Micelle catalyzed oxidative degradation of norfloxacin by chloramine-T

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ABSTRACT

Present work reports influence of micellar media (CTAB) upon the oxidative degradation of fluoro-quinolone family drug norfloxacin (NOR). The reaction has been studied at constant temperature (308 K). The stoichiometry of the reaction was found to be 1:4 and oxidation products were identified by LC–MS technique and other spectral studies. The reaction exhibited first-order-dependence on chloramine-T [CAT] and fractional-order dependence on [NOR]. The rate constant was independent of cationic micelles of cetyltrimethylammonium bromide [CTAB] at lower concentrations followed by a rapid increase in rate constant to a maximum and further gradual decrease in rate constant at higher CTAB was observed. In the presence of CTAB, both the oxidant and substrate are distributed between the aqueous and the micellar pseudo phases and then react to give the product. Compensation between water structure destruction and substrate–micelle interaction plays an important role in the presence of CTAB. The rate constants were obtained and the applicability of Piszkiewicz's, Raghvan–Srinivasan's and pseudo phase models allowed us to obtain the reactivity constants in the aqueous pseudo phase and in the micellar pseudo phase (k_2^w and k_2^m) and the binding constants of the reactants to the micellar phase (K_1, K_2). The effects of inorganic salts i.e. [SO_4^{2-}], [HSO_4^-], [Cl^-] and [Br^-] on reaction rate have also been studied.

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1. Introduction

Recently, presence and accumulation of pharmaceuticals and personal care products (PPCPs) in the aquatic environment have received increasing attention and putting a new challenge to drinking water, waste water and water treatment systems [1–3]. Due to their large quantities of uses, antimicrobial chemicals are continuously introduced to the aquatic environment via treated, untreated sewage, sludge, agricultural waste and runoffs. In this context, fluoroquinolones (FQs) are probably among the most important class of synthetic antibacterial agents as these are most commonly used in human and veterinary medicines. In fact most of these antibacterial agents are not fully metabolized in the body [4], therefore 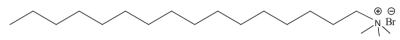entered the environment through wastewater effluents [5]. A perusal of literature shows that not so many studies focusing on the biodegradability and fate of FQs in the environment have been reported [6–9]. However, strong binding can be expected to delay degradation and may partly explain the apparent recalcitrance of FQs [10]. Several recent studies have reported the environmental presence of FQs in many countries such as Switzerland, the United States, Australia and China [11]. The presence of broad spectrum antibiotics like these in aquatic environment, even at low concentrations, may pose serious threats to the ecosystem and human health by inducing proliferation of bacterial drug resistance [12]. Studies on the oxidation of few FQs [13–15] and only two cases of oxidation of NOR [16,17] have been reported. However in natural water reservoirs already containing various surfactants as well as oxidants, the fate of these drugs is a new emerging aspect for researchers. This study reports the absolute kinetics and effects of cationic surface active agent cetyltrimethylammonium bromide (CTAB) on the oxidative degradation of one of the FQs, norfloxacine (NOR) by oxidant chloramine-T (CAT). This may be explaining how NOR gets transformed in the presence of an oxidant (CAT) and surfactant (CTAB) in aqueous media. During the water chlorination process behaviors of some FQs have been reported [18]. Our

investigation is based upon the influence of cationic surfactant on the transformation of NOR by CAT. The CAT itself is used as an antiseptic drug [19] and also most commonly used for various water treatment processes, disinfectant, deodorant, etc. [20].

The chemistry of aromatic sulfonyl haloamines (N-haloamines) is of interest due to its diverse behavior. N-haloamines are a group of mild oxidizing agents, which have been used extensively for the oxidation of several organic compounds. The versatile nature of N-haloamines is due to halonium cations and nitrogen anions in their structure, which can act as both a base and a nucleophile [21–25]. Thus, these compounds can react with a wide range of functional groups to cause a variety of molecular changes. The prominent member of this class of compounds is sodium-N-chloro-4-methylbenzensulfonamide, generally known as chloramine-T (CAT). Several reviews have been published on the oxidizing behavior of CAT [26–28] and a number of publications focus on the mechanistic aspects of the redox reactions in acidic media. In most of the studies one of the species, $RNHCl$ ($R = CH_3C_6H_4SO_2$), HOCl, or H_2OCl^+, has been considered as the reactive species [29,30]. Similar information on CAT in micellar medium is limited.

Surfactants of cationic nature like CTAB are well known antibacterial compounds.

Cetyltrimethylammonium bromide

They are also used as environmental cleaning products, in cosmetic formulations and pharmaceuticals [31,32]. Surfactant properties have attracted growing attention in biochemistry, biological and chemical research applications. Surfactants as reaction medium, affect reaction rates, position of the chemical equilibrium, products, and in some cases stereochemistry of the reactions [33,34]. Surfactants are having growing number of scientific and technological applications as these are found to control the size of synthesized microparticles and play an important role in solubilization and extraction. These surfactants are able to enhance reactions between non-hydro soluble organic substrates and hydro-soluble reagents, the kinetics of numerous reactions in microemulsions have been well studied [35]. In the presence of cationic micelles of CTAB, catalysis is observed when reactants are taken into the micellar pseudo phase. In fact, a greater reactivity has been reported in micellar pseudo phase as compared to the bulk solution. Analogies between enzyme and micellar catalysis have been widely discussed [36], but are discounted [37] because micellar catalysis generally lacks the substrate specificity and high catalytic activity of enzymes. Micellar effects on the rates are sensitive to the nature of counterions and to head group bulk [38]. Transition of spherical to larger micelles may be caused by salt or surfactant additions [39] or solute solubilization [40,41]. It is well known that the addition of a salt decreases the electrostatic interactions between monomers in the micelle and also affects the partitioning of organic compounds between micelles and bulk solvent [42]. Micellar catalysis can be enhanced by adding some salts indicating that the rate enhancement is sensitive to changes in micellar morphology and charge density [43].

2. Materials and methods

Analytical grade reagents were used without further purification and solutions were prepared in triple distilled water. The stock solution of CAT (Loba Chem.) was stored in dark colored bottle and the strength of CAT was checked iodometrically [44]. The NOR (USP powder, plama, m.p. 215–216 °C, 99.9%) was used as received and stock solution was prepared in 10% acetic acid which was further

purified by distillation. The NOR solution was also stored in dark colored bottle to prevent any photochemical reactions. To recrystallize CTAB (Merck), it was dissolved in minimum quantity of luke warm MeOH (Loba Chem.) at about 40 °C. Then Et_2O was then added with constant stirring until a permanent white precipitate was obtained. The content was cooled to room temperature and kept in the refrigerator for further cooling. Crystalline white solid so obtained was filtered in a Buchner funnel. Finally crystals were washed with excess cold ether and air dried.

All the kinetic measurements were carried out in a black-coated vessel at constant temperature (308 K) and experiments were carried out under pseudo first-order condition with [NOR] $\gg$ [CAT]. The reaction was initiated by rapid addition of known amounts of oxidants to the reaction mixture containing the required amounts of NOR, sulfuric acid, CTAB and water in glass stopper Pyrex boiling tubes, thermostated at the same temperature. Progress of reaction was monitored by iodometric determination of unconsumed [CAT] in known aliquots of the reaction mixtures at different time intervals. Each kinetic run was studied for ~80% reaction. Runs were reported twice and had <4% standard deviation. The rate constants of reactions in each kinetic run were determined by the slope of tangent drawn by plots of remaining log [CAT] against time data.

Excess of CAT over NOR was allowed to react in the presence of sulfuric acid. The residual oxidant in each case was determined iodometrically after 24 h. The results showed that 4 mol of CAT was required for each mole of NOR. On the basis of analysis of the reaction products, the stoichiometric equation is proposed in Scheme 1.

The reduced product of oxidant CAT i.e. p-toluene sulfonamide (PTS) was initially characterized by TLC [45]. Further confirmation was determined by its melting point, 139 °C, which was within close proximity to the reported temperature of 137–140 °C in previous works [46]. PTS was quantitatively determined by its reaction with xanthydrol to yield the corresponding N-xanthyl-p-toluenesulfonamide [47]. In a typical experiment, equal quantities of separated PTS and xanthydrol (0.20 g) were dissolved in 10 mL of glacial acetic acid. The reaction mixture was stirred for 3 min at room temperature and allowed to stand for 90 min. The derivative was filtered, recrystallized with dioxane/water (3:1), and dried at room temperature. The mass of PTS was obtained with 80–85% recovery in this case. Finally, the main oxidation product of NOR and other products were isolated and confirmed by GC–MS (JEOL-JMS, Mate-MS system, Japan) (Supporting information, Figs. S-1 and S-2). Carbon dioxide was identified by bubbling N_2 gas through the reaction mixture and passing liberated gas through a U-shaped tube containing a saturated $Ba(OH)_2$ solution. The oxidation product of NOR was also confirmed by FT-IR spectral studies (IR (KBr, $\gamma\,cm^{-1}$): 1730s, C=O; carboxylic, 1621s, C=O; 3059s, NH; 3500s, OH).

3. Results

To study the effects of concentration of various reactants on rate of oxidation reaction and with a view to ultimately propose a suitable reaction mechanism, concentration of each reactant was varied keeping concentration of other reactants constant. Firstly, the rate of reaction in the absence of cationic surfactant (CTAB) was determined and then the role of CTAB on the degradation of NOR by common chlorinating agent (during water treatment process) CAT, in acidic medium was analysed. The values of rate constants in the absence and presence of CTAB were found to be