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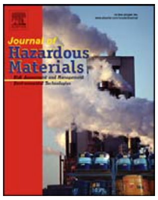

Oxidation by-products and ecotoxicity assessment during the photodegradation of fenofibric acid in aqueous solution with UV and UV/H_2O_2

Javier Santiago[a], Ana Agüera[b], María del Mar Gómez-Ramos[b], Amadeo R. Fernández Alba[b,c], Eloy García-Calvo[a,c], Roberto Rosal[a,c,*]

[a] Department of Chemical Engineering, University of Alcalá, E-28771 Alcalá de Henares, Spain
[b] Department of Analytical Chemistry, University of Almería, E-04010 Almería, Spain
[c] Advanced Study Institute of Madrid, IMDEA-Agua, Parque Científico Tecnológico, E-28805 Alcalá de Henares, Madrid, Spain

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ABSTRACT

The degradation of an aqueous solution of fenofibric acid was investigated using ultraviolet (UV) photolysis and UV/H_2O_2 with a low-pressure mercury lamp. We obtained quantum yields at different temperatures and the rate constant for the reaction of fenofibric acid with hydroxyl radicals. The maximum radical exposure per fluence ratio obtained was $1.4 \times 10^{-10}\ \mathrm{M\,L^{-1}\,mW^{-1}}$. Several reaction intermediates were detected by means of exact mass measurements performed by liquid chromatography coupled to quadrupole-time-of-flight mass spectrometry (LC-ESI-QTOF–MS). UV and UV/H_2O_2 pathways involve the decarboxylation of fenofibric acid to 4-chloro-4′-(1-hydroxy-1-methylethyl)benzophenone and other minor products, predominantly chlorinated aromatics. We detected several intermediates from reactions with hydroxyl radicals and some lower molecular weight products from the scission of the carbonyl carbon-to-aromatic-carbon bond. We recorded high toxicity in UV irradiated samples for the growth of *Pseudokirchneriella subcapitata* even after the total depletion of fenofibric acid; this was probably due to the presence of chlorinated aromatics. A degree of toxicity reappeared in highly irradiated UV/H_2O_2 samples, probably because of the formation of ring-opening products. The degree of mineralization was closely related to that of dechlorination and reached values of over 50% after 3–4 min before stabilizing thereafter.

1. Introduction

Fenofibric acid, 2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropanoic acid, is the active form of fenofibrate, a drug prescribed to reduce plasma triglycerides. Although its use is not widespread, it has often been encountered in wastewater treatment plants (WWTP). Rosal et al. [1] reported very low removal efficiency for fenofibric acid in a conventional WWTP located in Madrid with an average annual concentration of 79 ng/L. Stumpf et al. [2] obtained concentrations of up to 500 ng/L in the influent of several Brazilian WWTP and calculated a removal efficiency of 45% for conventional activated sludge treatment. Ternes et al. [3] reported the occurrence of 130 ng/L of fenofibric acid in the effluent of a German WWTP. Acero et al. [4] found 180 ng/L in the effluent of a WWTP located in Madrid. Fenofibric acid attracts particular attention due to its high toxicity for several aquatic microorganisms [5]. An additional reason for concern is that fenofibric acid and other pharmaceuticals are released in increasing quantities in complex mixtures. Recently, Rodea-Palomares et al. [6] and Rosal et al. [7] used the combination index-isobologram method and reported a synergistic behaviour for fenofibric acid in mixtures involving wastewater.

Advanced oxidation processes (AOP) are effective technologies for the removal of organic pollutants in wastewater. UV-based AOP have the advantage of using a fully commercialized technology due to the widespread use of UV systems for disinfection [8]. A drawback of these processes is the formation of oxidation by-products [9]. Over the last few years, it has been shown that the formation of by-products with enhanced toxicity for non-target organisms usually takes place at least under conditions of moderate carbon removal [10,11]. The identification of unknown transformation products is not an easy task. Liquid chromatography–mass spectrometry (LC–MS) combined with a new generation of high sensitivity MS systems provides abundant structural information for the elucidation of chemical structures. The objective of this work was to study the removal of fenofibric acid using UV and UV/H_2O_2 photolysis. We identified oxidation intermediates in order to propose a reaction pathway for the early oxidation stages. We also measured the ecotoxicity of partially oxidized mixtures.

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[*] Corresponding author at: Department of Chemical Engineering, University of Alcalá, E-28771 Alcalá de Henares, Spain. Tel.: +34 918855099; fax: +34 918855088.
E-mail address: roberto.rosal@uah.es (R. Rosal).

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2. Materials and methods

2.1. Reagents

Fenofibric acid was produced from fenofibrate (Sigma–Aldrich, +99% purity) as indicated elsewhere [5]. The product's purity was over 97%, as evaluated by high-performance liquid chromatography (HPLC). Pure water was obtained from a Milipore Mili-Q system with a resistivity of at least 18 MΩ cm at 298 K and a Millipore 0.22 μm Millipak Express filter (Billerica, MA). Hydrogen peroxide, sodium phosphate monobasic dihydrate and sodium hydrogen phosphate, sodium hydroxide and hydrochloric acid were analytical grade reagents used as received. p-Chlorobenzoic acid (pCBA), atrazine and 2,9-dimethyl-1,10-phenanthroline (DMP) were purchased from Sigma–Aldrich (+99% purity).

2.2. Analytical methods

Total organic carbon (TOC) was determined using a Shimadzu TOC-VCSH analyzer. Chlorine was determined using a Dionex DX120 Ion Chromatograph with a conductivity detector and an IonPac AS9-HC 4 mm × 250 mm analytical column with ASRS-Ultra suppressor. The eluent was 9.0 mM Na_2CO_3 flowing at 1.0 mL/min. The determination of extinction coefficients and colorimetric analyses was performed in a Shimadzu UV-1800 spectrophotometer. The analyses of fenofibric acid, pCBA and atrazine were performed by HPLC using an Agilent 1200 apparatus equipped with a reversed phase Kromasil 5u 100A C18 analytical column. The mobile phase (flow rate 1 mL/min) was a mixture of water containing 4 mL/L of orthophosphoric acid and 50 mL/L of methanol and acetonitrile in a proportion of 40:60 for pCBA separation and 50:50 for atrazine and fenofibric acid. UV detection was carried out at 280 nm and 228 nm for fenofibric acid, and atrazine and pCBA respectively. The volume injected was 50 μL in all cases. Hydrogen peroxide was measured using the colorimetric methods of Eisenberg [12] and Baga et al. [13].

A liquid chromatography-electrospray ionization-quadrupole-time-of-flight–mass spectrometry (LC-ESI-QTOF–MS) system, in positive and negative mode, was used to identify the transformation products in the samples. Samples collected at different irradiation times during the experiments were directly analyzed in the LC-TOF–MS system, without previous pre-concentration. The analytes were separated using a HPLC system (vacuum degasser, autosampler and a binary pump Agilent Series 1200, Agilent Technologies) equipped with a reversed-phase XDB-C_{18} analytical column of 4.6 mm × 50 mm, 1.8 μm particle size (Agilent Technologies). 0.1% formic acid and 5% MiliQ water in acetonitrile was used as mobile phase A and 0.1% formic acid in water (pH 3.5) as mobile phase B. The elution gradient went from 10% A (3 min) to 100% A in 22 min, and was kept at 100% A for 3 min. The flow rate was 0.5 mL/min and the injection volume 20 μL. The HPLC system was connected to a quadrupole-time-of-flight mass spectrometer (Agilent 6530 Q-TOF MS, Agilent Technologies, Santa Clara, CA). The instrument was operated in the 4 GHz High Resolution Mode. Ions were generated using an electrospray ion source with Agilent Jet Stream Technology. The operation conditions were: superheated nitrogen sheath gas temperature (400 °C) at flow rate (12 L/min), nozzle voltage (0 V), capillary, 4000 V; nebulizer, 60 psi; drying gas, 5 L/min; gas temperature, 250 °C; skimmer voltage, 65 V; octapoleRFPeak, 750 V; fragmentor (in source CID fragmentation), 90 V. The mass axis was calibrated using the mixture provided by the manufacturer over the m/z 40–3200 range. A second sprayer with a reference solution was used for continuous calibration in positive ion using the following reference masses: 121.0509 and 922.0098 m/z (resolution: 21,700 ± 500 at 922.0098 m/z), and in negative ion using the reference masses: 112.9856 and 966.0007. MS/MS spectra were acquired over the m/z 40–950 range at a scan rate of 0.5 s/spectrum. The collision energy was optimized to obtain the highest number of fragments. The full mass spectra data recorded were processed with Agilent MassHunter Workstation Software (version B.02.00).

2.3. Toxicity test and data analysis

The toxicities of fenofibric acid degradations by UV and UV/H_2O_2 treatments were evaluated in accordance with the algal growth inhibition test described in OECD TG 201 and using the *Pseudokirchneriella subcapitata* open system. Prior to the test, hydrogen peroxide was removed using 4 μL of catalase solution 5000 mg/L (3691 U/mg bovine liver from Sigma–Aldrich) per 1 mL of sample. Cultures were made in OECD growth medium at pH 8.0 ± 0.2. Algal cells were first cultured in 25 mL agitated flasks, in which growth was evaluated by cell counting. The prescribed amount of cells were then transferred to 96-well clear disposable microplates and exposed to pollutants during the logarithmic growth phase. The total volume occupied was 200 μL, each well containing 100 μL of sample and 100 μL of OECD growth medium. The microplates were placed in an algal growth chamber under continuous fluorescent illumination (approximately 100 $\mu E\, m^2\, s^{-1}$), and incubated at 22 ± 1 °C. The cell density was measured using an electronic particle counter (Coulter Counter Z2). The settings were: upper size limit, 8.0 μm; lower size limit, 2.5 μm; metered volume, 0.5 mL; aperture size, 50 μm. The tests were carried out with duplicate samples for each day of measurement and samples were taken at 24-h intervals over 72 h. Specific growth rates were calculated for each sample and treatment in order to obtain the inhibition percentage. EC_{50} value and 95% confidence limits for fenofibric acid were calculated using the concentration–inhibition relationship established by the logistic equation.

2.4. Experimental setup and procedure

Irradiation experiments were performed in a Heraeus 700 mL reactor equipped with a 15 W Heraeus Noblelight TNN 15/32 low-pressure mercury vapour lamp emitting at 254 nm with a secondary peak at 185 nm. The inner and outer radiuses were 2.4 and 4.5 cm respectively and the height of irradiated solution was 17 cm. The reactor was covered with black paper to avoid any reflection and in order to maintain a constant temperature the lamp was fitted in a quartz cooling tube refrigerated by means of a Huber Polystat cc2 thermostatic regulator. pH was kept constant using a 4 mM phosphate buffer; pH was monitored periodically to ensure a constant value within ±0.1 units. The experiments were carried out in batch mode and samples were withdrawn for analysis at set intervals.

Hydrogen peroxide actinometry experiments were performed to determine fluence rate. With respect to the annular geometry of the photoreactor, we assumed a linear source with emission in planes parallel to the lamp axis (LSPP). In this model the lamp is viewed as a consecutive line of points, each emitting radiation radially in all directions. The equation for the fluence rate is:

$$E'(r) = \frac{E'_o R_o}{r} e^{-\mu(r-R_o)} \tag{1}$$

where μ is the attenuation coefficient, R_o the radius of the internal wall of the photoreactor and E'_o the fluence rate at R_o expressed in $mW\, cm^{-2}$. By applying the LSPP model to the UV photolysis of hydrogen peroxide at high concentration, the exponent becomes negligible and the rate of hydrogen peroxide photolysis allows the