Holistic Investigation of Sustainable Tolperisone Hydrochloride Degradation from Water through Photodegradation

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Despite having only one planet to inhabit, environmental pollution remains a pressing global concern. Among the various threatened natural resources, the impact of pollution on drinkable water is particularly burdensome, affecting both life quality and the economy. One major contributor to water pollution is the presence of pharmaceutically active ingredients, posing significant risks. This study explores the use of heterogeneous photocatalysis as a sustainable alternative for the removal of tolperisone hydrochloride (TLP) from water. The research also delves into the analysis of the degradation pathway of TLP, employing various scavengers (NaF, *tert*-butanol, H_2O_2, EDTA × 2Na). The findings reveal a changing contribution of reactive species. Additionally, 12 photodegradation intermediates of TLP were identified through LC–ESI–MS/MS analysis.

Introduction

In recent decades, humanity is burdened with challenges such as global warming, climate change, and escalating water and soil pollution [1]. The scarcity of pure and sanitary water has emerged as a critical issue, impacting both quality of life and the global economy. The presence of micropollutants in aquatic environments, categorized as emerging pollutants per the European Directive 67/548/EEC [2], encompasses pharmaceuticals, personal care products, pesticides, and more. Tolperisone (TLP), a representative of skeletal muscle relaxants, is commonly employed in the treatment of various pathological conditions, such as multiple sclerosis, myelopathy, and painful muscle spasms associated with orthopedic and rheumatologic diseases [3]. Besides, TLP is identified as extremely harmful to aquatic ecosystems, warranting prevention from reaching groundwater, water courses, or sewage systems, even in minimal quantities. TLP Heterogeneous photocatalysis, recognized as a green and efficient technique for degrading persistent organic pollutants, falls under the domain of Advanced Oxidation Processes [4].

The primary objective of this study was to optimize the efficiency of photocatalytic degradation using chemometric analysis. Additionally, the research sought to investigate the photodegradation intermediates generated during the process of TLP degradation in water. Further experiments were carried out to identify these degradation intermediates and elucidate the potential degradation pathway of TLP, particularly in the presence of diverse scavengers.

Material and Methods

TLP (CAS No 3644-61-9, $C_{16}H_{24}ClNO$, M_r = 281.82, 99.5% purity, Goodwill Pharma, Subotica, Serbia) was used as the investigated organic pollutant. The following chemicals were used as the components of the mobile phase: acetonitrile (99.9%, Sigma−Aldrich, St. Louis, MO, USA) and orthophosphoric acid (85%, pro analysis, Sigma–Aldrich, St. Louis, MO, USA). The aqueous solution of TLP (0.05 mM) was prepared, and the heterogeneous photocatalytic experiments were carried out in the presence of TiO_2 Hombikat (anatase, surface area 35–65 m^2/g Sigma-Aldrich Chemie GmbH, Steinheim, Germany) and ZnO (≥99%, Sigma-Aldrich Chemie GmbH, Steinheim, Germany), as photocatalysts. Different scavengers were also used: NaF (*pro analysis*, Merck, Darmstadt, Germany), *tert*-butanol (≥99.5%, Sigma−Aldrich, St. Louis, MO, USA), H_2O_2 (30% (w/w), Sigma−Aldrich, St. Louis, MO, USA), ethylenediamine tetraacetic acid disodium salt (EDTA × 2Na) (≥99.5%, Dojindo Molecular Technologies, Rockville, MO, USA). The photocatalytic experiments were conducted in a photochemical cell made by Pyrex glass. The examinations under simulated sunlight irradiation (SSI) were performed using a 50 W halogen lamp (Philips), while in the experiments with UV irradiation, 125 W high-pressure mercury lamp (Philips, HPL N) was used. The samples were analyzed using a high-pressure liquid chromatograph with diode array detector (UFLC-DAD, Shimadzu Nexera, Tokyo, Japan) and Agilent Technologies 1200 series HPLC coupled with Agilent Technologies 6410A series electrospray ionization triple-quadrupole MS/MS and controlled by Agilent MassHunter Workstation B.03.03 software. Descriptive statistics provided information about the dataset. Continuous variables were tested by multivariate

analysis of variance (MANOVA). Pearson's linear correlation tested the relation between the pairs of continuous variables. Linear regression was employed to build and compare mathematical models.

Results and Discussion

The comprehensive optimization of the photocatalytic degradation process of TLP under varying experimental conditions was successfully achieved. To conclude, the highest removal efficiency of TLP was attained in the presence of TiO_2 as photocatalyst, with catalyst loading of 1.0 mg/mL, after 60.83 min of irradiation under UV light. To further assess the effectiveness of the aforementioned system, specific kinetic parameters were calculated and are presented in Table 1. Moreover, in this research, additional experiments were conducted employing the LC–MS/MS technique to comprehensively analyze potential photodegradation intermediates and elucidate a possible degradation pathway of TLP. According to the LC–ESI–MS/MS findings, a total of 12 degradation intermediates were identified in the analyzed samples. Notably, all these products exhibited an odd molecular weight, confirming the presence of a nitrogen atom, specifically indicating the retention of the piperidine ring. Additionally, the kinetics of the intermediates that appeared or disappeared during the photocatalytic degradation of TLP under the optimal conditions was investigated. To elucidate the photodegradation pathways of TLP, additional experiments were conducted under the optimal photocatalytic conditions (Fig. 1). The results indicate that NaF, adsorbed hydroxyl radical scavenger, did not exert a significant effect on the photocatalytic degradation of TLP when compared to TiO_2. The observed results suggest that the degradation occurred primarily through free hydroxyl radicals. This conclusion is supported by the significant decrease in the degradation efficiency of TLP in the presence of *tert*-butanol compared to TiO_2, indicating the effective trapping of free hydroxyl radicals. Similarly, under optimal photocatalytic conditions, analogous outcomes were observed with H_2O_2 as with TiO_2. This data implies that electrons did not play a substantial role in the degradation of TLP. On the other hand, a diminished photocatalytic activity was noted in the presence of EDTA × 2Na, as approximately 80% of TLP was degraded after 120 min of UV irradiation. Considering all aspects, it can be asserted that the photodegradation of TLP occurs through free hydroxyl radicals and positively charged holes.

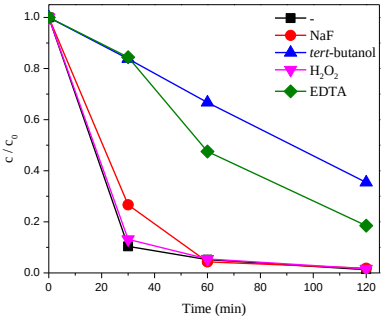

Figure 1. Effect of different scavengers (3.0 mM) on the photodegradation efficiency of TLP (0.05 mM) with TiO_2 (1.0 mg/mL) under UV light

Table 1. Kinetic data of TLP degradation under optimal experimental conditions.[a]

Degradation efficiency (%)	Degradation rate constant × 10^2 (min^{-1})	Degradation rate × 10^6 (μmol/(dm^3 min))	Half-reaction time (min)
100	8.44	4.22	8.21

[a] The kinetic parameters were calculated after 60 min of irradiation.

Conclusions

According to the experiments on photocatalytic degradation, it is evident that TLP was completely eliminated in the presence of TiO_2 under UV irradiation. Furthermore, the LC–ESI–MS/MS results revealed the presence of 12 distinct intermediates. Additionally, the degradation pathway of TLP was successfully defined. The data obtained suggests a change in the relative contribution of various reactive species.

Acknowledgments

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