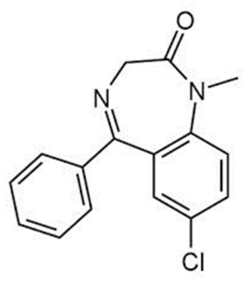
AOP Removal of Benzodiazepines from Contaminated Water: the Case of Diazepam

Carmen Tesoro [(a)], Sabino A. Bufo [(a,b)] ,Lee-Ann Modley [(b)], Laura Scrano [(c)], Rosanna Ciriello [(a)], Filomena Lelario [(a)]

[(a)] Department of Sciences, University of Basilicata, Via dell'Ateneo Lucano 10, Potenza, 85100, Italy
[(b)] Department of Geography, Environmental Management and Energy Studies, University of Johannesburg, Johannesburg, 2092, South Africa
[(c)] Department of European Cultures, University of Basilicata, Matera, 75100, Italy



INTRODUCTION

Nowadays, great attention is paid to pharmaceuticals and their metabolites as persistent pollutants in wastewater [1] due to their widespread consumption [2] and their incomplete removal during conventional wastewater treatments [3]. One important class of drugs is benzodiazepines, whose most commonly used representative is diazepam (7-chloro-lmethyl-5-phenyl-1,4-benzodiazepin-2-one) [4]. In the human body, diazepam produces several pharmacologically active metabolites (e.g., nordiazepam, temazepam, and oxazepam) that may transform further during wastewater treatment. The by-products could be of significant concern due to their potential toxicity [5]. To obtain diazepam's complete degradation, we experimented with an advanced oxidation process (AOP) by using TiO_2 as a catalyst.

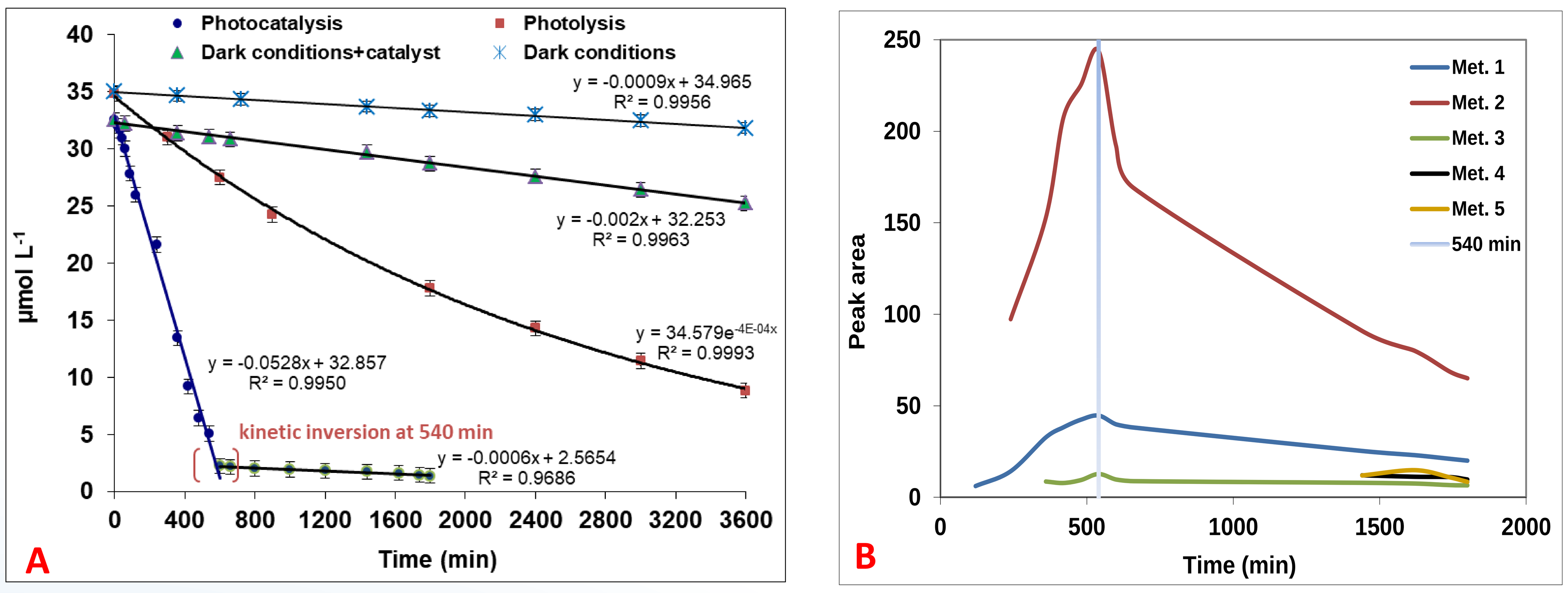


Figure 1. (A) Diazepam remaining under photolysis or photocatalysis. (B) Formation of diazepam byproducts during the photocatalytic process.

Table 1. Kinetic parameters of diazepam photodegradation: n, reaction order; $t_{1/2}$, half-life; k, kinetic constant; R^2, determination coefficient. Values were obtained based on three replicate experiments.

Oxidation Process	n	$t_{1/2}$	k	R^2
Photolysis	1	1853 (min) ÷ 30.89 (h)	$3.74x10^{-4}$ (μM min^{-1})	0.9993
Photocatalysis (0-540 min)	0	311 (min) ÷ 5.19 (h)	$528x10^{-4}$ (μM min^{-1})	0.9950
Photocatalysis (540-1800 min)	0	2034 (min) ÷ 33.90 (h)	$6.31x10^{-4}$ (μM min^{-1})	0.9686

EXPERIMENTAL CONDITION

All determinations were carried out using our LC system coupled to a Fourier Transform Ion Cyclotron Resonance (FT-ICR) Mass Spectrometer (Thermo Fisher Scientific-Bremen, Germany). Optimized MS conditions were used. The LC-MS analysis was performed in a isocratic mode with two solutions, solution A: water with formic acid (0.1% v/v) and solution B: acetonitrile (100% v/v). The elution flow rate was 1 mL min^{-1} and the injection volume was 20 μL in all samples. The irradiation apparatus used was an Heraeus Suntest CPS Instrument equipped with Xenon Arc lamp (1.8 KW)

RESULTS AND DISCUSSION

Photodegradation of diazepam was much faster under light irradiation + TiO_2 (half-life = 6 hours) than under the treatment in a solar simulator (half-life = 31 hours), as shown in figure 1 and table 1. The wastewater used as a control in the darkness and in presence of TiO2 shows a slight loss of soluble diazepam during the experiment due to its adsorption (from 6.6% at t=0, up to 27.5% at t=60h) on the surface of the catalyst. 84.5% of diazepam was degraded in 540min (9h) during the photocatalytical experiment with the formation of 5 by-products, which were under the limit of detection after 1800 min (30h). Further degradation of diazepam after the first 540 min (9h) was very slow with different kinetics. A summary of identified photoproducts is reported in Figure 2. Table 2 shows the accurate mass values and chemical formula.

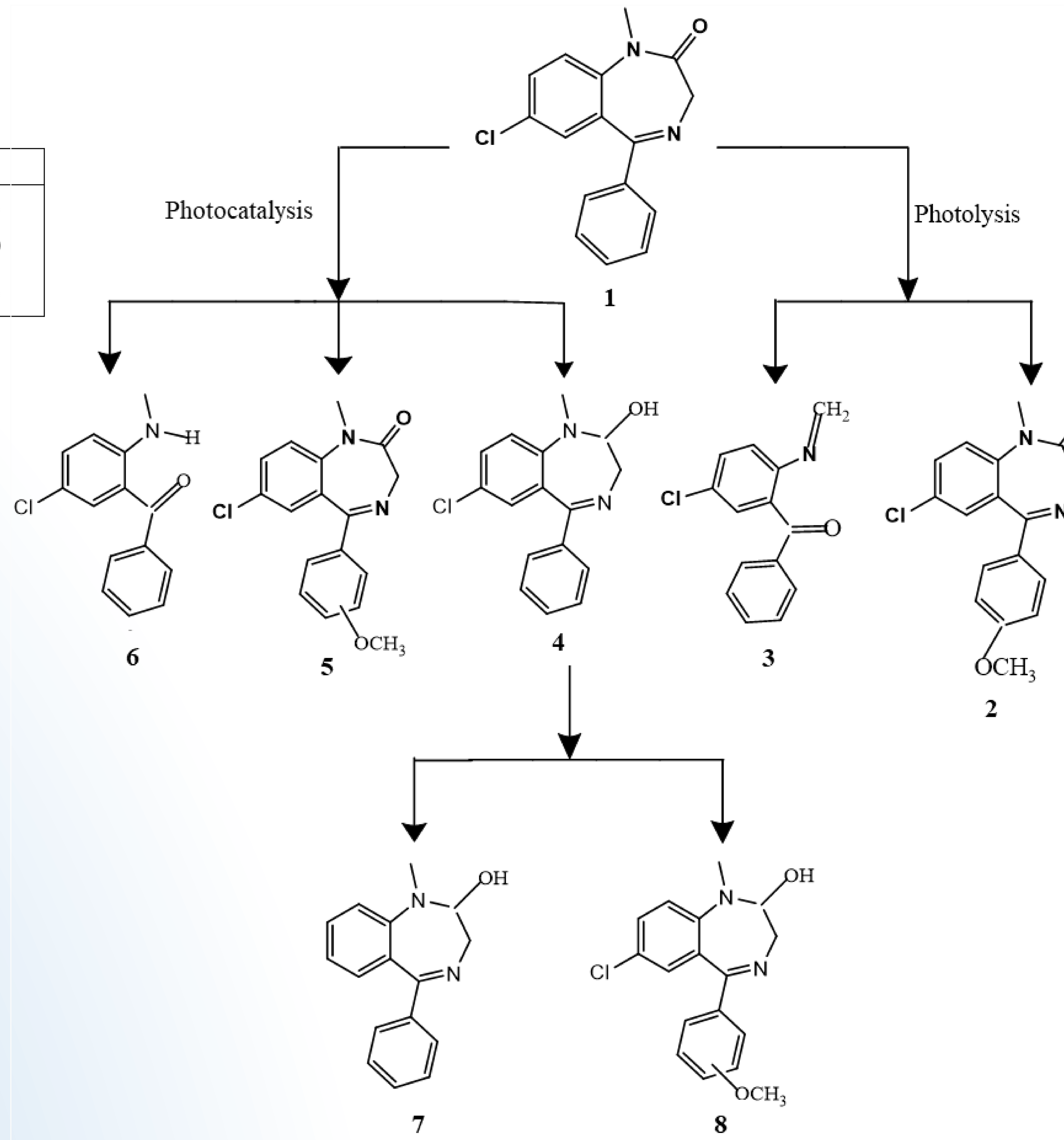


Figure 2. Summary of diazepam photoproducts structures under photolysis and photocatalysis processes.

Table 2. Photoproducts of diazepam

Compounds	Molecular formula	Accurate *m/z* [M+H]+	Error (ppm)
1	$C_{16}H_{14}ON_2Cl$	285.07910	+0.64
2	$C_{17}H_{16}O_2N_2Cl$	315.08948	+0.56
3	$C_{14}H_{10}NOCl$	244.05237	-0.0009
4	$C_{16}H_{16}ON_2Cl$	287.09957	+0.66
5	$C_{17}H_{16}O_2N_2Cl$	315.08997	-0.30
6	$C_{14}H_{13}ONCl$	246.06802	+ 0.57
7	$C_{16}H_{15}ON_2$	251.11789	+ 0.18
8	$C_{17}H_{18}O_2N_2Cl$	317.10513	+ 0.19

CONCLUSIONS

The results of this study suggest that the proposed approach could represent a valuable strategy for in-situ and ex-situ remediation of diazepam in wastewater.

All photoproducts (photolysis and photocatalysis) have been successfully identified using LC/ESI-FTICR-MS. Accurate masses were obtained, and molecular formulae were proposed based on known photochemical pathways and the structure of the mother molecule.

REEFERENCES

[1] Ashraf, M.A. Persistent organic pollutants (POPs): a global issue, a global challenge. Environ Sci Pollut Res 24, 4223–4227 (2017). https://doi.org/10.1007/s11356-015-5225-9.
[2] The Global Use of Medicines 2022 - Outlook to 2026. The IQVIA Institute, Durham, 2400 Ellis Rd, United States. Dec 09, 2021. https://www.iqvia.com/insights/the-iqvia-institute/reports/the-global-use-of-medicines-2022.
[3] Gros M., Petrović M., Ginebreda A., Barceló D., Removal of pharmaceuticals during wastewater treatment and environmental risk assessment using hazard indexes, Environ. Inter., 36, 2010, 15-26. https://doi.org/10.1016/j.envint.2009.09.002.
[4] Zhang M, Kou L, Qin Y, Chen J, Bai D, Zhao L, Lin H, Jiang G. A bibliometric analysis of the recent advances in diazepam from 2012 to 2021. Front Pharmacol. 2022 Nov 9;13:1042594. https://doi.org/10.3389/fphar.2022.1042594.
[5] Sulaiman S., Khamis M., Nir S., Scrano L., Bufo S.A., Karaman R., Diazepam stability in wastewater and removal by advanced membrane technology, activated carbon, and micelle–clay complex. Desalination and Water Treatment, (2014) 1–9. https://doi.org/10.1080/19443994.2014.981225.