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RESEARCH ARTICLE

Silver (I) catalyzed and uncatalyzed oxidation of levofloxacin with aqueous chlorine: A comparative kinetic and mechanistic approach

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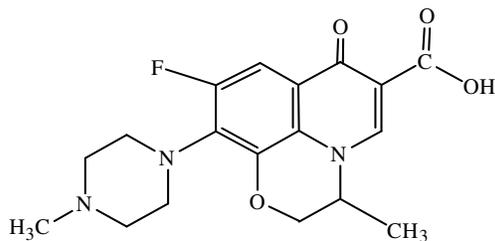
ABSTRACT:

The kinetics and mechanism of the Ag (I) ion catalyzed reaction of levofloxacin (LFC) by free available chlorine (FAC) during water chlorination processes was investigated for the first time between the pH values 4.2 and 8.2. The pH dependent second order rate constants were found to decrease with increase in pH. (e.g. Apparent second order rate constant for Ag (I) catalyzed reaction, $k_{app} = 114.40 \text{ dm}^{-3} \text{ mol}^{-1} \text{ sec}^{-1}$ at pH 4.2 and $k_{app} = 8.72 \text{ dm}^{-3} \text{ mol}^{-1} \text{ sec}^{-1}$ at pH 8.2 and at $25 \pm 0.2^\circ \text{C}$). The reaction rates revealed that Ag (I) catalyzed reaction was about six-fold faster than the uncatalyzed reaction. The products of the reaction were determined by Liquid chromatography and high resolution mass spectrometry. The reaction proceeds via formation of intermediate complex between Ag (I) ion and levofloxacin, then HOCl reacts with the complex to form chlorinated product. The effect of catalyst, effect of initially added product, effect dielectric constant and effect ionic strength on the rate of reaction was also studied. The effect of temperature on the rate of the reaction was studied at four different temperatures and rate constants were found to increase with increase in temperature and the thermodynamic activation parameters E_a , ΔH^\ddagger , ΔS^\ddagger and ΔG^\ddagger were evaluated for the reaction and discussed.

KEY WORDS: Kinetics, Chlorination, Levofloxacin, Mechanism, Silver (I), Catalysis, Oxidation.

INTRODUCTION:

Levofloxacin (LFC) is class of fluoroquinolone antibacterial agent. Antibacterial agents are the most important compounds used in medicine. Although, antibiotics have been used in large quantities for some decades, the existence of these substances in the environment has got little attention¹. LFC has higher renal clearance and greater renal concentration and has optimal choice for the treatment of complicated urinary tract infections.



Structure of levofloxacin(LFC)

Recently the pharmaceuticals of which antibacterial groups are important, which, have been also considered as environmental contaminants². Continuous exposure of antibiotic drugs to bacterial communities, promotes the bacteria to develop antibiotic resistance power. The possible induction of antibiotic resistance in bacteria is directly related to human health. The behavior of antibiotic drugs during water treatment process clearly plays a significant role in this aspect³. The behavior of fluoroquinolones moiety containing drugs plays an important role during water treatment process^{4,5}. Mechanisms of fluoroquinolone resistance include one or two of the three main mechanistic categories, alterations in the drug target, and alterations in the permeation of the drug to reach its target. No specific quinolone-modifying or -degrading enzymes have been found as a mechanism of bacterial resistance to fluoroquinolones, although some fungi can degrade fluoroquinolones by metabolic pathways⁶.

Transition metals catalyze many oxidation–reduction reactions since they involve multiple oxidation states. Recently the use of transition metal ions such as silver, ruthenium, osmium, palladium, manganese, chromium, iridium, copper either alone or as binary mixtures, as

catalysts in various oxidation-reduction processes have attracted considerable interest^{7,8}. The mechanism of catalysis depends on the nature of the reactant, oxidant and experimental conditions, it has been shown that metal ions act as catalysts by one of these different paths such as the formation of complexes with reactants or oxidation of the substrate itself or through the formation of free radicals⁹.

Silver is one of the commonly used transition metal as a catalyst in industry. Silver salts are commonly known as Lewis acids in the synthesis of organic compound¹⁰. Silver compounds are also used to catalyze intermolecular molecular carbene insertion carbon-halogen bonds, carbon-hydrogen and aromatic systems^{11,12}. The direct oxidations of alcohols, oxidative activation of alkenes and also simple alkanes have attracted interests as well¹³⁻¹⁵. Past efforts has been made to study by homogeneous silver-catalyzed organic transformations have mostly focused by using Lewis acid catalysis. Metal ions act as catalyst by one of these different paths¹⁶ such as formation of complexes with reactants. The role of Ag (I) as a catalyst has been discussed by Saxena Et al¹⁷. A silver form oxidation catalyst in solution has been less used in the past. Silver compounds are commonly employed as stoichiometric oxidants in both organic and inorganic synthesis¹⁸.

EXPERIMENTAL:

Apparatus

The absorbance and measurements and recordings absorption spectra of reactants and products were analyzed by using single beam CARY 50 study Bio UV-Vis Spectrophotometer (Varian BV, The Netherlands) with temperature controller with thermo stated conditions. The quartz sample cells of 1 cm were used throughout the present study. The pH measurements were made with digital Elico pH meter model LI 120. The temperature of reaction was maintained at 25.0 ± 0.2 °C. The quartz cells were cleaned by using 1:1 sulfuric acid to remove traces of any impurities deposited on it by prolongs use.

Materials and reagents

All the experimental chemicals were used of analytical grade. All the solutions were prepared by using double distilled water. A stock solution of levofloxacin (Dr. Reddy Laboratories) was prepared by dissolving appropriate quantity of sample in double distilled water. A stock solution of FAC was prepared by taking appropriate volume of 5% NaOCl (Thomas Baker) in distilled water according to the procedure described elsewhere¹⁹. Stock solution of silver nitrate (AgNO_3) (HIMEDIA) of known concentration was prepared in free chlorine distilled water. The stock solution of FAC was standardized by iodometry and DPD-FAS titrimetry respectively.²⁰ 0.02 mol dm⁻³ acetate (pH 4.2-5.0), phosphate (pH 7.0-7.4), and borate (pH 8.2) buffers were used to maintain constant pH during experiments conducted in reagent water system.

Instruments used

- For kinetics measurement, a CARY 50 study Bio UV-Vis Spectrophotometer (Varian BV, The Netherlands) with temperature controller and HPLC system (Agilent 1100 series, USA) were used
- For product analysis, LC/MSD Trap systems (Agilent 1200 series, USA) were used.
- For pH measurement an Elico pH meter model LI 120 was used.

Kinetic procedure

All the chemical reactants were placed in a thermostatic bath at 25.0 ± 0.2 °C for at least 30 minutes to attain thermal equilibrium. The kinetic measurement were followed under pseudo first order condition with FAC is at least ten fold molar excess over LFC at a constant ionic strength using 0.02 mol dm⁻³ buffers in both uncatalyzed and catalyzed reactions. The reaction was started by mixing solutions of LFC, AgNO_3 , FAC and with the necessary volume of buffers thermostat. The cause of the reaction was followed by monitoring decrease in the absorbance of LFC as a function of time in a 1 cm path length quartz cell of Carry 50 Bio UV-Visible spectrophotometer.

The application of Beer's law of LFC at λ_{max} 294 nm had been verified giving $\epsilon = 59475 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$. Pseudo first-order rate constants, k'_{obs} , were evaluated from the plots of $\log (A_t - A_\infty)$ versus time, where 'A' refers to absorbance at any time t and t_∞ is at infinite time which excludes the absorbance of any products of LFC during the reaction. The first order plots in almost all the cases were linear upto 80% completion of the reaction and k'_{obs} values were reproducible within $\pm 6-7\%$ (Table 1).

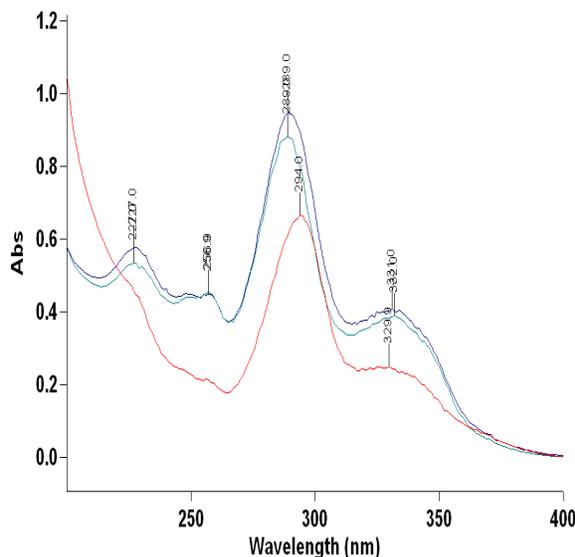


Fig.1. Spectral changes during the chlorination of levofloxacin (LFC) by FAC in the presence of Ag(I) catalyst at 25 ± 0.2 °C

Table 1 Effect of variation of [FAC] on the silver catalyzed chlorination of levofloxacin at 25 °C. Ionic strength = 0.02 mol dm⁻³ ± 6-7 % Error

pH	10 ⁴ [FAC] (mol dm ⁻³)	10 ⁶ [LFC] (mol dm ⁻³)	10 ⁸ [Ag ⁺] (mol dm ⁻³)	10 ³ k _{obs.} (s ⁻¹) (Total) Found	10 ⁴ k _{obs.} (s ⁻¹) (Uncatalyzed)	10 ³ k _{obs.} (s ⁻¹) (catalyzed)
4.2	0.40	6.0	5.0	1.15	8.3	0.32
	1.11	6.0	5.0	6.70	14.3	5.27
	1.30	6.0	5.0	8.25	19.0	6.35
	1.60	6.0	5.0	16.5	27.0	13.8
	2.00	6.0	5.0	18.2	32.0	15.0
5.0	0.40	6.0	5.0	0.70	5.9	0.11
	1.11	6.0	5.0	1.77	10.4	0.77
	1.30	6.0	5.0	2.31	14.2	0.89
	1.60	6.0	5.0	4.47	19.0	2.56
	2.00	6.0	5.0	7.14	23.4	4.80
7.0	0.40	6.0	5.0	0.43	3.5	0.08
	1.11	6.0	5.0	1.20	6.2	0.58
	1.30	6.0	5.0	1.66	8.4	0.82
	1.60	6.0	5.0	2.30	10.6	1.24
	2.00	6.0	5.0	3.30	13.7	1.93
7.4	0.40	6.0	5.0	0.25	2.0	0.05
	1.11	6.0	5.0	0.41	3.3	0.08
	1.30	6.0	5.0	0.75	4.6	0.29
	1.60	6.0	5.0	1.11	5.8	0.53
	2.00	6.0	5.0	1.50	7.7	0.73
8.2	0.40	6.0	5.0	0.16	1.4	0.02
	1.11	6.0	5.0	0.25	1.8	0.07
	1.30	6.0	5.0	0.37	2.0	0.17
	1.60	6.0	5.0	0.50	2.4	0.26
	2.00	6.0	5.0	1.00	5.6	0.44

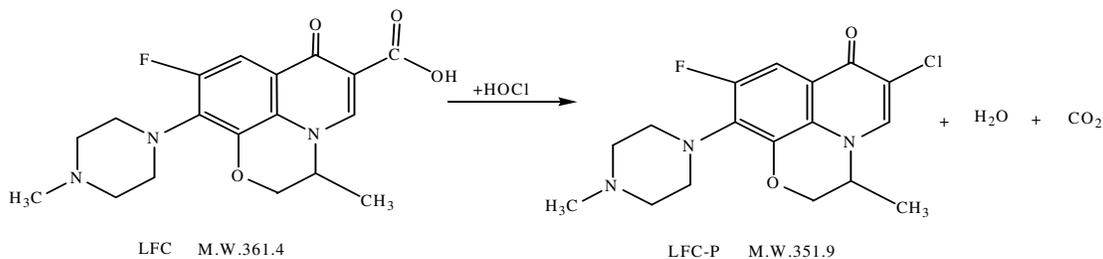
Spectral changes during the chlorination of levofloxacin (LFC) by FAC at 25±0.2°C as shown in UV-Vis spectra as shown in fig.1. It is evident from the figure that the concentration of LFC decreases as the reaction proceeds. Further evidence for complex formation was obtained from the UV-Vis spectra of reaction mixtures in which hypsochromic shift of 5 nm from 294 to 289 nm and hyperchromicity at 289 nm was observed. The Parent compound loss was also monitored by HPLC system (Agilent 1100 series, USA) with RX-C18 column (4.6 mm × 250 mm, 5 μm) with UV diode array detector. The observed rate constants from HPLC method were in good agreement with UV visible methods. FAC concentration was measured by DPD – colorimetry or DPD-FAS titrimetry¹⁷ at the conclusion of each kinetic experiment. During the calculation of pseudo first order rate constants (k_c) for catalyzed and (k_u) uncatalyzed has also been considered during calculation.

Thus

$$k_t = k_c + k_u \quad (1)$$

$$k_c = k_t - k_u \quad (2)$$

Uncatalyzed reaction

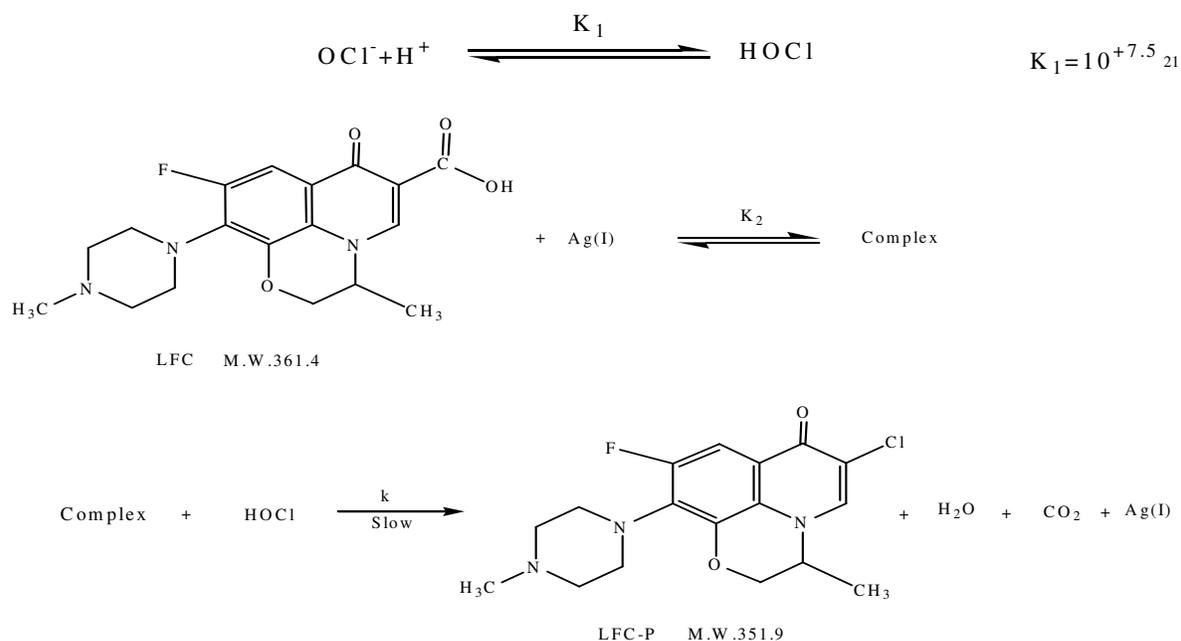


The rate constants, k_c were obtained within ± 6 error (Table 1). Regression analysis data was performed with Microsoft Office Excel-2007.

Product analysis

Different sets of reaction a mixture containing varying ratios levofloxacin was added to 0.02 moldm⁻³ pH 7 phosphate buffers to achieve starting concentration of 100 mg dm⁻³. HOCl solution was subsequently added to initiate reactions at oxidant: substrate molar ratios ranging from 1:2 to 5:1 in uncatalyzed reaction and a constant amount of Ag (I) in catalyzed reaction were kept for 12 hrs and the products were analyzed using LC/MSD Trap system (Agilent 1200 series, USA) MS analyses were conducted using positive mode electro spray ionization (ESI⁺), over a mass scan range of 50-1000 m/z. The observed peaks of LC/MS spectra (Fig.2.) interpreted in accordance with the proposed structure of the product. The major identified product in the reaction is shown below (Scheme1).

Catalyzed reaction



Scheme 1. Proposed reaction for major product LFC /FAC reaction based on LC/MS

RESULTS AND DISCUSSION:**Products of levofloxacin**

LC-ESI-MS analysis of levofloxacin reaction indicated that major product molecular ions of m/z 352.4 (LFC-P) Fig.2. This has an LFC structure, in which the quinolone carboxylic group was displaced by a Cl atom. Decarboxylation (resulting in a mass loss of 45 daltons) and monochlorination (leading to mass gain of 35 daltons) would yield a net loss of 10 daltons relative to the parent LFC molecule, in accordance with the mass difference between LFC and LFC-P. LFC occurs at the N(4) amine nitrogen of piperazine ring. Levofloxacin undergoes chlorination under the influence of UV-visible light in acidic medium with HOCl in both Ag (I) catalyzed and uncatalyzed reactions are carried out. In catalyzed reaction, Catalyst reacts with LFC forms complex, which on decomposition forms LFC radical and reacts with HOCl to form chlorine substituted product. The major chlorinated product is formed in both catalyzed and uncatalyzed product.

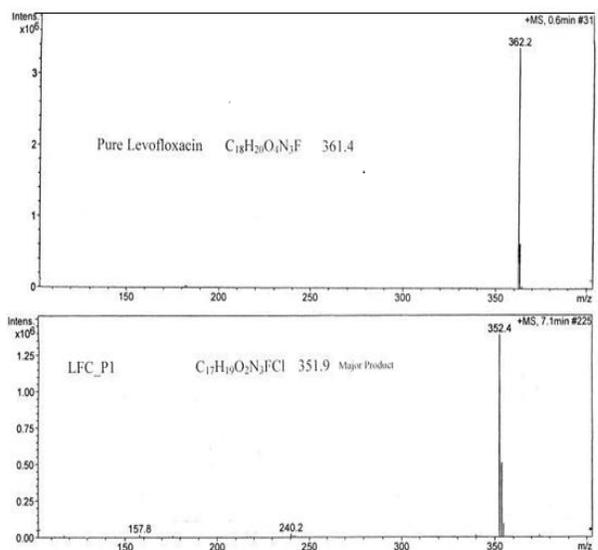


Fig.2 LC/MS spectra of levofloxacin and levofloxacin chlorination major product

Reaction orders

A plot of $\log k'_{\text{obs}}$ versus $\log [\text{FAC}]_0$ yielded a line with slope equal to 1 for total reaction (Fig.3.), indicating that this reaction can be treated as first order with respect to FAC.

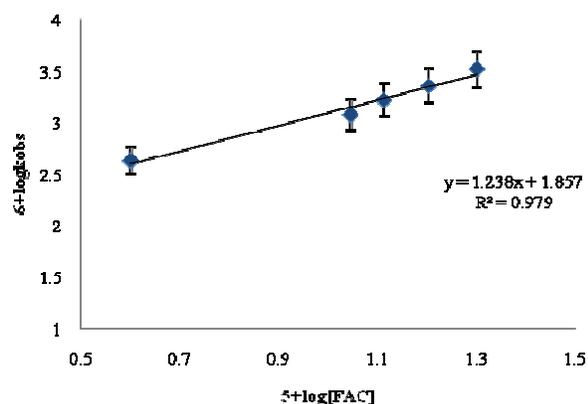


Fig. 3. Plot of $\log (k_{\text{obs}})$ versus $\log [\text{FAC}]$ at pH 7

Effect of Variation of FAC on the reaction

The FAC concentration was varied in the range of 0.4×10^{-4} mol dm^{-3} to 2.0×10^{-4} mol dm^{-3} with constant concentrations of LFC, 6×10^{-6} mol dm^{-3} , silver (I), 8×10^{-8} mol dm^{-3} and at constant ionic strength of 0.02 mol dm^{-3} . The plots of $\log [\text{FAC}]$ versus time, for different initial concentrations of FAC are found to be linear (Fig.3.) ($R^2 > 0.994$) and constant the pseudo-first order rate constants; k_{obs} values (Table 1) indicated that the order with respect to $[\text{FAC}]$ was unity.

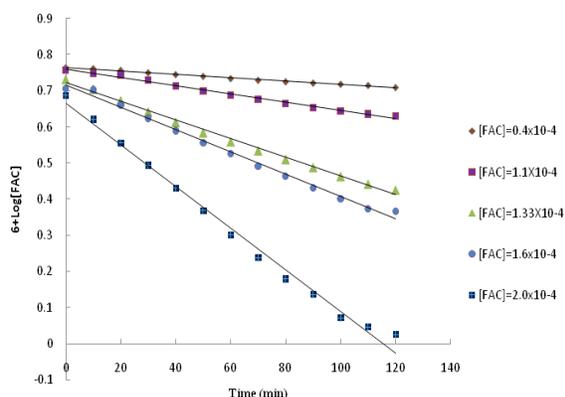


Fig.3. Sample individual time plots for $\log [\text{FAC}]$ for various concentrations at pH=4.2. $[\text{LFC}] = 6 \times 10^{-6}$ mol dm^{-3} , $[\text{Ag(I)}] = 8 \times 10^{-8}$ mol dm^{-3} , $[\text{FAC}] = 0.4 \times 10^{-4}$, 1.1×10^{-4} , 1.33×10^{-4} , 1.6×10^{-4} , 2.0×10^{-4} mol dm^{-3} .

Effect of pH on the reaction

The pH of the reaction mixture varied from pH = 4.2 to 8.2 by using acetate, phosphate and borate buffers, keeping the other conditions constant throughout the experiment. The rate was found to decrease with increase in pH. The graph of apparent second order rate constant, k''_{app} versus pH for uncatalyzed, catalyzed and total reaction (Fig.4) The pH dependent apparent second order rate constant for the catalyzed and uncatalyzed reaction were calculated from the plot of $k''_{\text{app}} = (k_{\text{obs}} / [\text{FAC}]_{\text{T}})$. The variation in k''_{app} from pH 4.2 to 8.2 can be attributed to the varying importance of

specific reaction amongst the individual acid -base conditions of LFC and FAC

When sodium hypochlorite is dissolved in water, it hydrolysis rapidly and combines with H^+ ions according to the equation 3 and 4



Hypochlorous acid is weak acid, it undergoes partial ionization as shown in equation (5)

$$K_a = \frac{[\text{H}^+][\text{OCl}^-]}{[\text{HOCl}]} \quad (5)$$

Where, K_a is called dissociation constant, $[\text{H}^+]$, $[\text{OCl}^-]$ and $[\text{HOCl}]$ are the concentration of H^+ , OCl^- and HOCl respectively.²² The p^{K_a} value of HOCl is 7.54 at 25 °C and p^{K_a} value of HOCl is 7.82 at 0 °C.²³ At lower pH HOCl dominant active species and at higher pH OCl^- dominant weaker species. Hence rate of reaction decreases with increase in pH.

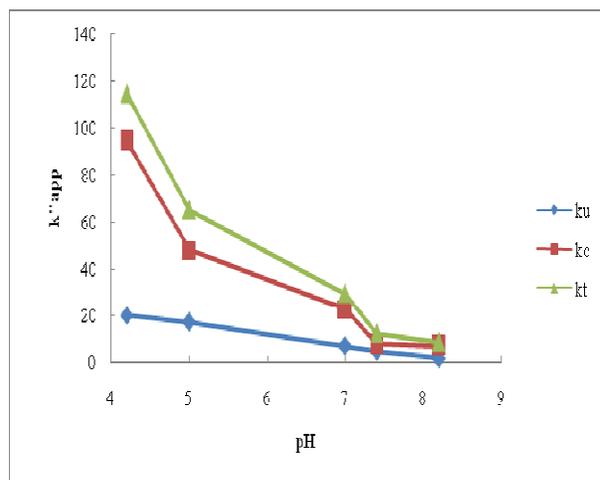


Fig.4. The second order rate constants catalyzed, uncatalyzed and total reaction plot of k''_{app} vs pH

Effect of varying ionic strength

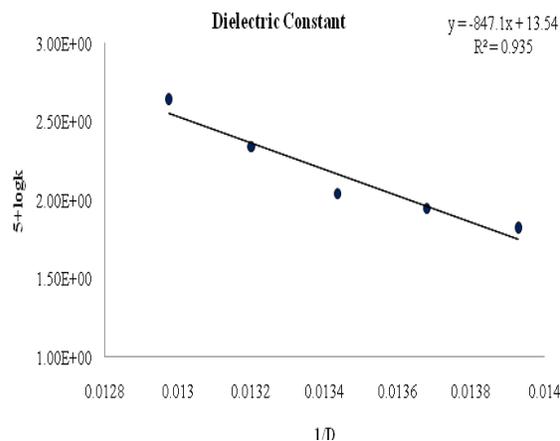
The effect of ionic strength (I) 25°C temperature at was studied by varying the buffer concentration from 0.002 to 0.01 mol dm^{-3} at p^{H} 7.0 and 9.0 conditions was carried out. It was observed that no significant effect of ionic strength on the rate constant. The solvent did not react with the oxidant under experimental conditions. (Table 2) The observed negligible 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 species²⁴.

Table 2 Effect of ionic strength on the chlorination of levofloxacin at different pH 25°C. [HOCl]= 1.6×10⁻⁴ mol dm⁻³, [LFC] = 6×10⁻⁶ mol dm⁻³, [Ag⁺]=1×10⁻⁸ mol dm⁻³ and Ionic strength = 0.02 M

pH	[Buffer] (× 10 ⁻³ mol dm ⁻³)	k _{obs.} (× 10 ⁴ s ⁻¹)	pH	[Buffer] (× 10 ⁻³ mol dm ⁻³)	k _{obs.} (× 10 ⁴ S ⁻¹)
	2	4.76	2		4.0
	4	4.91	4		3.8
7	6	3.96	6		3.4
	8	4.40	8		3.2
	10	4.50	10		3.2

Effect dielectric constant

The effect of dielectric constant (D) was studied by varying the t- butanol water content in the reaction mixture with all other conditions being maintained constant. The D values were calculated from the equation, $D = D_W V_W + D_B V_B$, where D_W and D_B are dielectric constants of pure water and t-butyl alcohol respectively, and V_W and V_B are the volume fractions of components water and t-butyl alcohol, respectively, in the total volume of the mixture. The rate constant k'_{obs} decreases with decrease in the dielectric constant of the medium. The plot of $\log k'_{obs}$ versus $1/D$ with was linear with a negative slope of 847.13 and $r^2 \geq 0.935$. (Fig.5) The effect of solvent on the reaction kinetics has been described in detail in well known monographs of²¹ and for a limiting case of zero angle approach between two dipoles or an ion dipole system Amis²⁵ has shown that a plot $\log k_{obs}$ vs $1/D$ gives a straight line with negative slope for interaction between negative ions and dipole or two dipoles. In the present study the rate constant at pH =7 decreased with decrease in dielectric constant of the medium.

**Fig.5.** Effect of dielectric constant on the chlorination of LFC in the presence of Ag (I) catalyst**Effect of LFC variation**

The LFC concentration was varied in the range of 2×10^{-6} mol dm⁻³ to 10.0×10^{-6} mol dm⁻³ with constant concentrations of FAC, 1.33×10^{-4} mol dm⁻³, and catalyst Ag (I), 5.0×10^{-8} mol dm⁻³ at constant ionic strength of 0.02 mol dm⁻³ both uncatalyzed and catalyzed reaction. The pseudo-first order rate constant remains constant. The k_{obs} values (shown in Table 3) indicated that the order with respect to [LFC] was unity.

Effects of initially added products

Initially added products, such as chloramines or combined chlorine (CC) did not have any significant effect on the rate of reaction. The experimental rate law is given as follows

$$\text{Rate} = -\frac{d[\text{LFC}]}{dt} = kK_1K_2[\text{OCl}^-][\text{H}^+][\text{LFC}][\text{Ag}^+]$$

$$\frac{\text{Rate}}{[\text{LFC}]} = k_{obs} = kK_1K_2[\text{OCl}^-]^{1.25}[\text{H}^+]^{0.24}[\text{Ag}^+]^{0.82}$$

Table 3 Effect of variation of [LFC] on the uncatalyzed and silver catalyzed chlorination on the rate at of reaction Ionic strength = 0.02 mol dm⁻³ at 25±0.2 °C

pH	10 ⁴ [FAC] (mol dm ⁻³)	10 ⁶ [LFC] (mol dm ⁻³)	10 ⁸ [Ag ⁺] (mol dm ⁻³)	10 ³ k _{obs.} (s ⁻¹) (Total) Found	10 ⁴ k _{obs.} (s ⁻¹) (Uncatalyzed)	10 ³ k _{obs.} (s ⁻¹) (catalyzed)
	1.33	2.0	5.0	1.04	8.41	0.20
	1.33	4.0	5.0	1.10	8.45	0.26
7.0	1.33	6.0	5.0	1.06	8.41	0.22
	1.33	8.0	5.0	1.11	8.43	0.27
	1.33	10.0	5.0	1.08	8.45	0.24

Effect of temperature

The kinetics was studied at four different temperatures with varying LFC and FAC by keeping other conditions constant, the rate was found to increase with increase in temperature. The second order rate constant k''_{app} at four different temperatures 15, 20, 25 and 30°C were obtained. The energy of activation corresponding to these rate constants was evaluated from the Arrhenius plot of $\log k$ versus $1/T$ ($r^2 > 0.959$) and from which other activation parameters were obtained. Effect on the rate of reaction in both the catalyzed and uncatalyzed reactions (Table 3). The positive value of ΔH and ΔG (Table 4) indicate that the transition state is highly solvated, increasing the size of transition state. The moderate values of ΔH and ΔG were both favorable for electron transfer processes²⁶. The negative value of ΔS indicates that transition state is more ordered than the reactants.

Table 4. Activation and thermodynamic parameters for the oxidation of LFC by FAC with respect to the slow step of the reaction

a) Effect of temperature

Temperature (Kelvin)	$10^3 k (s^{-1})$
288	1.85
293	2.44
298	2.65
303	3.18

(b) Activation parameters

Activation parameters	Values Catalyzed)	Values (Uncatalyzed)
E_a (kJ mol ⁻¹)	24.88±2.0	28.6 ± 3.0
ΔH (kJ mol ⁻¹)	22.43±1.0	26.1 ± 2.7
$\Delta S \pm$ (JK ⁻¹ mol ⁻¹)	-27.32±2.5	-12.4 ± 1.5
$\Delta G \pm$ (kJ mol ⁻¹)	30.16±1.0	29.8 ± 3.0

Effect of varying [Ag (I)] catalyst

The [Ag (I)] catalyst concentrations were varied from 2×10^{-8} to 16×10^{-8} moldm⁻³ range, at constant concentrations of LFC, HOCl and constant ionic strength. The rate of the reaction increases with increase in the concentration of Ag

(I). The order in [Ag (I)] was found to be unity from the linearity of the plot of k_c versus [Ag (I)] as shown in Fig.6.

Activity of catalyst

It is observed by Moelwyn-Hughes²⁷ in both the uncatalyzed and catalyzed reactions proceed simultaneously, so that

$$k_t = k_u + K_c [Ag(I)]^x$$

Where, k_t is the observed pseudo first order rate constant in the presence of Ag(I) catalyst, k_u is the pseudo first order rate constant for uncatalyzed, K_c is the catalytic constant and 'x' the order of the reaction with respect to Ag(I). In the present investigation, x values for the standard run were considered to be unity. Discussion Then, the value of K_c is calculated using the equation,

$$K_c = \frac{[k_t - k_u]}{[Ag(I)]^x} = \frac{k_c}{[Ag(I)]^x} \quad (\text{Where } k_t - k_u = k_c)$$

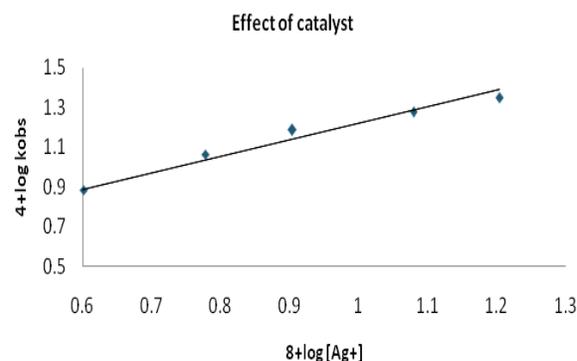
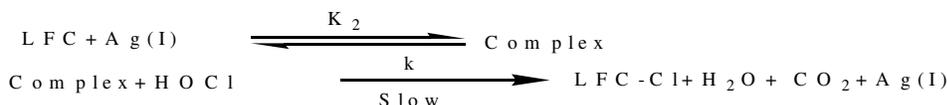


Fig.6. First order rate constant for the reaction of LFC and FAC at different concentrations of Ag (I)

The rate law can be calculated from the proposed mechanism



$$Rate_C = Rate_T - Rate_U$$

$$Rate = k [Complex] = k [Complex] [HOCl]$$

$$= k K_2 [HOCl] [LFC] [Ag(I)]$$

$$= k K_1 K_2 [OCl^-] [H^+] [LFC] [Ag^+] \quad \text{-----(2)}$$

$$[LFC]_T = [LFC]_f + [Complex]$$

$$= [LFC]_f + K_2 [LFC] [Ag^+]$$

$$[LFC]_f = \frac{[LFC]_T}{1 + K_2[Ag^+]} \quad \text{----(3)}$$

$$[Ag^+]_f = \frac{[Ag^+]_T}{1 + K_2[LFC]} \quad \text{----(4)}$$

$$\begin{aligned} [OCI^-]_T &= [OCI^-]_f + [HOCI] \\ &= [OCI^-]_f + K_1[OCI^-][H^+] + k[HOCI][Complex] \\ &= [OCI^-]_f + K_1[OCI^-][H^+] + kK_1[OCI^-][H^+][Complex] \\ &= [OCI^-]_f + K_1[OCI^-][H^+] + kK_1K_2[OCI^-][H^+][LFC][Ag^+] \end{aligned}$$

$$[OCI^-]_f = \frac{[OCI^-]_T}{1 + K_1[H^+] + kK_1K_2[H^+][LFC][Ag^+]}$$

The term $1 \gg kK_1K_2[H^+][LFC][Ag^+] \approx 0$

$$[OCI^-]_f = \frac{[OCI^-]_T}{1 + K_1[H^+]} \quad \text{----(5)}$$

$$\begin{aligned} [H^+]_T &= [H^+]_f + [HOCI] \\ &= [H^+]_f + [H^+][OCI^-] \end{aligned}$$

$$[H^+] = \frac{[H^+]_T}{1 + K_1[OCI^-]} \quad \text{----(6)}$$

Substitute the values from equations (3) to (6) in equation (2)

$$Rate = kK_1K_2 \left[\frac{[OCI^-]_T}{1 + K_1[H^+]} \right] \left[\frac{[H^+]_T}{1 + K_1[OCI^-]} \right] \left[\frac{[LFC]_T}{1 + K_2[Ag^+]} \right] \left[\frac{[Ag^+]_T}{1 + K_2[LFC]} \right]$$

$$Rate = \frac{kK_1K_2 [OCI^-]_T [H^+]_T [LFC]_T [Ag^+]_T}{\{1 + K_1[H^+]\} \{1 + K_1[OCI^-]\} \{1 + K_2[Ag^+]\} \{1 + K_2[LFC]\}} \quad \text{----(7)}$$

$$Rate = \frac{kK_1K_2[OCI^-]_T [H^+]_T [LFC]_T [Ag^+]_T}{\{1 + K_1[H^+] + K_1[OCI^-]\} \{1 + K_2[Ag^+]\} \{1 + K_2[LFC]\}}$$

$$Rate = \frac{kK_1K_2[OCI^-][H^+][LFC][Ag^+]}{\{1 + K_1[H^+] + K_1[OCI^-]\} \{1 + K_2[Ag^+]\} \{1 + K_2[LFC]\}}$$

$$Rate = \frac{kK_1K_2[OCI^-][H^+][LFC][Ag^+]}{1 + K_2[Ag^+] + K_2[LFC] + K_1[H^+] + K_1K_2[H^+][Ag^+] + K_1K_2[H^+][LFC] + K_1[OCI^-] + K_1K_2[OCI^-][Ag^+] + K_1K_2[OCI^-][LFC]} \quad \text{----(8)}$$

At very lower concentrations of silver and LFC the equation (8) reduces to

$$\frac{Rate}{[LFC]} = k_{obs} = \frac{kK_1K_2[OCI^-][H^+][Ag^+]}{1 + K_1[OCI^-] + K_1[H^+]} \quad \text{----(9)}$$

Equation (9) confirms all the observed orders with respect to different species, which can be verified by rearranging it to

$$\frac{1}{k_{obs}} = \frac{1}{kK_1K_2[OCI^-][H^+][Ag^+]} + \frac{1}{kK_2[H^+][Ag^+]} + \frac{1}{kK_2[H^+][OCI^-]} \quad \text{----(10)}$$

$$\frac{[Ag^+]}{k_C} = \frac{1}{kK_1K_2[OCI^-][H^+]} + \frac{1}{kK_2[H^+]} + \frac{1}{kK_2[OCI^-]} \quad \text{----(11)}$$

Environmental implications of fluoroquinolone degradation products

LFC is fluoroquinolones class of antibacterial agent has the ability to inhibit bacterial DNA replication and is believed to be linked to their quinolone moieties²⁸. Suggesting that piperazine and quinolone fragmentation may lead to elimination of antibacterial activity. The product of major channel involves halodecarboxylation of quinolone moiety and it may retain the antibacterial activity but the products of minor channel involve degradation at both piperazine and quinolone moieties, may lose the antibacterial activity.

CONCLUSION:

In drinking water treatment, toxic organic compounds could combines with chlorine. pH plays an important factor affecting the chlorination process. Levofloxacin reacts rapidly with chlorine over the range of pH 4.2 to 8.2 with different rates. It undergoes faster reaction in acidic medium becomes slower in basic medium by maintaining conventional chlorination conditions likely to be observed in conventional water chlorination processes. The observed product the formation of major product involves electrophilic halodecarboxylation of quinolone moiety and hence, it may retain the antibacterial activity as observed in ciprofloxacin and enrofloxacin. Further toxicological studies on the degradation products of LFC are required to understand the environmental implications of the LFC reaction with FAC.

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