenton process, photolytic and photo catalytic etc. was carried out in both acidic and alkaline medium[26–30]. There are no reports on the oxidation of MF by DPC from kinetic and mechanistic points of view. Copper(III) periodate complex as an oxidant shows multiple equilibria between different copper(III) species and it would be important to know which of the active species as an oxidant. Such studies are of importance in understanding the mechanistic pathways of oxidation of MF and to provide an insight into the interaction of metal ions with substrates. Hence, the present investigation is aimed to elucidate the reactivity of MF towards DPC, to arrive at a plausible mechanism and to understand the reactive species.

Materials and methods

Chemicals:

All chemicals were used in this investigation of analytical grade. Reaction solutions were prepared by requisite quantity of reagents in double distilled water. Solution of MF (KORES India Limited, Mumbai) was always freshly prepared before experiment. KOH and KNO_3 (BDH, Mumbai) were employed to maintain the required alkalinity and ionic strength respectively in reaction solutions. Corning glassware was employed both for storing the solutions and the kinetics of the reaction unless specified otherwise.

Preparation of diperiodatocuprate(III):

A stock solution of oxidant, DPC was prepared by dissolving copper sulphate (3.54 g), potassium meta periodate (6.8 g), potassium persulphate (2.2 g) and KOH (9.0 g) in 250 cm^3 water. The mixture was heated to boil on a hotplate with constant stirring till it turns to dark red and the boiling was continued for another 20 min for the completion of the reaction. The mixture was then cooled, filtered through sintered glass crucible (G-4). Filtrate was diluted to 250 cm^3 with distilled water. The solution obtained was found fairly stable at room temperature for several months in the presence of periodate. The complex was characterized by its UV-Visible spectrum, which exhibits strong broad absorption band at 415 nm. The aqueous solution of DPC was standardized by standard method[31].

Instrumentation:

For kinetic measurements, a Peltier accessory (temperature-Controlled) attached to a double beam U.V.3000$^+$, UV-Visible spectrophotometer (LABINDIA, Navi Mumbai) with UV path length 1.0 cm in the spectral range 200–800 nm, was used. For product analysis sample spectrum was recorded from the Fourier Transform Infrared (FT-IR) spectrophotometer (ALPHA-T, Bruker, Germany) in the range of 400–4000 cm^{-1} by mixing the sample with dried KBr (in 1:20 weight ratio) with a resolution of 4 cm^{-1} and Liquid Chromatography-Mass Spectroscopy (LC-MS) (Q-TOF Micromass, WATERS Company, UK), was used. The sample was subjected to LC-MS analysis at the rate of 5 μL/min in the applied voltage of 30 kV with a glass micro syringe.

Kinetic measurements:

The reactions were carried out in stoppered flask at 30±1°C with all ingredients of the reaction mixture except DPC and the reaction was initiated by adding a known volume of DPC. Aliquot (2 ml) of the reaction mixture was withdrawn periodically. The progress of the reaction was followed by observing the absorbance of DPC in the reaction mixture at 415 nm in a placed in the cell compartment of an UV-Visible spectrophotometer, that there was no interference from other species in the reaction mixture at this wave length. The UV spectra indicates gradually disappearance of Cu(III) band with time as a result of its reduction to Cu(II) (Fig. 1).

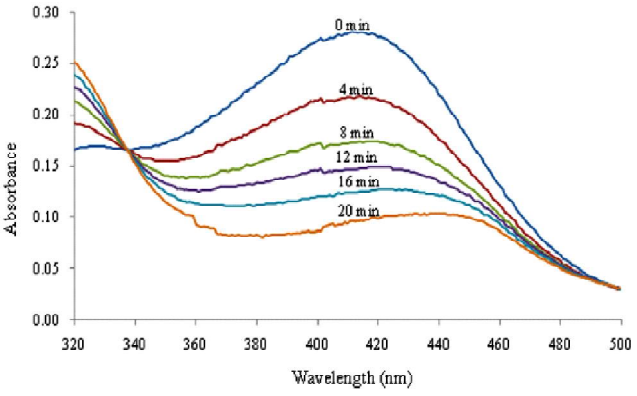


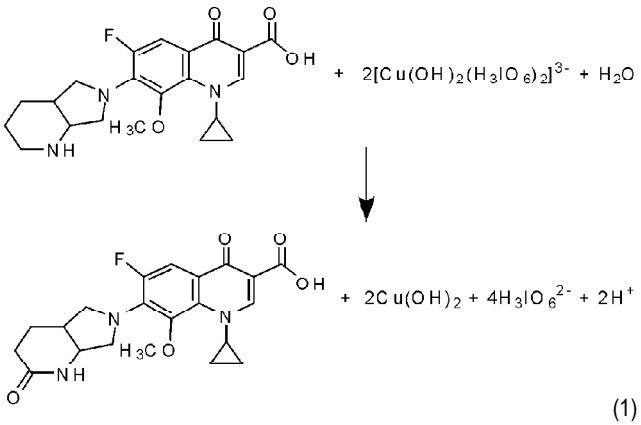
Fig. 1. Spectral changes during the oxidation of MF by DPC in alkaline medium at 30°C. [DPC] = 5.0×10^{-5}, [MF] = 1.0×10^{-3}, [OH^-] = 1.0×10^{-2}, [IO_4^-] = 2.0×10^{-4} and I = 2.0×10^{-2} mol dm^{-3}.

The application of Beer's law of DPC at 415 nm had been verified giving ε = 6230 dm^3 mol^{-1} cm^{-1}, pseudo-first order rate constant (k_{obs}) was calculated from the plot of the logarithm of absorbance versus time[32]. The pseudo-first order plots were linear up to 80% completion of the reaction and k_{obs} value was reproducible within ±6%.

Results and discussion

Stoichiometry and product analysis:

The stoichiometry of the reaction determined by various sets of reaction mixtures containing different concentration of DPC and MF in aqueous alkaline medium at constant ionic strength for 12 h at 30°C in a closed vessel to ensure the completion of the reaction. The excess of DPC was estimated spectrophotometrically (Table 1) and the results correspond to the stoichiometry as represented by eq. (1)



(1)

The product was separated out with ether after the completion of the kinetic experiments. The main oxidative product 1-cyclopropyl-6-fluoro-1,4-dihydro-7-(octahydro-2-oxopyrolol[3,4-*b*]pyridine-6-yl)-8-methoxy-4-oxo-quinolone-3-carboxylic acid was identified with the help of LC-MS and FT-IR analysis.

LC-MS data were obtained on a Q-TOF Micromass, spectrometer. The mass spectrum showed a molecular ion peak at *m/z* 416 amu which corresponds to oxidation of the piperazine ring[29] (Fig. 2). The presence of C=O bond was confirmed by FT-IR analysis which showed C=O stretching at 1693.98 cm^{-1} and -NH stretching of the -NH group at 3322.92 cm^{-1} (Fig. 3) and the remaining peaks are of the parent compound.

Diperiodatocuparate(III) dependence:

The concentration of the oxidant, DPC was varied from 1.0×10^{-5} to 1.0×10^{-4} mol dm^{-3} at constant concentration of MF, OH^-, IO_4^- and ionic strength at 30°C. The k_{obs} values are nearly constant indicating the order with respect to DPC concentration is unity (Table 2). This was also confirmed from the linearity of plots of log (absorbance) versus time to about 80% completion of the reaction (Fig. 4).

Moxifloxacin dependence:

The effect of MF on the rate of reaction was studied at constant concentration of DPC, IO_4^-, ionic strength and two different concentration of alkali. The substrate, MF was varied in the range of 5.0×10^{-4} to 5.0×10^{-3} mol dm^{-3}. The rate of reaction increases with increasing concentration of MF in the both alkali conditions and tends towards a limiting at higher concentration of MF (Table 2). The order with respect to MF concentration was obtained from the plot of log k_{obs} versus log [MF] and found to be less than unity.

Hydroxyl ion dependence:

The effect of concentration variation of sodium hydroxide on the rate of reaction was studied in the concentration range 0.5×10^{-2} to 30.0×10^{-2} mol dm^{-3} at fixed concentration of DPC, OH^-, IO_4^- and ionic strength at 30°C. The rate decreases quickly with increase in $[OH^-]$ till 2.0×10^{-2} mol dm^{-3}, and then increases with continuous increase in $[OH^-]$ (Fig. 5). The effect of hydroxyl ion on the rate of reaction indicate the reaction proceed by two paths in the mechanism.

Periodate ion dependence:

The concentration of KIO_4 was varied from 2.0×10^{-4} to 3.5×10^{-4} mol dm^{-3} at constant concentration of MF, ionic

Table 1. Stoichiometry of the reaction diperiodatocuprate(III) with moxifloxacin in aqueous alkaline medium

Sr. No.	10^5 [DPC] (mol dm^{-3})	10^5 [MF] (mol dm^{-3})	$\frac{\Delta[DPC]}{\Delta[MF]}$
1.	6.0	2.0	2.08
2.	5.0	3.0	2.04
3.	8.0	2.0	2.08
4.	8.0	3.0	1.99
5.	12.0	5.0	2.02

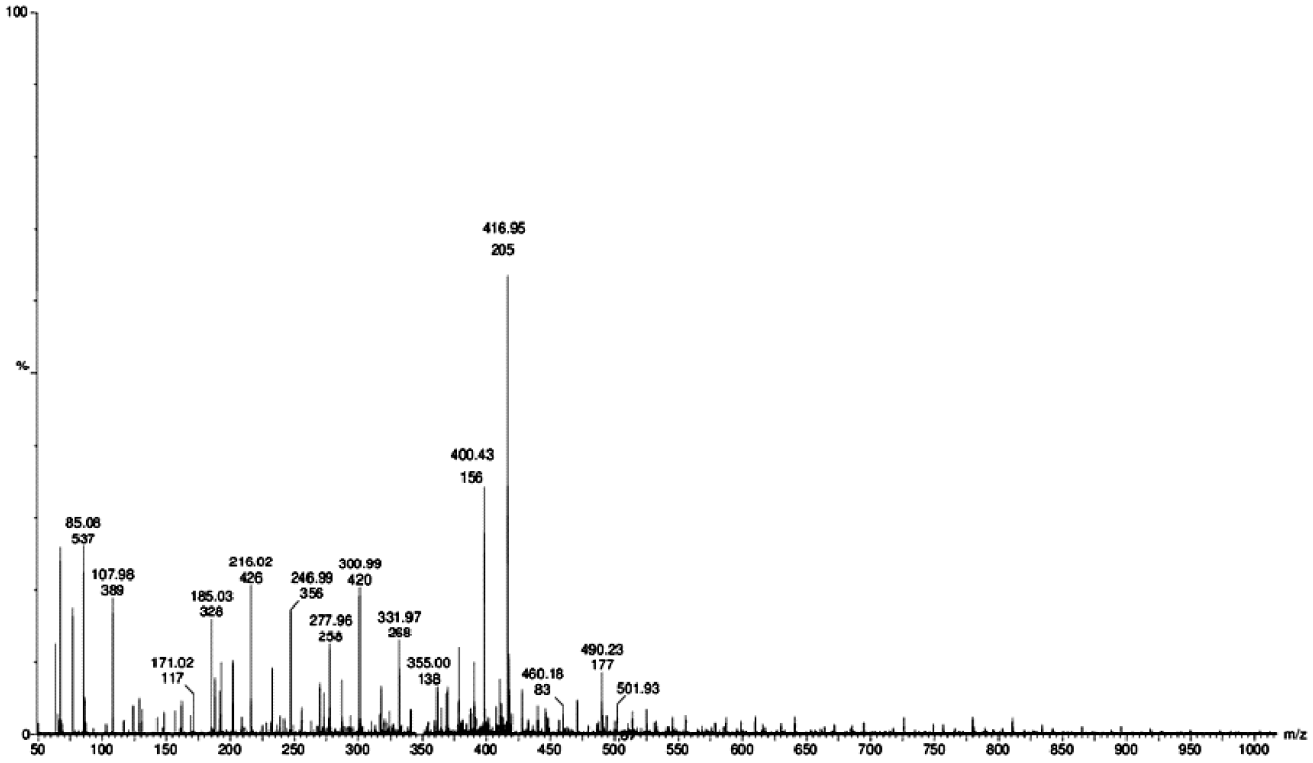


Fig. 2. LC-MS spectra of oxidation product of MF.

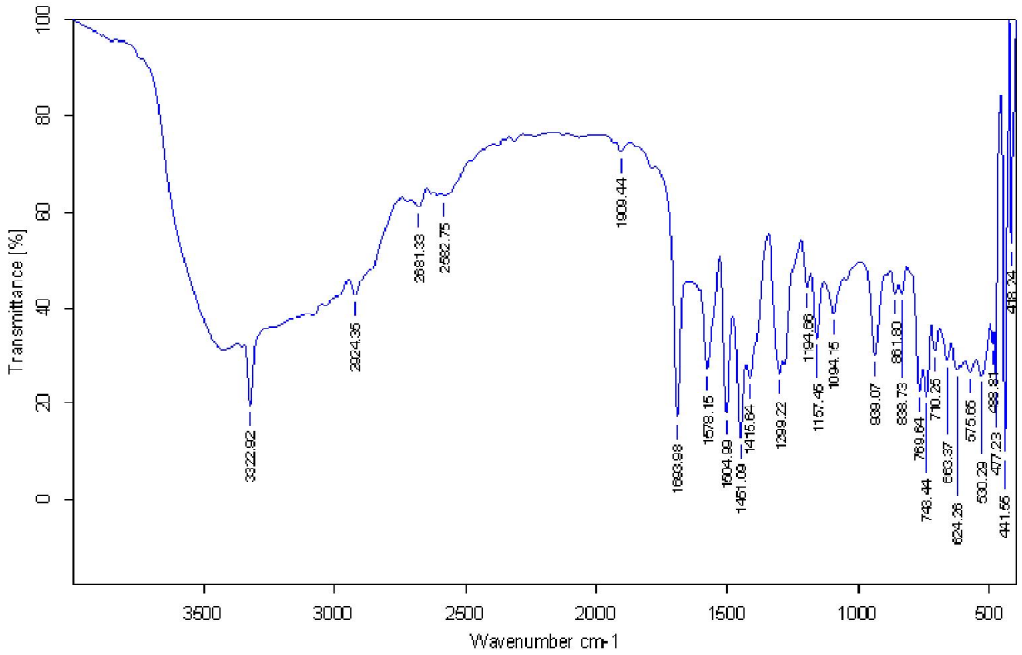


Fig. 3. FT-IR spectra of the product of oxidation of MF by DPC.

Table 2. First order rate constants (k_{obs}) for the reaction of MF with DPC in aqueous alkaline medium at I = 2.0×10^{-2} mol dm^{-3} and temperature = 303 K

10^5 [DPC] (mol dm^{-3})	10^4 [MF] (mol dm^{-3})	10^2 [OH$^-$] (mol dm^{-3})	10^4 [IO_4^-] (mol dm^{-3})	10^4 k_{obs} (s^{-1})
1.0	10.0	1.0	2.0	10.73
2.5	10.0	1.0	2.0	10.70
3.0	10.0	1.0	2.0	10.72
5.0	10.0	1.0	2.0	10.73
7.0	10.0	1.0	2.0	10.70
7.5	10.0	1.0	2.0	10.73
8.0	10.0	1.0	2.0	10.71
10.0	10.0	1.0	2.0	10.69
5.0	5.0	1.0	2.0	7.41
5.0	7.5	1.0	2.0	9.32
5.0	10.0	1.0	2.0	10.73
5.0	20.0	1.0	2.0	14.21
5.0	30.0	1.0	2.0	16.24
5.0	40.0	1.0	2.0	17.50
5.0	50.0	1.0	2.0	18.10
5.0	5.0	30.0	2.0	60.00
5.0	7.5	30.0	2.0	78.02
5.0	10.0	30.0	2.0	90.04
5.0	20.0	30.0	2.0	120.02
5.0	30.0	30.0	2.0	136.01
5.0	40.0	30.0	2.0	145.04
5.0	50.0	30.0	2.0	150.03
5.0	10.0	1.0	2.0	10.73
5.0	10.0	1.0	2.5	12.40
5.0	10.0	1.0	3.0	13.90
5.0	10.0	1.0	3.5	15.70

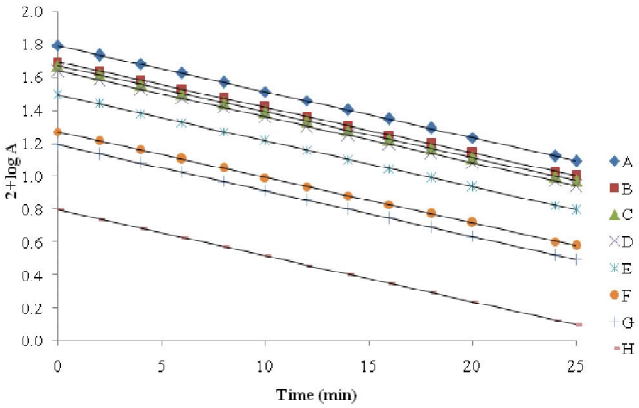


Fig. 4. First order plots of the variation of DPC concentration at 30°C. [MF] = 1.0×10^{-3}, [OH$^-$] = 1.0×10^{-2}, [IO_4^-] = 2.0×10^{-4} and I = 2.0×10^{-2} mol dm^{-3}. [DPC]$\times10^{-5}$ mol dm^{-3} = (A) 10.0, (B) 8.0, (C) 7.5, (D) 7.0, (E) 5.0, (F) 3.0, (G) 2.5, (H) 1.0.

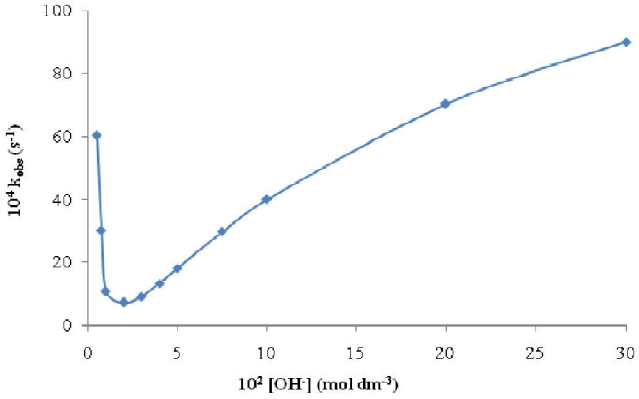


Fig. 5. Plots of k_{obs} versus [OH$^-$] at 30°C. [DPC] = 5.0×10^{-5}, [MF] = 1.0×10^{-3}, [IO_4^-] = 2.0×10^{-4} and I = 2.0×10^{-2} mol dm^{-3}.

strength and two different hydroxyl ion at 30°C. The effect of IO_4^- on the rate of reaction was studied to show up the active forms of Cu(III) periodate complex. At low [OH$^-$] (1.0×10^{-2} mol dm^{-3}), the rate constant k_{obs} increased with increase in [KIO_4]. But at high [OH$^-$] (30.0×10^{-2} mol dm^{-3}), k_{obs} decreased with increase in [KIO_4]. The effect of KIO_4 on rate of reaction is suggested that the involvement of DPC in the multiple equilibria[33].

Effect of ionic strength and dielectric constant:

At constant concentration of reactants, the ionic strength was varied by varying concentration of potassium nitrate at 30°C while other reactant concentration and condition constant. The results indicate the ionic strength had negligible effect on the rate of reaction. At constant acidity and other constant conditions, as the t-butyl alcohol content increase from 0 to 50% (v/v) in the reaction, change in dielectric constant had negligible effect on the rate of reaction. The negligible effect of ionic strength on the rate of reaction suggests that the reaction is either between two neutral species or a neutral and a charged species.

Effect of added product:

The initial added product, Cu(II) ($CuSO_4$) was studied in the range of 1.0×10^{-4} to 1.0×10^{-3} mol dm^{-3} while other reactants concentration and conditions constant, did not have any significant effect on the rate of reaction. Results indicate no involvement of the product in the reaction.

Test for free radical:

To test the intervention of free radicals, the reaction mixture, to which a known quantity of acrylonitrile had been added initially, was kept for two hours under nitrogen atmosphere. On dilution with methanol, white precipitate of polymer was formed, indicating the presence of intervention of free radicals in the reaction.

Mechanism:

In aqueous alkaline medium $[Cu(IO_6)_2]^{7-}$ or DPC gets hydrated which was expressed as $Cu(HL)_2$[34] in which HL represents the $H_3IO_6^{2-}$. The three following equilibria (a-c) were found in alkaline medium,

$$2IO_4^- + 2OH^- \overset{\beta_1}{\rightleftharpoons} H_2I_2O_{10}^{4-} \quad (a)$$

$$IO_4^- + 2OH^- + H_2O \overset{\beta_2}{\rightleftharpoons} H_3IO_6^{2-} \quad (b)$$

$$IO_4^- + 2OH^- \overset{\beta_3}{\rightleftharpoons} H_2IO_6^{3-} \quad (c)$$

Thus, under the present experimental conditions the main species are expected to be $H_2IO_6^{3-}$ and $H_3IO_6^{2-}$ and the dimer form $[H_2I_2O_{10}^{4-}]$ is negligible under these conditions[34]. So the total concentration of $[IO_4^-]$ added in the reaction was as follows:

$$[IO_4^-] = [H_3IO_6^{2-}] + [H_2IO_6^{3-}]_e$$

(e = equilibrium concentration of substrate)

Substitute eqs. (b) and (c) in the above equation, then

$$[H_3IO_6^{2-}] = [HL] = \frac{\beta_2}{\beta_2 + \beta_1 [OH^-]} [IO_4^-]_T$$

$$\text{If } \frac{\beta_2}{\beta_2 + \beta_1} = \frac{1}{\phi}$$

$$\text{Then } [HL] = \phi[OH^-][IO_4^-]_T \quad (d)$$

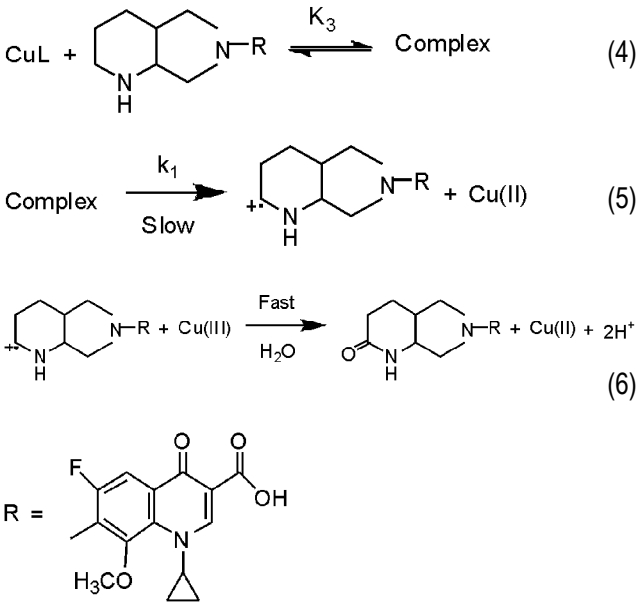
Based on the experimental results and above discussion the possible mechanism could be as follows:

$$Cu(HL)_2 + 2OH^- \overset{k_1}{\rightleftharpoons} CuL(HL) + H_2O \quad (2)$$

$$Cu(HL) \overset{k_2}{\rightleftharpoons} CuL + HL \quad (3)$$

where CuL and $Cu(HL)_2$ are two active species of DPC in the reaction.

(I) At higher concentration of $[OH^-]$, the equilibria of eqs. (2) and (3) shift left to right and CuL form exist as active species of DPC, then mechanism are proposed as Scheme 1.



Scheme 1. Proposed mechanism for the oxidation of MF by DPC at higher concentration of $[OH^-]$.

The Scheme 1 will lead to the following rate expression

$$\frac{-d[Cu(III)]_T}{dt} = 2k_1[C] = 2k_1K_3[CuL][MF] \quad (7)$$

where [C] is the concentration of the intermediate adduct.

The total concentration of $[Cu(III)]_T$ is given by eq. (8)

$$[Cu(III)]_T = [Cu(HL)_2] + [CuL(HL)] + [CuL] + [C]$$

$$[Cu(III)]_T = \frac{[CuL][HL] + K_1[OH^-][CuL][HL] + K_1K_2[OH^-][CuL] + K_1K_2K_3[OH^-][MF][CuL]}{K_1K_2[OH^-]} \quad (8)$$

Substitute eq. (8) in (7) then we get eq. (9)

$$\frac{-d[Cu(III)]_T}{dt} = \frac{2k_1K_1K_2K_3[OH^-][Cu(III)]_T[MF]}{[HL] + K_1[OH^-][HL] + K_1K_2K_3[OH^-][MF] + K_1K_2[OH^-]} \quad (9)$$

Eq. (9) conforms the reaction is first order with respect to DPC, under pseudo-first order conditions $[MF] > [Cu(III)]_T$,

the pseudo-first order rate constant k_{obs} is as follows:

$$k_{obs} = \frac{2k_1K_1K_2K_3[OH^-][MF]}{[HL]\{1 + K_1[OH^-]\} + K_1K_2K_3[OH^-][MF] + K_1K_2[OH^-]} \quad (10)$$

Taking the reciprocal of eq. (10) and after rearrangement obtained eq. (11) is

$$\frac{1}{k_{obs}} = \frac{K_1K_2[OH^-] + [HL] + K_1[OH^-][HL]}{2k_1K_1K_2K_3[OH^-]} \bullet \frac{1}{[MF]} + \frac{1}{2k_1} \quad (11)$$

Eq. (d) is substituted into eq. (11), then

$$\frac{1}{k_{obs}} = \frac{K_1K_2 + \phi[IO_4^-] + K_1\phi[OH^-][IO_4^-]}{2k_1K_1K_2K_3} \bullet \frac{1}{[MF]} + \frac{1}{2k_1} \quad (12)$$

From eq. (12) k_{obs} decreases with increase in periodate $[IO_4^-]$ concentration, which confirms to our results. The equation (11) is consistent with our experimental results and plot between $1/k_{obs}$ versus 1/[MF] (Fig. 6) from the intercept of the plot the value of slow step rate constant k_1 were obtained at different temperature[20]. The plot of log k_1 against $1/T$ was made and calculates the values of activation parameters.

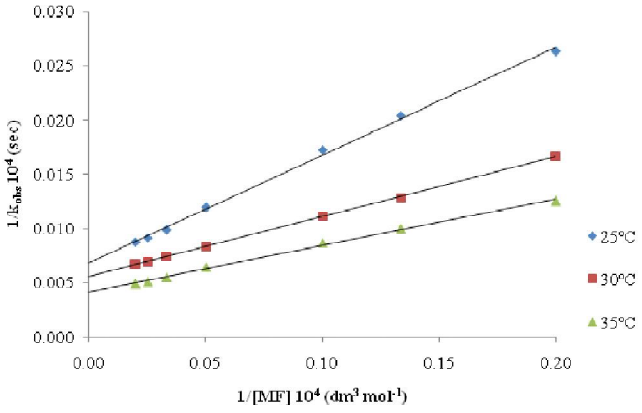
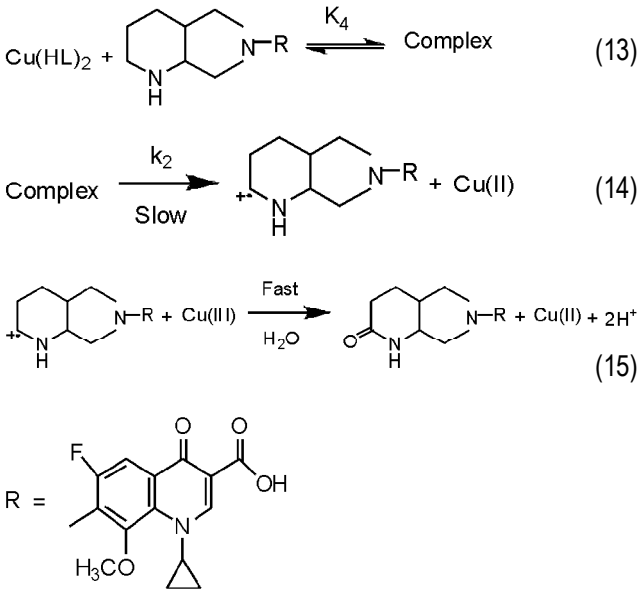


Fig. 6. Plot of $1/k_{obs}$ versus 1/[MF] at different temperatures. [DPC] = 5.0×10^{-5}, $[OH^-] = 30.0\times10^{-2}$, $[IO_4^-] = 2.0\times10^{-4}$ and I = 2.0×10^{-2} mol dm^{-3}.

(II) At low concentration of $[OH^-]$, DPC complex exist mainly in $Cu(HL)_2$ form, which means $Cu(HL)_2$ >> [CuL], so mechanism are as Scheme 2.



Scheme 2. Proposed mechanism for the oxidation of MF by DPC at low concentration of $[OH^-]$.

The above Scheme 2 will leads to the following rate law

$$\frac{-d[Cu(III)]_T}{dt} = 2K_1[C] = 2k_2K_4[Cu(HL)_2][MF] \quad (16)$$

The total concentration of Cu(III) are given as

$$[Cu(III)]_T = [Cu(HL)_2] + [CuL(HL)] + [CuL] + [C]$$

$$[Cu(III)]_T = [Cu(HL)_2]\left\{1 + K_1[OH^-] + \frac{K_1K_2[OH^-]}{[HL]} + K_4[MF]\right\} \quad (17)$$

Thus

$$[Cu(HL)_2] = \frac{[Cu(III)]_T[HL]}{[HL] + K_1[OH^-][HL] + K_1K_2[OH^-] + K_4[MF][HL]} \quad (18)$$

Substituting eq. (18) into (16) then resulting

$$\frac{-d[Cu(III)]_T}{dt} = \frac{2k_2K_4[Cu(III)]_T[MF][HL]}{[HL] + K_1[OH^-][HL] + K_1K_2[OH^-] + K_4[MF][HL]} \quad (19)$$

Hence the reaction is first order with respect to DPC so eq. (19) becomes

$$k_{obs} = \frac{2k_2K_4[MF][HL]}{[HL] + K_1[OH^-][HL] + K_1K_2[OH^-] + K_4[MF][HL]} \quad (20)$$

The rearranging of eq. (20)

$$\frac{1}{k_{obs}} = \frac{1}{2k_2K_4}\frac{(1 + K_1[OH^-] + K_1K_2[OH^-][HL])}{[MF]} + \frac{1}{2k_2} \quad (21)$$

Eq. (d) is substituted into eq. (21), then

$$k_{obs} = \frac{2k_2K_4\phi[OH^-][IO_4^-]_T[MF]}{\phi[OH^-][IO_4^-]_T + K_1[OH^-]\phi[OH^-][IO_4^-]_T + K_1K_2[OH^-] + K_4[MF]\,\phi[OH^-][IO_4^-]_T} \quad (22)$$

$$k_{obs} = \frac{2k_2K_4[MF]}{1 + K_1[OH^-] + K_4[MF]} + \frac{\phi[OH^-][IO_4^-]_T}{K_1K_2[OH^-]} \quad (23)$$

From eq. (23) k_{obs} increases with increase in periodate $[IO_4^-]$ concentration, which confirms to our results. A plot of graph between $1/k_{obs}$versus 1/[MF] gives straight line at different temperature and the intercept of the graph gives the value of slow step rate constant k_2 (Fig. 7)[35]. A plot of log k_2 obtained at different temperatures were made against $1/T$, yielded a straight line and determine the activation parameters (Table 3).

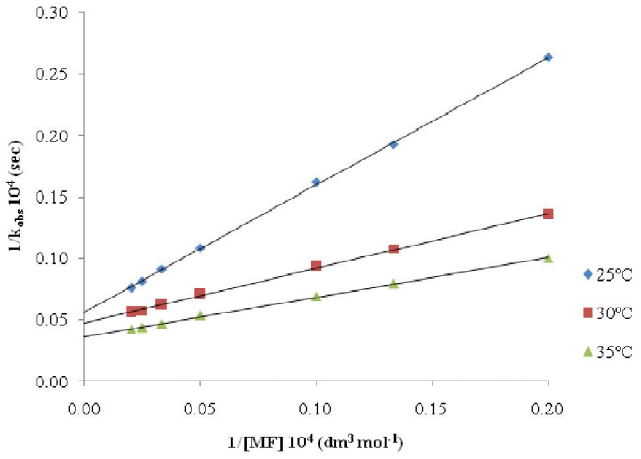


Fig. 7. Plot of $1/k_{obs}$versus 1/[MF] at different temperatures. [DPC] = 5.0×10^{-5}, $[OH^-] = 1.0\times10^{-2}$, $[IO_4^-] = 2.0\times10^{-4}$ and I = 2.0×10^{-2} mol dm^{-3}.

Table 3. Activation parameters for the reaction of diperiodatocuprate(III) with moxifloxacin in aqueous alkaline medium

Activation parameters	Values from k_1 at high $[OH^-]$	Values from k_2 at low $[OH^-]$
E_a (kJ mol^{-1})	21.06	25.85
$\Delta H^{\#}$ (kJ mol^{-1})	18.54	23.33
$\Delta S^{\#}$ (JK^{-1} mol^{-1})	–217.13	–219.23
$\Delta G^{\#}$ (kJ mol^{-1})	84.35	89.75

The entropy of activation ($\Delta S^{\neq}$) tends to be more negative for reaction of an inner-sphere nature, where as the reactions of positive $\Delta S^{\neq}$ values proceed via an outer-sphere mechanism. The obtained large negative values of $\Delta S^{\neq}$ express that the mechanism is one-electron transfer of inner-sphere nature which indicate that there is a decrease in the randomness during the reaction proceed by both two paths reaction process. This leads to the formation of intermediate complex and such activated complex is more ordered than the reactants due to loss of degree of freedom[36]. Whether, the positive value of $\Delta H^{\neq}$ indicates that the complex formation is endothermic and the value of $\Delta G^{\neq}$ suggests enhanced formation of the intermediate with raising temperature as well as to the non-spontaneity of the complex formation.

Conclusion

Oxidation of MF by DPC in aqueous alkaline medium was found to be first order with respect to oxidant and fractional order with respect to substrate. Among the various species of DPC, CuL and $Cu(HL)_2$ are two active species of DPC at different concentration of alkali. The reaction pathway involves complex formation and free radical mechanism. Rate constant of slow step and other equilibrium constants involved in the mechanism are evaluated and activation parameters with respect to the slow step of the reaction were computed. The overall sequence discussed here is dependable with all experimental results, including the product, mechanistic and kinetic studies. The results of the study are expected to useful for evaluating the potential risk of antibacterial agents.

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