MOF-Based Photocatalytic Degradation Of The Antidepressant Drug Duloxetine

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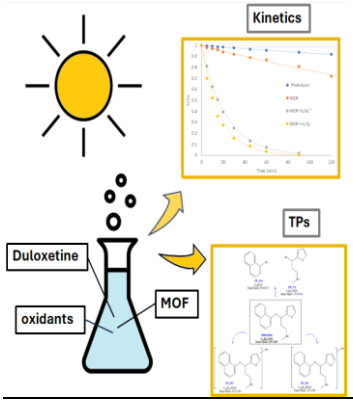
***D. N. Bikiaris*[1]**, *A.S. Rapti*[1], *E.N. Evgenidou*[1,2], *D.A. Lambropoulou*[1,2].
(1) Department of Chemistry, Aristotle University of Thessaloniki, GR-541 24 Thessaloniki, Greece
(2) Centre for Interdisciplinary Research and Innovation Balkan Center, Thessaloniki, GR 57001, Greece



In this study, the metal–organic framework (MOF)-based photocatalytic treatment of duloxetine was investigated. Basolite F300 was used as catalyst, however no significant degradation of the target compound was observed when applied solely. Addition of an oxidant (H_2O_2, $S_2O_8^{2-}$) appears to enhance the process possibly by triggering heterogeneous Fenton-type reactions. Both processes led to the elimination of duloxetine within 90 min of treatment. The effect of the oxidants dose was explored, while the optimum amount proved to be 100 mg/L for both oxidants. The arising transformation products (TPs) were also detected, while the main transformation pathways were hydroxylation, hydrogenation-hydroxylation and cleavage of the ether bond. Ecological structure-activity relationship (ECOSAR) predictions revealed the formation of many toxic and harmful TPs while some of them were even more toxic than the parent compound.

Introduction

Antidepressants are a class of pharmaceutical compounds that are frequently prescribed and usually for a long-term use. Depression and anxiety that originated in the population during the COVID-19 pandemic led to a considerable increase in their consumption. Moreover, due to their physicochemical properties they exhibit moderate removal in WWTPs thus finding their way to enter the water cycle. The increased stability in the aquatic matrices led to their continuous determination in various environmental compartments [1]. Even at low concentrations, antidepressants can present adverse effects on aquatic microorganisms and consequently their removal is an urgent environmental issue [2].

Advanced oxidation processes (AOPs) are an attractive alternative for pharmaceuticals' treatment. Among the various techniques, MOFs have been chosen as advantageous semiconductors for various heterogeneous photocatalytic studies while Fe-MOFs exhibit some Fenton-type activity. Even though iron based-MOFs are applicable in visible light photocatalysis, they often suffer from increased recombination rates. However, this can be hindered with the addition of electron acceptors/oxidants due to their facile implementation and quantum yield increase. The use of iron-based MOFs, such as Basolite F300, is highly advantageous, due to the iron biocompatibility and low toxicity [3].

Under this light, the MOF-based photocatalytic degradation of duloxetine has been investigated. The main objectives were: i) to evaluate the degradation kinetics in the presence of the MOF catalyst, ii) to study effect of the addition of two different oxidants (H_2O_2, $S_2O_8^{2-}$), iii) to identify the produced TPs and iv) to assess their *in silico* toxicity.

Material and Methods

Duloxetine (>99%) was supplied by Sigma Aldrich (Germany). The photocatalyst Basolite® F300 (Fe-BTC, Iron 1,3,5-benzenetricarboxylate; produced by BASF) was purchased from Sigma Aldrich/ Merck (Germany). Sodium persulfate ($Na_2S_2O_8$, 99+%) was supplied from Chem-LabNV (Zedelgem, Belgium). Hydrogen peroxide (H_2O_2, 30% w/v) was purchased from Panreac (Barcelona, Spain). LC-MS-grade solvents (methanol, water) were purchased from Merck (Germany). Formic acid of LC-MS grade (98%) was obtained from Sigma Aldrich (Germany). Ultrapure water was acquired from a purification system (18.2 MΩ × cm, Milli-Q, Millipore, USA). All photocatalytic experiments were conducted in the solar simulator Atlas Suntest CPS+ (Germany) equipped with an air-cooled xenon lamp (1.5 kW) providing a simulated solar light (SSL) with irradiance intensity of 500 W m^{-2}. The determination of DUL concentration and the identification of the formed TPs were conducted using ultra-high performance liquid chromatography– high resolution mass spectrometry (HRMS). The available system consisted of a UHPLC unit coupled to a benchtop QExactive Focus-Orbitrap mass spectrometer (Thermo Scientific). At the UHPLC system, the mobile phase consisted of (A) water (0.1% formic acid) and (B) methanol (0.1% formic acid). The instrument was operated with electrospray ionization (ESI) in positive and negative mode. The Orbitrap analyzer was operated at 70,000 resolution for full-scan MS (FS) and 17,500 for data-dependent acquisition (ddMS2). The mass range was set at 100–1000 Da and 50–1000 Da for FS and ddMS2, respectively.

Results and Discussion

Preliminary studies showed that photolytic

degradation of duloxetine proceeded in a slow rate achieving less than 10% degradation within 2h of irradiation while by the same time, in the presence of MOF catalyst, a 29% degradation is observed. Addition of oxidants strongly accelerates the reaction process and the target compound is completely degraded within 90 min (**Figure 1**).

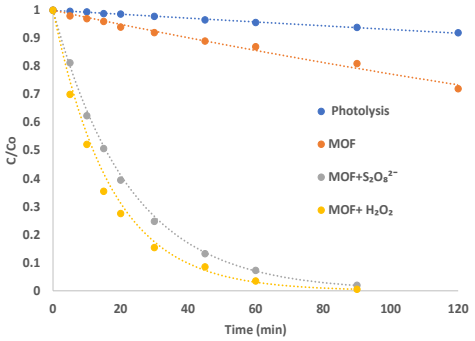


Figure 1. Photolytic and photocatalytic degradation of duloxetine

Exploring the effect of the addition of the oxidants, experiments were conducted with different concentrations of oxidants ranging from 100 to 300 mg/L. However, higher concentrations than 100 mg/L didn't achieve higher reaction rates due to scavenging effects to the oxidative radicals.

In addition to the degradation kinetics, the TPs formed during the photocatalytic process were also investigated. The degradation of the target compound leads to the generation of ten TPs arising from three basic transformation routes; namely hydroxylation, hydrogenation-hydroxylation and cleavage of the ether bond (**Figure 2**).

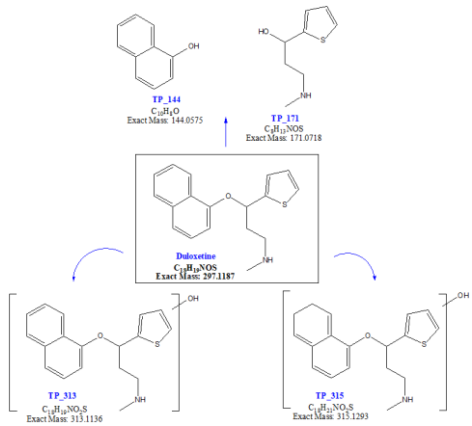


Figure 2. Main degradation pathways of duloxetine

The in Silico toxicity od duloxetine and its TPs was calculated using the ECOSAR software. The calculated values of the major TPs are presented in **Table 1**.

Table 1. Predicted acute and chronic toxicity of DUL and its major TPs

Compounds	Acute toxicity (mg/L) ($EC_{(50)}/LC_{(50)}$)			Chronic toxicity (mg/L) (ChV)		
	Fish	*Daphnids*	*Green algae*	*Fish*	*Daphnids*	*Green algae*
DUL	0.99	0.16	0.07	0.02	0.02	0.03
TP_144	7.50	3.07	13.20	0.84	0.58	6.15
TP_171	202	20.97	22.81	18.03	1.50	6.85
TP_313	2.16	0.33	0.17	0.06	0.04	0.07
TP_315	4.04	0.59	0.32	0.13	0.06	0.13

Not harmful	Harmful	Toxic	Very Toxic

Conclusions

The photocatalytic degradation of the antidepressant duloxetine has been studied in the presence of MOF. Addition of oxidants appears to strongly enhance the degradation process. Ten TPs were identified during photocatalytic treatment arising through hydroxylation, hydrogenation-hydroxylation and cleavage of the ether bond. The arising TPs retained the toxic properties of the parent compound.

Acknowledgments

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