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Photocatalytic degradation and mineralization of tramadol pharmaceutical in aqueous TiO_2 suspensions: Evaluation of kinetics, mechanisms and ecotoxicity

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ABSTRACT

In the present study the transformation and mineralization of a common aquatic pollutant, Tramadol (TRA) was investigated for the first time by means of TiO_2 photocatalysis. The degradation kinetics for both TRA and total organic carbon (TOC) followed apparent first-order model with rate constants of $k_{app} = 15.3 \times 10^{-2}$ min^{-1} and $k_{app} = 9.7 \times 10^{-3}$ min^{-1} and half lives ($t_{1/2}$) of 4.5 min and 71.4 min, respectively. The transformation products (TPs) of TRA, were identified by high resolution accurate mass liquid chromatography (HR-LC–MS) suggesting that hydroxylation, oxidation and dealkylation are the main transformation pathways. The reactions were found to occur mainly at the surface of the photocatalyst via surface-bound $HO^\bullet$ radicals rather than by free diffusion into the homogeneous phase. The potential risk of TRA and its TPs to aqueous organisms was investigated using Microtox bioassay before and during the process. The acute toxicity increased in the first stages and then decreased rapidly to very low values within 120 min of the photocatalytic treatment. The increase in the toxicity is associated with near additive or low synergistic effects between two TPs generated during the process i.e. N-desmethyl and N-oxide tramadol.

1. Introduction

Pharmaceutical compounds are a group of emerging contaminants which are found in surface waters and wastewaters at levels up to a few μg L^{-1}, raising major concerns about their potential impact on ecosystems and public health [1–3]. Aquatic toxicity, resistance development in pathogenic bacteria, genotoxicity and endocrine disruption are the main possible adverse effects caused by the frequent occurrence of pharmaceuticals in the aquatic environment [3–6]. Pharmaceuticals are generally designed with high stability for their intended effects on humans and they are poorly removed in wastewater treatment plants (WWTPs) thus, enter the environment as unchanged parent compounds, metabolites or conjugates of both [1,2]. A representative example of persistent pharmaceutical contaminant is Tramadol (TRA), a centrally acting synthetic opioid analgesic, used worldwide to treat moderate to severe acute or chronic pain. TRA is excreted via urine as an unchanged compound up to 30% and undergoes extensive metabolism, primarily resulting in *N*-desmethyl-(*N*-DES) and *O*-desmethyl-(*O*-DES) tramadol [6–8].

TRA is partially removed in conventional wastewater treatment plants and as a result it has been frequently detected in sewage outflows as well as in surface water worldwide. According to a European-wide monitoring study on the occurrence of organic micropollutants in WWTP effluents, TRA was one of the most frequent detected contaminants with mean and maximum concentration levels up to 256 and 1116 ng L^{-1}, respectively [5–7].

Advances in water and wastewater treatment have led to the development of promising technologies termed as advanced oxidation processes (AOPs), involving highly reactive hydroxyl radicals ($HO^\bullet$), for the treatment of many emerging contaminants, including pharmaceuticals, poorly eliminated by conventional biological treatment processes [9,10]. Heterogeneous photocatalysis using titanium dioxide (TiO_2) as a catalyst is a well-established AOP, providing promising results for both removal and total mineralization of various pharmaceuticals and other micro-pollutants from aqueous phase [11–13]. Heterogeneous photocatalysis typically involves the formation of $HO^\bullet$, h^+, $HO^\bullet{}_2$, $O_2{}^{-\bullet}$, and $^1O_2$, etc. as

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oxidizing species and either hydrated electrons (e^-_{aq}) or hydrogen atoms ($H^\bullet$) as reducing species, which can contribute to the degradation of the contaminants [13–16]. However, only few studies have focused on the identification of photocatalytic transformation products and possible degradation pathways of pharmaceutical compounds [17].

Despite the extensive presence of TRA in various environmental matrices, only a few AOPs such as ozonation and ferrate oxidation [16], electrochemical oxidation [18], and UV/chloramines/H_2O_2 treatment [19] have been successfully employed for its degradation in aquatic matrices. In the first study, different pathways and major transformation products (TPs) between ozonation and ferrate oxidation were reported while in both cases complete mineralization was not achieved [16]. In the second study, further TPs were formed in the presence of halogen ions while TRA removal was achieved but only a minor reduction of total organic carbon (TOC) was reported [18]. Similarly, different TPs and partial removal of TOC were also observed in the latter study [19].

In this context, no data is currently known regarding the photocatalytic transformation process, the degradation mechanisms and pathways of TRA as well as the toxicity assessment of the treated TRA aquatic solution and its individual transformation products. Photocatalytic reactions proceed via parallel and often interconnected pathways that do not lead always to complete mineralization or detoxification of the treated solution and sometimes more persistent or toxic compounds are formed during the degradation process [20]; thus the identification and the toxicity assessment of the transformation products are significant milestones for the assessment of the process. Such integrated studies are of great importance for the purposes of proper water and wastewater treatment by photocatalytic process. In addition, oxidation, degradation and transformation of pharmaceuticals via photo-induced reactions (direct and indirect photochemical mechanisms) take place after their release in environmental media. Photocatalytic redox mechanisms are useful for simulating environmental or metabolic degradation processes, thus providing important knowledge on the transformation products of the studied pollutants [21].

The objective of this study was to investigate the photocatalytic degradation of TRA, as a model compound in the opioid analgesics and antidepressants families, providing a fundamental understanding on the applicability and effectiveness of the process for removing the parent compound and transformation products as well as for the detoxification of the aqueous solutions. The transformation kinetics and mechanisms of TRA TiO_2 photocatalytic degradation and mineralization were studied for the first time. The possible degradation pathways of TRA were proposed by identifying the major transformation products using high resolution accurate mass liquid chromatography (HR-LC–MS) and scavenging experiments. The continuous monitoring/assessment of potential toxicity during the treatment was also followed in order to ensure the appropriate degree of treatment and to contribute in the optimization of operating conditions. Moreover, the ecotoxicological potential effects of the major transformation products were determined, providing important knowledge regarding their ecotoxicological potency in aquatic media and giving useful insight on the application of the treatment as additional step in water and wastewater treatment.

In the majority of previously published photocatalytic degradation studies of various pharmaceuticals, toxicity has been generally taken as the overall toxicity of the solution without providing information on potential ecotoxicity of the TPs as well as additives, synergistic or antagonistic effects between them. In this sense, the present work provides various new data regarding the systematic elucidation of the photocatalytic process of this ubiquitous pharmaceutical pollutant in the water.

2. Experimental

2.1. Materials

Tramadol hydrochloride salt, anisole and phenol analytical grade (99.9%) were purchased from Sigma-Aldrich (USA). High purity (99.9%) standards of *N*-desmethyl-tramadol (*N*-DES), *N*,*N*-bidesmethyl-tramadol (Bi-DES) and N-oxide-tramadol (N-OX) analytical grade (99.9%), were purchased from LGC Standards (Germany). Titanium dioxide Degussa P25 (particle size, 20–30 nm; crystal structure, 80% anatase and 20% rutile; surface area, $56\,m^2g^{-1}$) was used as photocatalyst. HPLC-grade solvents (acetonitrile, isopropanol, methanol and water) were supplied by Merck (Darmstadt, Germany). Sodium azide (NaN_3), potassium iodide (KI), sodium fluoride (NaF) and potassium dichromate ($K_2Cr_2O_7$) were obtained from Sigma-Aldrich. Superoxide dismutase (SOD) was purchased from Carl Roth GmbH+ Co., KG. (Karlsruhe). HA 0.45 μm filters were supplied by Millipore (Bedford, USA). Oasis HLB (divinylbenzene/N-vinylpyrrolidone copolymer) cartridges (60 mg, 3 mL) from Waters (Mildford, MA, USA) were used for the by-products evaluation.

2.2. Irradiation procedures

Irradiation experiments were performed using a Suntest XLS+ solar simulator (Atlas, Germany). The illumination was performed using a vapor xenon lamp (2.2 kW) equipped with special glass filters restricting the transmission of wavelengths below 310 nm. Photocatalytic degradation of TRA was conducted in a Pyrex reactor with a total volume of 250 mL and a double-walled cooling-water jacket to keep the temperature of the solutions at about 25 °C throughout all experiments. Before illumination, suspensions of TRA solutions ($10\,mg\,L^{-1}$) containing $100\,mg\,L^{-1}$ TiO_2 were stirred at 600 rpm in the dark for 30 min to achieve adsorption–desorption equilibrium.

2.3. Analytical methods

A Dionex P680HPLC equipped with a Dionex PDA-100 Photodiode Array Detector was used for TRA determination and quantitation. TRA analysis was performed on a Discovery C18, (250 mm length × 4.6 mm ID, 5 μm particle size) column from Supelco (Bellefonte, PA, USA), thermostated at 40 °C. The elution was performed isocratically using LC-grade water at pH 3 (30%) and acetonitrile (70%) solution as the mobile phase at a flow rate of $1\,mL\,min^{-1}$. Quantification was realized at 215 nm. The detection limit was $40\,\mu g\,L^{-1}$ using a signal-to-noise ratio (S/N) equal to 3. TOC removal was followed via a Shimadzu, TOC V-csh Analyzer. NO_3^- ions released during the process were determined by a Dionex ICS-1500 equipped with ASRS Ultra II self-regenerating suppressor. Ammonium ions (NH_4^+) were analyzed by a UV–vis spectrophotometer (Hitachi, model U-2000) using the colometric method based on indophenol blue formation [22].

2.4. LC–MS analysis

For the identification of TPs, aliquots of 20 mL the irradiated solutions were extracted by means of solid-phase extraction (SPE), using Oasis HLB (divinylbenzene/N-vinylpyrrolidone copolymer) cartridges (60 mg, 3 mL) from Waters (Mildford, MA, USA). SPE was performed using a 12-fold vacuum extraction box (Visiprep, Supelco, Bellefonte, PA, USA). The cartridges were activated and conditioned with 3 mL of methanol and 3 mL LC-grade water at a