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Photocatalytic degradation of paracetamol: Intermediates and total reaction mechanism

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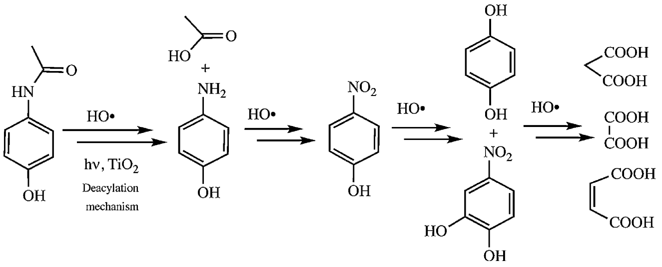
HIGHLIGHTS

- ► The advanced oxidation of paracetamol with TiO_2/UV was investigated.
- ► HPLC indicated the formation of hydroquinone, benzoquinone, *p*-aminophenol and *p*-nitrophenol.
- ► IR studies indicated that *p*-nitrophenol and *p*-aminophenol are also produced.
- ► PAM photocatalytic reaction mechanism includes an alternative deacylation pathway.

GRAPHICAL ABSTRACT



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ABSTRACT

The advanced oxidation of paracetamol (PAM) promoted by TiO_2/UV system in aqueous medium was investigated. Monitoring this reaction by HPLC and TOC, it was demonstrated that while oxidation of paracetamol is quite efficient under these conditions, its mineralization is not complete. HPLC indicated the formation of hydroquinone, benzoquinone, *p*-aminophenol and *p*-nitrophenol in the reaction mixtures. Further evidence of *p*-nitrophenol formation was obtained following the reaction by UV–vis spectroscopy. Continuous monitoring by IR spectroscopy demonstrated the breaking of the aromatic amide present in PAM and subsequent formation of several aromatic intermediate compounds such as *p*-aminophenol and *p*-nitrophenol. These aromatic compounds were eventually converted into trans-unsaturated carboxylic acids. Based on these experimental results, an alternative deacylation mechanism for the photocatalytic oxidation of paracetamol is proposed. Our studies also demonstrated IR spectroscopy to be a useful technique to investigate oxidative mechanisms of pharmaceutical compounds.

1. Introduction

In recent years, there is a growing interest in the environmental relevance of pharmaceutical compounds in waters. There are different sources for this type of pollution like waste from chemical industries, disposal from household, and excretion after administration in humans and animals. Several pharmaceutical compounds have been detected as minor pollutants in industrial waste, surface and ground waters [1]. Many of these compounds are extensively used as anti-inflammatories, analgesics, lipid regulators, antibiotics, antiepileptics, antiseptics and disinfectants [2–5].

To avoid further accumulation of pharmaceutical compounds in the aquatic environment, several research groups are utilizing advance oxidation processes (AOP), where a highly reactive intermediate like $HO^•$ is generated, to achieve the destruction of these contaminants in water. The successful application of ozonation and other AOP (O_3/H_2O_2, H_2O_2/UV, and H_2O_2/Fe^{+2}/UV) for the oxidation of pharmaceuticals and their metabolites has been reported [5–8].

An important AOP is the photocatalytic oxidation of organic pollutants by the use of a semiconductor catalyst that upon

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photolysis with UV light undergoes a surface reaction in which electrons move from the valence band to the conduction band (e^-) leaving positive holes (h^+) behind [9–13]. Both highly reactive species (e^- and h^+) initiate oxidation and reduction reactions on the surface of a TiO_2 catalyst. Organic compounds (D) can be oxidized directly by positive holes (h^+). In an aqueous suspension, h^+ reacts with water molecules and surface HO^- groups to give $HO^\bullet$ radicals, which are known to be strong oxidizing species. Oxygen is bubbled through the reaction mixture to trap free electrons in order to inhibit the recombination step. Other reaction intermediates contribute to the production of $HO^\bullet$ radicals, which react with organic pollutants and eventually mineralize them [11,14]. It has been demonstrated by electron spin resonance spectroscopy that $HO^\bullet$ is the most abundant intermediate in aqueous TiO_2 suspensions [15]. The photocatalytic reaction mechanism could be summarized in the following cascade of reactions [9,12,16]:

$$TiO_2 \xrightarrow{h\nu} e^- + h^+ \tag{1}$$

$$e^- + h^+ \rightarrow \text{ recombination} \tag{1a}$$

$$h^- + H_2O \rightarrow HO^\bullet + H^+ \tag{2}$$

$$h^- + HO^- \rightarrow HO^\bullet \tag{3}$$

$$h^+ + D \rightarrow D^+ \text{(Direct oxidation of organic compounds)} \tag{4}$$

$$HO^\bullet + D \rightarrow D_{\text{oxidized}} \text{(Oxidation of organic compounds by } HO^\bullet \text{ radicals)} \tag{5}$$

$$e^- + O_2 \rightarrow O_2{}^{\bullet -} \tag{6}$$

$$O_2{}^{\bullet -} + HO_2{}^\bullet + H^- \rightarrow H_2O_2 + O_2 \tag{7}$$

$$H_2O_2 + e^- \rightarrow HO^- + HO^\bullet \tag{8}$$

Paracetamol (PAM, Fig. 1) also known as 4-hydroxyacetanilide, 4-acetamidephenol or acetaminophen is widely used as analgesic and antipyretic agent. In contrast to aspirin, it does not cause gastric irritation and it is a component of more than one hundred medications [17]. When it is used in excess or with alcohol, paracetamol could cause liver failure and even death [18]. This toxicity has been attributed to the production of a highly toxic metabolite (NAPQI, Fig. 1) formed by enzymatic oxidation in the liver. PAM occurrence in environment has attracted interest as a potential contaminant for waters. Concentration levels on the range of 1–6 μg/L have been detected in European sewage treatment plant effluents and up to 10 μg/L in water samples from natural sources in the USA [4].

An insight into the advanced oxidation chemistry of PAM was reported by Vogna et al. [19]. They investigated the oxidation of PAM with UV/H_2O_2 to determine the intermediate and final break down products in this reaction utilizing a combination of analytical techniques such as GC–MS, HPLC, and NMR. In a subsequent investigation on ozonation and H_2O_2 photolysis of PAM, it was demonstrated that both oxidative systems are able to destroy the aromatic ring of the substrate but low mineralization in the order of 30% was determined by TOC analysis [20]. Main reaction intermediates and products were identified for both systems by HPLC and GC–MS. To improve the amount of mineralization, the degradation of PAM has been investigated with several oxidative systems such as O_3/UV with Fe^{+3} and Cu^{+2} as catalysts [21], electrogenerated H_2O_2/UV with Fe^{+3} and Cu^{+2} as catalysts [22], and anodic oxidation with boron-doped diamond electrode [23].

The first advanced oxidation of PAM promoted by TiO_2/UV system in aqueous medium was investigated [24]. Continuous monitoring by several techniques, such as HPLC, TOC, ESI-MS and GC–MS revealed that PAM removal was quite efficient under these reaction conditions. Fragmentation pathways were also proposed based on MS analysis of aliquots taken at consecutive oxidation reaction times. Prior to MS analysis, all samples were submitted to a derivatization procedure to give the more stable trimethylsilyl derivatives. In two subsequent studies, the degradation of PAM by TiO_2 photocatalysis was also investigated to determine the optimal operating conditions [25,26].

In this study, we investigated the photocatalytic oxidation of PAM, a reagent extensively used in medicine, in the presence of TiO_2. This reaction was monitored by a combination of techniques such as UV–vis, IR and HPLC. The mineralization of paracetamol was followed by total organic carbon analysis (TOC). Based on these experimental results a total reaction mechanism for the oxidation of PAM is proposed. In addition to the quinone and hydroquinone oxidation pathway, involving the lost of acetamide, previously reported by others [19,20,24], an alternative deacylation oxidation route is presented.

2. Experimental

2.1. Materials

PAM, *p*-aminophenol, *p*-nitrophenol, benzoquinone, hydroquinone and 1,2,4-trihydroxybenzene were purchased from Aldrich. Other organic and inorganic acids and salts were purchased from J.T. Bayer. Spectroscopic and chromatographic grade solvents were purchased from Mallinckrodt. Double distilled water, filtered through 0.45 μm HA cellulose acetate membranes (Millipore Corp. Bedford, MA) was used throughout.

2.2. Photocatalytic oxidation experiments

Photocatalytic oxidation experiments were carried out in a reactor system described in previous publications [12]. This unit is configured with a Pyrex glass tube reactor (400 mL) irradiated with four 15 W UV light lamps (Cole Parmer E-09815-55, $\lambda_{max} = 365$ nm). It has a fan to cool down the reaction mixture to room temperature. For each set of experiments, 250 mL of a PAM standard solution were placed inside the glass reactor and slurried with 2 g/L of TiO_2. This suspension was mixed with a magnetic stirrer. Pure oxygen can be bubbled through the reaction mixture at a constant rate of 100 mL/min. Under these conditions, the initial pH of the solution was 7.9 ± 0.2, and it was measured with a 710A Orion pH meter. Samples were taken from time to time to monitor the progress of the reaction by different analytical techniques. Before analysis, all reaction mixtures were filtered through a 0.22 μm GV cellulose acetate membrane (Millipore Corp. Bedford, MA).

To identify the intermediate organic products generated through photocatalytic degradation reactions, 300 mL of an aqueous solution of PAM (300 ppm) were mixed with 2 g/L of TiO_2 and irradiated in the photoreactor for several hours. The solution slurry was kept under a constant flow of oxygen of 100 mL/min. A volume (100 mL) of mixture was removed at different times of reaction (2, 4 and 6 h). The aqueous mixture was extracted three times with ethyl acetate. The solvent was dried with anhydrous sodium sulfate and removed in a rotary evaporator to yield an oil that was placed in KBr cells for subsequent analysis by FT-IR spectroscopy.

2.3. Analytical methods

For the determination of PAM and some intermediate compounds, reaction mixtures at different irradiation times were analyzed by high performance liquid chromatography (HPLC) in a 600E Waters instrument equipped with a UV–vis Waters 490 detector tuned at 242 nm. A Novapack-Phenyl column (4 μm,