Transformation of acetaminophen using manganese dioxide – mediated oxidative processes: Reaction rates and pathways

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HIGHLIGHTS

▶ APAP was rapidly oxidized by δ-MnO$_2$.
▶ APAP transformation were increased with the decreased pH or increased temperature.
▶ APAP transformation was inhibited by some inorganic ions and phenols co-solutes.
▶ The UV–Vis spectra show that APAP may polymerize to form oligomer.
▶ The products of APAP were formed by the coupling oxidation of aromatic carbon.

ARTICLE INFO

ABSTRACT

This study investigates the oxidative transformation kinetics of acetaminophen (APAP) by δ-MnO$_2$ under different conditions. APAP was rapidly oxidized by δ-MnO$_2$ with the generation of Mn^{2+}. The measured APAP reaction rate considerably increased with an increase in initial δ-MnO$_2$ and APAP concentration, but decreased as pH increased. The APAP reaction rate also increased with an increase in temperature. The addition of inorganic ions (Mn^{2+}, Ca^{2+}, and Fe^{3+}) and substituted phenols (guaiacol, caffeic acid, and p-coumaric acid) as co-solutes remarkably decreased the transformation rate of APAP. The UV–Vis absorption spectra exhibited the $\pi \rightarrow \pi^*$ transition, typical for aromatic rings. In addition, the intensity of the absorption peak gradually improved with increasing reaction time, suggesting that APAP can polymerize to form oligomers. Moreover, the secondary mass spectra of the dimers elucidated that the dimers were formed by the covalent bonding of phenol aromatic rings. Moreover, the higher-degree oligomers were formed by the coupling polymerization of phenolic and anilidic groups of dimers. These results are useful in understanding the fate of APAP in natural systems.

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1. Introduction

A number of new compounds are continually being manufactured and released in the environment. Environmental contaminations by pharmaceuticals and personal care products (PPCPs) draw extensive public attention as pervasive problems. In PPCPs, acetaminophen (APAP) is an intensively used analgesic and antipyretic drug globally. APAP is one of the top 200 prescriptions in the United States in 2003 and the third most required medicine in the United Kingdom [1]. The consumption of APAP is up to 1.0×10^9 g in Japan in 2003 [2–4].

According to a previous study, about 58%–68% of APAP is excreted from the body during therapeutic use [5]. However, the removal of APAP is incomplete in wastewater treatment plants (WWTPs). The reported removals vary from almost complete to 80% in hospital WWTPs and 86% in municipal WWTPs, respectively [6–10]. Thus, APAP is frequently detected in drinking water, surface water, and WWTP effluents. For example, Rabiet et al. [11] detected 211 ng L^{-1} of APAP in drinking water wells. In surface waters, up to 10 and 15.7 μg L^{-1} of APAP have been reported in the United States and Taiwan, and even more than 65 μg L^{-1} of APAP in the Tyne River, United Kingdom [12–14]. APAP has also been detected in European WWTP effluents ranging from several hundred nanograms up to 11.3 μg L^{-1} [7,11,15]. APAP is introduced into the soil environment through dispersion of manure and sewage sludge as field fertilizers [16]. Such considerable amounts of APAP residues in nature result in the emergence and spread of resistant microorganisms, which could have potential impacts on ecosystems and on human health [17–19].

Most studies on APAP focus on analgesic action mechanism and toxicity [17–26]. Studies on the transformation and removal of APAP are relatively limited. These studies mainly focused on

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photodegradation with catalysis of TiO_2, ozonation, H_2O_2, and Fe(III)/oxalate, and transformation by biological, laccase, dichromate and electro-Fenton [2,3,27–32]. Minimal attention was placed on the potential transformation of APAP in the manganese dioxide (MnO_2) system. MnO_2 is typically present in soils and sediments, and is among the most important naturally occurring reactants or catalysts in the organic transformation of soil and sediments. MnO_2 has high reaction potency with various organic pollutants, including anilines, phenols, antibacterial agents, and atrazine [33–38]. Although MnO_2-mediated abiotic transformation may be an important chemical process of APAP in soil and aquatic environments, current understanding of this transformation processes remains limited.

In this study, we sought to obtain a mechanistic understanding of the transformation processes of APAP in the δ-MnO_2 system, and to evaluate the factors influencing APAP transformation by δ-MnO_2. Experiments were conducted to determine the reaction kinetics and products of APAP oxidized by the δ-MnO_2 system. The influences of environmental conditions (e.g., pH and temperature) and the presence of co-solutes (e.g., metal ions and organic matter) on reaction kinetics were also assessed. Based on the kinetic results and product identification, reaction schemes of APAP with δ-MnO_2 were proposed.

2. Materials and methods

2.1. Chemical reagents

APAP (98.0%) was purchased from Dr. Ehrenstorfer GmbH (Augsburg, Germany). Guaiacol (99%), caffeic acid (98%), p-coumaric acid (98%), and 2,6-dimethoxyphenol (99%) were obtained from Adamas–Beta (Basel, Switzerland). δ-MnO_2 was purchased from Acros (New Jersey, USA). High-performance liquid chromatographic (HPLC)-grade methanol (MeOH) was purchased from Tedia (Fairfield, OH, USA). All other reagents were of analytical grade and received from Guangzhou Chemicals Inc. (Guangzhou, China). APAP stock solutions were prepared in ultrapure water to obtain a final concentration of 2 mM in a 100 mL brown volumetric flask protected from light and stored at 4 °C. The APAP stock solution was diluted with buffer solutions to constitute solutions with different concentrations on the day of the experiment.

2.2. Kinetic experiments

Reactions of APAP with δ-MnO_2 were conducted in 15 mL amber borosilicate glass bottles with brown screw caps and Teflon septa at 25 °C under constant shaking at 200 rpm. Sodium chloride (NaCl) was added to adjust the ionic strength (I = 10 mM). Ultrapure water and containers were sterilized at 130 °C for 30 min prior to use excluding the influence of microbial effects on the reaction. δ-MnO_2 solutions were prepared at suspensions of 125, 175, 250, 325, and 375 mg L^{-1} via continuous stirring for 8 h on magnetic stirrers with thermostatic water bath to homogenize the solution prior to use. Reaction samples were periodically collected at time points from 0 min to 80 min. Rapid filtration through 0.22 μm GVWP membranes (Millipore) were used to quench the reaction.

Environmental influences (e.g., pH and temperature) and the presence of co-solutes (e.g., metal ions and organic matter) on the reaction kinetics were also assessed. The reaction pH range of 4.0–6.0 was adjusted using a 5 mM glacial acetic acid (HAc)-sodium acetate (NaAc) buffer system at 25 °C. Temperature effect was studied by changing the reaction temperatures in the range of 15, 25, and 35 °C at pH 4.5. The effects of inorganic ions and organic

substituted phenols were also investigated at pH 4.5 in buffer solutions with inorganic ions (K^+, Mn^{2+}, Zn^{2+}, Mg^{2+}, Ca^{2+}, Fe^{3+}, NO_3^-, SO_4^{2-}, and PO_4^{3-}) and organic substituted phenols (guaiacol, caffeic acid, and p-coumaric acid) at 25 °C. The final concentration of APAP and MnO_2 were 40 μM and 50 mg L^{-1}, respectively, in 15 mL brown glass bottles for reactions. Two sets of control reactors, namely, pure buffer with APAP and pure buffer with δ-MnO_2, were also set up to verify the influence of the buffer solution on the reaction.

2.3. Analysis of APAP and Mn^{2+}

APAP concentrations were analyzed by HPLC (Shimadzu LC-200 pump, Technologies XDB-C18, 4.6×150 mm, 5 μm), with a flow rate of 0.5 mL min^{-1} and UV absorbance detection at 243 nm. The mobile phase was a CH_3OH/H_2O mixture (30/70, v/v), and the injection volume was 20 μL. Under these conditions, APAP had a retention time of 5.9 min.

The concentration of Mn^{2+} was detected by TAS-986 flame-type atomic absorption spectrometer. The experimental conditions were as follows: operating current, 7 V; spectral bandwidth, 0.2 nm; combustion gas height, 6 mm; and absorption wavelength, 279.5 nm.

2.4. UV–Vis spectroscopy

Absorption spectra at wavelengths from 200 nm to 450 nm were obtained using a UV–Vis spectrophotometer (Evolution 60, Thermo Scientific, USA) with a 1-cm quartz cuvette. The spectra of the initial solution contained 40 μM of APAP and 50 mg L^{-1} of MnO_2, with 0.01 M NaCl as background electrolyte, at 25 °C and pH 4.5. Reaction samples were periodically collected at time points from 0 min to 80 min.

2.5. Product identification

The initial pH was increased to 7.0 to obtain adequate reaction intermediates and possible products for analysis. All reactors were rapidly quenched by filtration through 0.22 μm GVWP membranes (Millipore) after 80 min. The supernatants and δ-MnO_2 solids were collected separately. The supernatants of all reactors were combined and extracted using a LC-C_{18} solid-phase extraction (SPE) cartridge (3 mL) purchased from Sigma–Aldrich (PA, USA) at a flow rate of 1 mL min^{-1}. After extraction, the products were eluted with 3 mL MeOH from the cartridge, and subsequently concentrated to 1 mL with a gentle N_2 gas stream.

The sample was analyzed by using a mass spectrometer (MS) and a tandem mass spectrometer (MS/MS) (Waters, Milford, MA) with infusion injection. The MS was operated in negative electrospray ionization mode (ESI), with the capillary potential set at −2.78 kV. Nitrogen (Airgas, >99.99% purity) was used as nebulizer and drying gas, maintained at flow rates of 45 and 300 L h^{-1}, respectively. The desolvation temperature was 300 °C and the source block temperature at 80 °C. Cone voltage was set to −78 V and the extractor at −4 V. The mass analyzer was first run at scan mode. Secondary MS spectra were then generated for selected ions via collision induced dissociation, using Ar (Airgas, >99.9% purity) as collision gas. Fragmentor voltages and collision energy (CE) were experimentally optimized.

The sample was separated and analyzed using a Waters 2690 HPLC (Waters, Milford, MA) coupled with MS (HPLC/MS). For optimum MS signals and chromatogram, a binary gradient elution consisting of water (A) and methanol (B) at a flow-rate of 0.5 mL min^{-1} was used as mobile phase for the HPLC/MS analysis