Photocatalytic decomposition of Nimesulide by treatment with TiO_2 nanoparticles

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Abstract During the last two decades, pharmaceuticals have been recognized as environmental contaminants. Nimesulide, is a NSAID with analgesic and antipyretic properties, usually used for the treatment of acute pain and has been detected from several researchers through the years in environmental samples. In this study, we explored the application of heterogeneous photocatalysis (TiO_2 in suspension) for the degradation of Nimesulide. Different factors that affect the photocatalytic process were compared: load of catalyst and pH. Under optimal conditions (100 mg L^{-1} TiO_2 at pH 6), 5 mg L^{-1} Nimesulide can be removed within 45 min (k= 0.152 min-1) by using Degussa P-25. The transformation products generated during the treatment were investigated and characterized by means of liquid chromatography coupled to high resolution mass spectrometry. Also, the toxicity of Nimesulide and its transformation products was evaluated. The main Nimesulide phototransformation pathways were observed to be hydroxylation and fragmentation. Finally, mineralization and ion analysis was performed and a feasible transformation mechanism is proposed.

Keywords: Nimesulide, photocatalysis, kinetics, transformation products, TiO_2

1. Introduction

Pharmaceuticals enter the environment mostly through domestic use to wastewater treatment plants (WWTPs). Their spread through surface waters is basically a result of the incomplete removal of some of these pollutants during conventional wastewater treatment (Jones *et al*., 2007; Rodríguez-Álvarez *et al*., 2013). A great number of monitoring investigations have been contacted worldwide since the 1970s, that prove the presence of pharmaceuticals in various water samples, such as sewage water influence, surface and even groundwater (Aherne *et al*., 1990; Caldwell *et al*., 2014; Comoretto and Chiron, 2005; Hignite and Azarnoff, 1977; Phillips *et al*., 2015).

For instance, non-steroidal anti-inflammatory drugs (NSAIDs) are among the most frequently detected drugs in the environment, in concentrations ranging from ng L-1 to μg L-1,due to their extended use in human and animal health care (Manzo *et al*., 2014). Nimesulide belongs to the group of sulfanilamide derivatives and it's a partially selective cyclooxygenase 2 enzyme (COX-2) inhibitor (Rainsford, 2006). Despite the fact that Nimesulide causes relatively low occurrence of gastrointestinal injury, compared to other anti-inflammatory drugs (Bernareggi, 1998), rare but mild to serious associated hepatic adverse effects have been reported and mitochondrial injury and oxidative stress have been implicated in contributing to liver damage in susceptible patients (Monteiro *et al*., 2011).

Nimesulide has been detected from several researchers through the years in environmental samples. Lacey *et al*. detected Nimesulide in influents and effluents of wastewater treatment plants , in concentrations ranging from non-detected up to 0.441 μg L^{-1}(Lacey *et al*., 2008). In fact the concentrations of Nimesulide detected in that study, were very close in influents and effluents. This is a proof that conventional wastewater treatment plants, are unable to remove effectively Nimesulide. In this light, application of efficient methods for the removal of pharmaceuticals, such as Nimesulide, from wastewater is extremely necessary.The main objectives of this study were: (i) the application and optimization of TiO_2 treatment under simulated solar irradiation, the evaluation of the Nimesulide elimination efficiency by means of mineralization, (ii) the identification of the TPs formed during the photocatalytic treatment (iii) the examination of the changes in toxicity during photocatalysis.

2. Methods

2.1 Photocatalytic degradation experiments

Photocatalytic experiments were carried out at a solar simulator Atlas Suntest CPS+ with the same Pyrex glass UV reactor, at various amounts of TiO_2 (50-400 mg L^{-1}), while the pH ranged from 2 to10 (adjustment by H_2SO_4 0.01M and NaOH 0.01M). The suspension was kept in the dark for 30 min, prior to illumination to reach adsorption equilibrium onto semiconductor surface. The initial concentration of Nimesulide was 5 mg L^{-1}.

2.2 Analytical procedures

For the determination of Nimesulide concentrations, an HPLC system consisted of a SIL 20A autosampler with

the volume injection set to 20mL and LC-20AB pump both from Shimadzu (Kyoto, Japan), was used. The analytical column used was a C18, 150 x 4.6 mm with 5μm particle size (Restek, USA). Detection was carried out using a SPD 20A DAD detector coupled in series with the LC–MS 2010EV mass selective detector, equipped with an atmospheric pressure electrospray ionization (ESI) source. The samples were analyzed using the ESI interface in negative ionization (PI) mode. The HPLC mobile phase was a mixture of LC-MS grade water-0.1% formic acid (30%) and acetonitrile (70%) with a flow rate of 0.4 mL min^{-1}. The total run analysis lasted 8 min. The TPs were identified by high resolution accurate mass liquid chromatography (HR-LC–MS) (Kosma *et al*., 2017).

3. Results and discussion

3.1 Effect of TiO_2 loading

The effect of TiO_2-P_{25} concentration was studied at concentrations varying from 50 to 400 mg L^{-1}.The experiments were carried out at pH 6 (initial pH of Ultrapure water), while the rate constants were calculated by the linear fit of each degradation curve for the first 20 min of reaction. It is observed that when low concentrations of catalyst are used (50-200mg L^{-1}), the rate constant increases by the increase of catalyst. From a certain concentration and above it (200-400 mg L^{-1}) the rate constant stays stable. The increase of the initial reaction rate for concentrations up to 200 mg L^{-1} is attributed to the increase of the photogenerated active sites in the catalyst surface resulting to the formation of greater amounts of reactive oxygen species (ROS). Further increase of TiO_2 concentration leads to a reduction of the reaction rate due to the increase of the light-scattering by the suspended particles of the catalyst and the blocking of the light passage. In order to obtain slower kinetics in further experiments on degradation and mineralization of CY, a lower concentration (100 mg L^{-1}) of P25-TiO_2 catalyst was selected.

3.2 Effect of pH

The effect of pH on the photocatalytic reaction is generally attributed to the surface charge of TiO_2. For pH values lower than the point of zero charge (pzc) of catalyst, which is 6.3 for TiO_2 , the catalyst is positively charged and at higher pH values it is negatively charged (Evgenidou *et al*., 2005). The higher rate constant was observed for pH 6 (0.152 min^{-1}), which is close to the pzc of TiO_2.

3.3 Mineralization process

The results of TOC and inorganic ions for the photocatalytic degradation, are presented in Fig.1. After 3h of irradiation, the TOC reduction is approximately 85%, while the NO_3^- ions are almost 50% released, after the first 2h of irradiation. Additionally, sulfate ions were not detected at all.

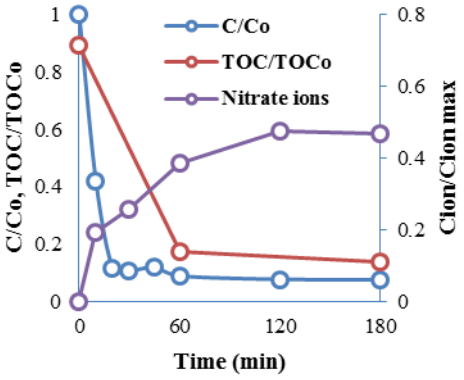

Figure 1. Nimesulide mineralization process under TiO_2 treatment (5 mg L^{-1} Nimesulide, 100 mg L^{-1} TiO_2).

3.4 Evaluation of transformation products

A total number of 5 TPs was identified based on high resolution mass spectrometry and tentative structures were proposed based on accurate mass measurements of m/z ions, which are depicted on Table 1. The main Nimesulide phototransformation pathways were observed to be hydroxylation and fragmentation (Fig. 2).

3.5 Toxicity evaluation

In the present study, a *V. fischeri* toxicity bioassay was applied to aqueous samples taken in different photocatalytic time intervals and the inhibition percentage of each sample after 15 min exposure of the bacterium was determined. The results are presented in Fig.3. The initial CY solution appears to have low toxicity, since the inhibition does not exceed 16%. On the other hand, the TPs generated during the first min of photocatalytic treatment present higher toxicity levels, approaching 45% inhibition at 20 min of irradiation. This rise in toxicity can be attributed to the formation of more toxic reaction intermediates than the parent compound or due to synergistic effects among the TPs formed (Antonopoulou *et al*., 2015; Antonopoulou and Konstantinou, 2016). However, inhibition appears to decrease after a while, reaching 5% after 180 min of treatment.

4. Conclusions

TiO_2/SSL process was studied for the photocatalytic degradation and mineralization of anti-inflammatory drug, Nimesulide. High percentages of mineralization were accomplished after 3h irradiation (TOC removal ~ 85%). The TPs formed during the photocatalytic degradation of Nimesulide were identified for the first time using high resolution LC–MS techniques. Overall, the results of the present study demonstrated that TiO_2/SSL process can eliminate parent compound and its toxicity, offering a promising alternative approach to treat Nimesulide contaminated aqueous media. However, toxicity screening after advanced treatment is recommended, since some TPs formed during the process are more toxic than the Nimesulide.

Table 1. High resolution mass spectra data for Nimesulide and identified TPs derived from mass spectrometric analysis.

Code name	Pseudo-molecular ion formula	Theoretical m/z $[m-H]^-$	Experimental m/z $[m-H]^-$	Δ (mm)	RDBE
Nimesulide	$C_{13}H_{11}N_2O_5S$	307.0389	307.0388	0.481	9.5
TP1	$C_{12}H_9N_2O_3$	229.0613	229.0617	0.531	9.5
TP2	$C_7H_7N_2O_5S$	231.0076	231.0079	0.581	5.5
TP3	$C_{13}H_{11}N_2O_6S$	323.0338	323.0340	0.567	9.5
TP4	$C_{13}H_{11}N_2O_7S$	339.0287	339.0288	0.652	9.5
TP5	$C_{13}H_{11}N_2O_8S$	355.0236	355.0236	0.538	9.5

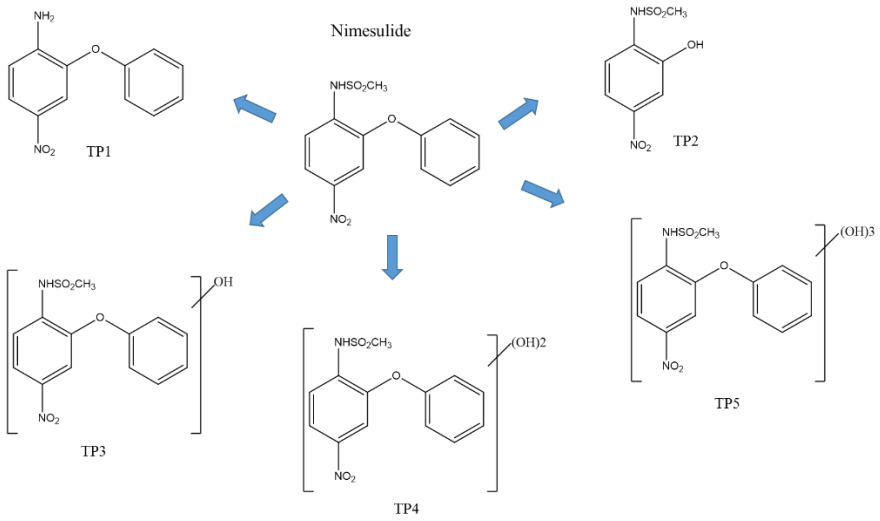

Figure 2. Transformation products of Nimesulide.

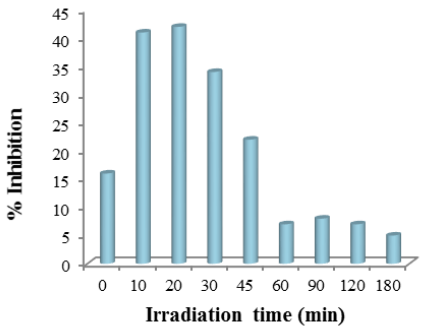

Figure 3. Toxicity evolution as a function of photocatalytic treatment time (C_0 (Nimesulide) = 30 mg L^{-1}, C (TiO_2)= 300 mg L^{-1}

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