

PREPARATION OF COLLOIDAL MANGANESE DIOXIDE AND THEIR APPLICATION IN DEGRADATION OF ANTIBACTERIAL DRUG

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ABSTRACT

Pharmaceuticals, especially fluoroquinolone antibiotics, have received increasing global concern, since they have been recognized as emerging environmental pollutants. Degradation of antibiotics, such as oxidative degradation by metal oxides, often plays an important role in the elimination of antibiotics from the environment. The kinetics of oxidation of moxifloxacin by colloidal manganese dioxide has been studied in aqueous acidic medium at 25 °C temperature. The stoichiometry for the reaction indicates that the oxidation of one mole of moxifloxacin requires one mole of manganese dioxide. The reaction is second order that is first order with respect to manganese dioxide and moxifloxacin. The rate of reaction increases with the increasing $[H^+]$ ion concentration. A probable reaction mechanism, in agreement with the observed kinetic results, has been proposed and discussed.

Keywords: Colloidal Manganese dioxide, Kinetics, Moxifloxacin and Oxidation.

I. INTRODUCTION

Moxifloxacin (MF), 1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-[(4a*s*,7*a*s)-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 [1]. The use of this newer generation fluoroquinolone is increasing due to expand antibacterial spectrum. But these are not fully metabolized in the body and are partially excreted in its pharmaceutically active form. Due to the limited biodegradability and widespread use of these antibiotics, an incomplete removal is obtained in typical waste water treatment plants and analogous huge quantities are discharged into the environment. For the removal of these Fluoroquinolone many studies are used, in which oxidation process is mostly used and degrade them from the environment. A literature survey revealed that the kinetics and mechanism of oxidation of MF by different oxidants was carried out in both acidic and alkaline medium [2-5]. Manganese dioxide (MnO_2) is one of the most active and important oxidative component, showing high potency in degrading various organic pollutants such as antibacterial agents [6]. Perez-Benito et al. found first time that water-soluble manganese dioxide can be prepared from reduction of aqueous potassium permanganate by sodium thiosulphate under neutral condition [7]. A literature survey confessed that the kinetics and mechanism of degradation of some antibiotics by MnO_2 in aqueous acidic/alkaline medium have been

studied earlier [8, 9]. But yet lack of literature on the oxidative degradation of MF by MnO_2 in aqueous acidic medium has been reported, so the title reaction prompted us to understand the mechanism of the reaction.

II. EXPERIMENTAL

2.1 Chemicals

The solution of LEV (KORES India Limited) was prepared by dissolving known amounts of the samples in double distilled water. Solutions of LEV were always freshly prepared before experiment. Potassium permanganate (MERCK) and sodium thiosulfate (BDH) were used as received. Sulphuric acid (MERCK), sodium sulphate (MERCK) was used to maintain the acidity and ionic strength respectively. All other reagents were of AR or GR MERCK quality. Double distilled water was employed throughout the study.

2.2 Instrumentation

For kinetic measurements, a Peltier accessory (temperature-Controlled) attached to a double beam U.V.3000⁺, UV-Visible spectrophotometer (LABINDIA) with U.V. path length 1.0 cm in the spectral range 200-800 nm, was used.

2.3. Preparation of MnO_2

According to the Perez-Benito method, for the preparation of water soluble MnO_2 , the required volume of $\text{Na}_2\text{S}_2\text{O}_3$ solution (20 cm^3 , $1.88 \times 10^{-2} \text{ mol dm}^{-3}$) was added to a standard solution of KMnO_4 (10 cm^3 , 0.1 mol dm^{-3}) and the reaction mixture was diluted by the required volume of water in 2 dm^{-3} standard flask. The resulting solution was dark brown and perfectly transparent and stable for several weeks. The absorption spectrum of the reaction mixture consists of one broad band covering the whole visible region of the spectrum with λ_{max} 390 nm. The application of Beer's law of MnO_2 at 390 nm had been verified giving $\epsilon = 15660 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ [10].

2.4. Kinetic measurements

The reaction was initiated by mixing the solutions of MnO_2 and MF which also contained the required concentration of H_2SO_4 and Na_2SO_4 at 25°C . The progress of the reaction was followed by spectrophotometrically at 390 nm, that there was no interference from other species in the reaction mixture at this wave length. Initial rates were computed employing plane mirror method. The pseudo first order plots were also made wherever, reaction conditions permitted. Results in triplicate were reproducible to within $\pm 6\%$.

2.5. Stoichiometry and product analysis

The stoichiometry of the reaction was determined with various ratio of reactants and constant concentration of other reactants. After completion of the reaction, unreacted MnO_2 was indicated that one mole of MF was oxidized by one mole of MnO_2 , exhibiting 1:1 ratio for the reaction of reductant to oxidant

III. RESULTS AND DISCUSSION

1.1. Effect of manganese dioxide concentration

The concentration of MnO_2 was varied in the range $(0.75 \text{ to } 7.5) \times 10^{-5} \text{ mol dm}^{-3}$ at two but fixed concentration of MF to be 5×10^{-5} and $6 \times 10^{-5} \text{ mol dm}^{-3}$, $[\text{H}_2\text{SO}_4] = 2 \times 10^{-4} \text{ mol dm}^{-3}$ and $[\text{Na}_2\text{SO}_4] = 3 \times 10^{-4} \text{ mol dm}^{-3}$ at 25°C . Initial rates ($k_i \text{ mol dm}^{-3} \text{ s}^{-1}$) were calculated employing plane mirror method and a plot of initial rate (k_i) versus $[\text{MnO}_2]$ was made that yielded a straight line passing through the origin ascribing first order dependence with respect to MnO_2 . Second order plots were also made by making plots of $\log ([\text{MF}]_t/[\text{MnO}_2]_t)$ against time.

3.2 Effect of Moxifloxacin concentration

The concentration of MF was varied from $(1.0-10.0) \times 10^{-5} \text{ mol dm}^{-3}$ at two but fixed concentration of MnO_2 viz. 2×10^{-5} and $3 \times 10^{-5} \text{ mol dm}^{-3}$ at 25°C . Initial rates ($k_i \text{ mol dm}^{-3} \text{ s}^{-1}$) were calculated and a plot of initial rate ($k_i \text{ mol dm}^{-3} \text{ s}^{-1}$) against $[\text{MF}]$ was made, a straight line passing through the origin was obtained confirming first order dependence with respect to MF. Certain reactions were also undertaken under pseudo first order conditions ($[\text{MF}] \gg [\text{MnO}_2]$) under identical experiment conditions varying from $(1.0-10.0) \times 10^{-4} \text{ mol dm}^{-3}$, pseudo first order plots were made and pseudo first order rate constants ($k_{\text{obs}}, \text{ s}^{-1}$) evaluated from these plots were found to increase proportionately with the increasing concentration of MF.

3.3 Effect of hydrogen ion and sulphate ion

The actual concentration of $[\text{H}^+]$ and $[\text{SO}_4^{2-}]$ i.e., $[\text{H}^+]_f$ and $[\text{SO}_4^{2-}]_f$ were calculated from acid-sulfate equilibrium constant for the different concentration of sulfuric acid. The effect of concentration variation of $[\text{H}^+]$ ion on the rate of reaction was studied in the concentration range $(0.08-0.75) \times 10^{-4} \text{ mol dm}^{-3}$ at fixed concentration of MF, MnO_2 , ionic strength and $[\text{SO}_4^{2-}] = 1.0 \times 10^{-4} \text{ mol dm}^{-3}$ at three temperatures viz. 20° , 25° , 30°C respectively. Pseudo first order rate constant (k_{obs}) was found to be increased with increase in $[\text{H}^+]$.

The effect of sulfate ion concentration was also studied in the concentration range $(0.5-1.5) \times 10^{-4} \text{ mol dm}^{-3}$, all other reaction conditions being constant and $[\text{H}^+]$ at $0.5 \times 10^{-4} \text{ mol dm}^{-3}$ keep constant with the required concentration of H_2SO_4 concentrated from acid and sulfate equilibrium constant for different added $[\text{SO}_4^{2-}]$. The results indicate that $[\text{SO}_4^{2-}]$ did not have significant effect on the rate of reaction.

3.4. Effect of ionic strength and dielectric constant

At constant concentration of reactants, the ionic strength was varied by varying concentration of sodium sulfate $(0.3-3.0) \times 10^{-4} \text{ mol dm}^{-3}$ at 25°C . 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.

3.5. Effect of added product

In order to observe the effect of externally added Mn(II) on the rate of reaction was studied by varying concentration of MnCl_2 (1.0×10^{-5} to $10 \times 10^{-5} \text{ mol dm}^{-3}$) keeping other experimental conditions constant. The results indicates that the rate of reaction is unaffected by the addition of Mn(II).

3.6. Test for free radical

The formation of free radical was confirmed by the addition of acrylonitrile in the reaction mixture. After 5 h then diluted with methanol, while precipitate was formed, indicating the presence of free radical during the progress of reaction.

The negligible effect of ionic strength and dielectric constant on the rate of reaction suggests that the reaction is either between two neutral species or a neutral and a charged species.

3.7. Mechanism

On the basis of above results, the mechanism of oxidation of MF by MnO_2 in acid aqueous media is given by the scheme 1.

(2)

(3)

(4)

(5)

Scheme 1 Proposed mechanism for the oxidation of MF by MnO_2 .

On the basis of above mechanism the following rate equations can be proposed

$$Rate = kK_1K_2[MnO_2][MF][H^+]$$

(6)

$$\frac{\text{Rate}}{[\text{MnO}_2]} = k_{obs} = kK_1K_2[\text{MF}][\text{H}^+]$$

(7)

$$\frac{k_{obs}}{[\text{MF}]} = k' = kK_1K_2[\text{H}^+]$$

(8)

Where k' is second order rate constant.

$$\frac{1}{k'} = \frac{1}{kK_1K_2[\text{H}^+]}$$

(9)

Plot of $1/k'$ versus $1/[\text{H}^+]$ gives straight line passing through the origin (Fig.1) to support the rate law.

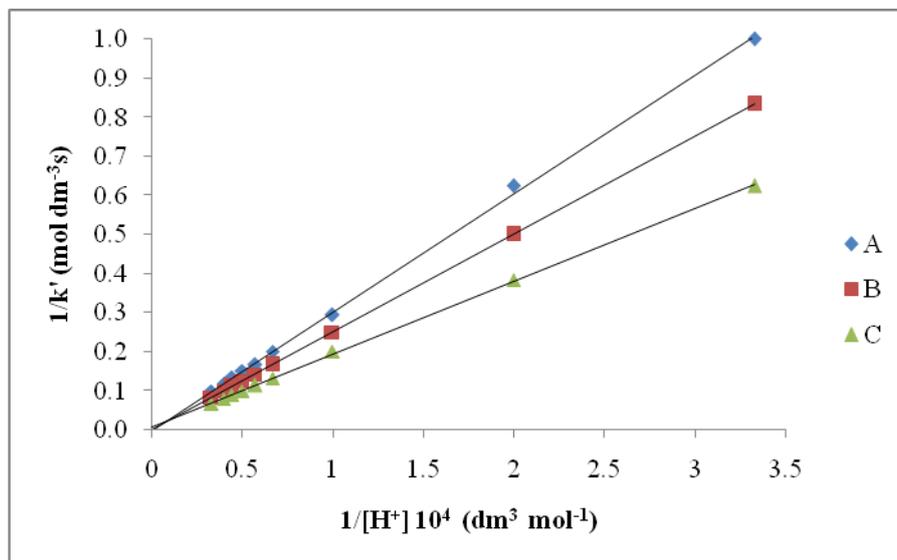


Fig. 1 Plot of $1/k'$ versus $1/[\text{H}^+]$ at three temperatures (A=20°C, B=25°C, C=30°C) $[\text{MnO}_2] = 3.0 \times 10^{-5} \text{ mol dm}^{-3}$, $[\text{MF}] = 5.0 \times 10^{-4} \text{ mol dm}^{-3}$, $I = 5 \times 10^{-4} \text{ mol dm}^{-3}$.

IV. CONCLUSION

A kinetic and mechanistic study of MF oxidation by MnO_2 has been first time investigated in aqueous acidic medium. The reaction follow first order kinetics with respect to MnO_2 , MF and H^+ ion under first order reaction conditions. Results and mechanism indicate that H_2MnO_3 is reactive species of MnO_2 . Since dealkylated products are obtained in the present study, it is evident that the products of the title reaction have antimicrobial activity after oxidation. Thus the degradation of fluoroquinolones plays an important role in the field of waste water treatment.

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