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Photocatalytic degradation of rosuvastatin: Analytical studies and toxicity evaluations

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HIGHLIGHTS

- The photocatalytic degradation of rosuvastatin was studied under UV irradiation.
- Commercial catalyst ZnO was used.
- Initial rosuvastatin concentration, photocatalyst loading and pH were evaluated.
- The byproducts generated during the oxidative process were detected and identified.
- Acute toxicity tests using *Daphnia magna* were carried out.

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ABSTRACT

Photocatalytic degradation of rosuvastatin, which is a drug that has been used to reduce blood cholesterol levels, was studied in this work employing ZnO as catalyst. The experiments were carried out in a temperature-controlled batch reactor that was irradiated with UV light. Preliminary the effects of the photocatalyst loading, the initial pH and the initial rosuvastatin concentration were evaluated. The experimental results showed that rosuvastatin degradation is primarily a photocatalytic process, with pseudo-first order kinetics. The byproducts that were generated during the oxidative process were identified using nano-ultra performance liquid chromatography tandem mass spectrometry (nano-UPLC–MS/MS) and acute toxicity tests using *Daphnia magna* were done to evaluate the toxicity of the untreated rosuvastatin solution and the reactor effluent.

1. Introduction

Statins are drugs used to lower blood cholesterol levels. Currently, the most frequently employed statins are lovastatin (Mevacor), pravastatin (Pravachol), simvastatin (Zocor), fluvastatin (Lescol), atorvastatin (Lipitor) and rosuvastatin (Crestor) (Nirogi et al., 2007; Lee et al., 2009). Due to their recalcitrance in sewage treatment systems, these drugs have been detected in surface waters (Miao and Metcalfe, 2003; Hernando et al., 2007; Piecha et al., 2010) and can pose a risk to humans and other living organisms (Klavarioti et al., 2009). Therefore, it is necessary to remove them from aqueous municipal and industrial effluents before they enter into environment.

Advanced Oxidation Processes (AOPs) have been previously evaluated for the removal of pharmaceuticals in water (Andreozzi et al., 2003; Arslan-Alaton and Dogruel, 2004; Kaniou et al., 2005; Zhang et al., 2007; Rizzo et al., 2009; Elmolla and Chaudhuri, 2010; De la Cruz et al., 2013). One of the most promising techniques among these processes is heterogeneous photocatalysis. This involves the generation of hydroxyl radicals by the irradiation of a semiconductor in water, which in turn can be used to promote the decomposition of organic contaminants. Although the most widely employed semiconductor is TiO_2 (Reyes et al., 2006; Yurdakal et al., 2007; Sakkas et al., 2007; Mendez-Arriaga et al., 2008; Yang et al., 2008; Piecha et al., 2010; Razavi et al., 2011; De la Cruz et al., 2013), ZnO has been received more attention due to its low cost and high activity in several photochemical processes. Also, ZnO has an energy band gap similar to that of TiO_2 (3.2 eV). Some published studies have shown that ZnO is slightly

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more efficient than TiO_2 in pharmaceuticals degradation (Kaniou et al., 2005; Chatzitakis et al., 2008).

There are few studies of the photocatalytic degradation of statins and none of these have examined rosuvastatin. Piecha et al. (2010) observed the formation of non-toxic byproducts arising from the TiO_2-assisted photocatalysis of aqueous lovastatin, pravastatin and simvastatin. Razavi et al. (2011) also reported substantial efficiency of TiO_2 in the degradation of fluvastatin, lovastatin, pravastatin and simvastatin. While degradation mechanisms were proposed, no toxicological studies were carried out in this previous study. As such, still little is known about the photocatalytic behavior of statins in water.

This work studied the photocatalytic degradation of rosuvastatin in aqueous solutions containing commercial ZnO in suspension. Byproducts were detected and identified and their toxicity evaluated to determine the efficiency, safety and feasibility of the photocatalytic processes applied. The effect of photocatalyst and rosuvastatin concentration and the initial pH were also evaluated to determine the optimal operating conditions for the photocatalytic setup.

2. Material and methods

2.1. Chemicals

Rosuvastatin calcium (≥99%) (Johnson Pharmacy) and the photocatalysts zinc oxide (ZnO, Merck) were used in the photocatalytic experiments. Ultrapure water used in the experiments was provided by a Millipore purification system (Direct Q 3 UV). Acetonitrile (HPLC grade) (Merck), formic acid (Sigma-Aldrich) and an Acquity UPLC BEH130 C18 column (18 μm × 100 mm, 1.7 μm particle size) from Waters were used in the analyses of byproducts by nano-UPLC–MS/MS.

2.2. Instruments and methods

To evaluate photodegradation kinetics and mineralization potential of the photocatalytic processes, the Total Organic Carbon (TOC) of initial and irradiated mixtures were measured using a Shimadzu VCSH TOC analyzer packed with a platinum catalyst supported on alumina pellets.

Byproducts arising from the degradation of rosuvastatin were identified by nano-ultra performance liquid chromatography tandem mass spectrometry (nano-UPLC–MS/MS) on a Waters nanoAcquity UPLC system (Waters Corp., Milford, MA) equipped with a binary solvent delivery system and an autosampler with the volume injection set to 2 μL. Chromatographic separation was carried out on an Acquity UPLC BEH130 C18 column with a mobile phase consisting of (A) 0.1% formic acid (v/v) in ultrapure water and (B) 0.1% formic acid (v/v) in acetonitrile and was programmed with a gradient starting at 70% A. After 2 min, the percentage of A decreased linearly to 10% within 5 min, and after more than 5 min, the percentage of A was increased linearly to 95%. These conditions were held for 15 min; next, the mobile phase composition was restored to the initial composition in 1 min and was maintained for column regeneration for another 4 min. The flow rate was 0.6 μL min^{-1} and the total chromatographic run time, including the reconditioning time of the column, was 30 min.

Accurate mass MS and MS/MS analyses were performed on a Q-TOF Micro™ (Micromass, Manchester, UK). MS analysis detection was carried out with an electrospray (ESI) interface operating in the positive ionization mode with a capillary voltage of +3300 V. The source temperature was 100 °C. Nitrogen was used as the cone and desolvation gases. The cone gas flow was set to 5 L h^{-1}, and the desolvation gas flow was set to 30 L h^{-1}. MS spectra were acquired from *m/z* (mass to charge) 100 to 1200. Product ion MS/MS spectra were acquired at low and/or high collision energies using argon as the collision gas at a pressure of ~15 psi. External mass calibration for the positive ESI mode was conducted prior to analysis within the *m/z* range 100 to 2000 by infusing a solution of acetonitrile: water (50:50) and phosphoric acid 0.1% at a flow rate of 0.6 μL min^{-1}. A phosphoric acid solution was used as the internal lock mass. All MS data handling, including the calculations of the accurate masses and the elemental compositions of the precursor and product ions, was performed with the software package MassLynx V4.1. MS spectra were processed using a noise filter followed by smoothing and measuring the peak top with a centroid top of 80%.

Toxicological evaluation of the byproducts arising from the ZnO-assisted photocatalysis of rosuvastatin was carried out with *Daphnia magna* according to ABNT NBR 12713 (2009). An untreated rosuvastatin solution and the reactor effluent were used for these tests, which consist of a control (prepared only with dilution water) and sample dilutions, with one of four replicates using a total volume of 15 mL. Each bottle was covered with plastic and stored in an incubator with a photoperiod of 16 h of light and a controlled temperature of 20 ± 2 °C. After 48 h, the number of mobile individuals in each sample was determined.

2.3. Photodegradation experiments

The experiments were carried out in a batch photochemical reactor (Fig. 1) irradiated with a modified mercury vapor lamp (Philips HPL-N 125 W) emitting only UV-A (365 nm) with an incident irradiance of 5.4 mW cm^{-2} as determined at the start of each experiment by a radiometer (Cole-Parmer Instrument, Radiometer Series 9811). Aeration was achieved by a 15 W compressor, the agitation of the reaction mixture was maintained using a magnetic stirrer and the temperature was monitored using a K-type thermocouple.

The rosuvastatin solution was prepared using ultrapure water and maintained under vigorous magnetic stirring for approximately 2 h. For photocatalysis experiments, various loadings (0.3 to 1.5 g L^{-1}) of ZnO were added to 330 mL aqueous rosuvastatin solution. Before an irradiation, the adsorption–desorption equilibrium for the drug on the photocatalyst surface was determined and carried out in the dark for 1 h. Photocatalysis experiments were then commenced and the reaction progress monitored by collecting samples (10 mL) at fixed intervals 0, 5, 15, 30 and 60 min. The collected samples were then centrifuged and stored in amber glass bottles. Subsequently, the rosuvastatin content was analyzed quantitatively by measuring the absorbance at 241 nm using Cary 100 (Varian) Spectrophotometer. A calibration curve was used to relate the rosuvastatin concentration in the collected samples during the tests to its absorbance at a wavelength of maximum absorption (241 nm), according to the Lambert–Beer Law.

The pseudo-first order degradation rate constant and the percentage degradation of rosuvastatin were used as parameters to compare results obtained. All experiments were carried out in duplicate or triplicate, as necessary, and the average values used as the results.

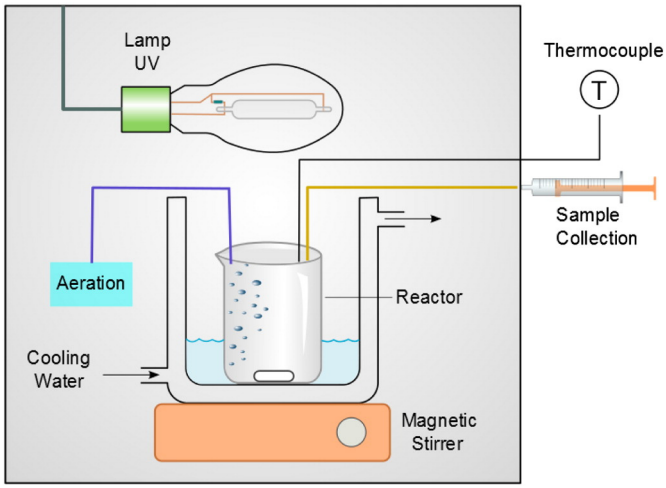

Fig. 1. Photochemical reactor used in the photocatalysis of rosuvastatin in water.