PHOTOLYTIC AND PHOTOCATALYTIC DEGRADATION OF PHARAMCEUTICALS

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Summary

Pharmaceuticals are highly diverse group of compounds used for treating and preventing diseases in humans and animals. They are designed to be biologically active and therefore they might negatively affect non-target living organisms. Owing to the advances of different analytical methodologies during the last decade, the widespread occurrence of these compounds in the environment was demonstrated. Although they are present in the environment in ng/L concentrations the proof of their existence in the environment lead to an arising social and scientific awareness. Many studies showed that the main point of collection and subsequent release of pharmaceuticals into the environment are wastewater treatment plants, suggesting that their upgrade and implementation of advanced treatment technologies are required.
This work presents the results of use of some AOPs - photolytic and photocatalytic degradation of three pharmaceuticals (sulfamethazin, febantel and praziquantel) from different groups. In the experiments with UV-C radiation both photolytic and photocatalytic degradation processes occur, whereas with UV-A radiation only photocatalytic treatment was driven. Although photocatalytic experiments with UV-A are not as efficient as those with UV-C, they have a potential for practical use since natural UV-A solar radiation, which lowers the overall cost of the treatment, can be used.

Keywords: photolysis, photocatalysis, TiO_2 film, pharmaceuticals

Introduction

One of the major challenges faced around the world is the limited quantity of unpolluted water available for future use as a resource for drinking water supply. Until recently the impact of chemical pollution has focused on the conventional “priority” pollutants (pesticides, polycyclic aromatic hydrocarbons (PAHs), persistent organic pollutants (POPs), heavy metals...). However, the growing use of pharmaceuticals worldwide, the so-called emerging contaminants, has become a new environmental problem, which has great

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concern among scientists in the last decade (Glassmeyer et al., 2008). Pharmaceuticals are complex molecules with different physicochemical and biological properties and functionalities. They have an important role in the treatment and prevention of disease in both humans and animals. Because of their nature they can also have unintended effects on animals and micro-organisms in the environment. As these compounds are frequently transformed in the body, a combination of unchanged pharmaceuticals and metabolites are excreted by humans. Human-use pharmaceuticals enter raw sewage via urine and feces and by improper disposal. These pharmaceuticals are discharged from private households and from hospitals and eventually reach municipal wastewater treatment plants (WWTPs). If pharmaceuticals are only partially eliminated, residual quantities enter surface or groundwater. However, direct inputs into natural waters are also possible through veterinary practice when manure is spread on fields. If not degraded, pharmaceuticals may end up in soil or groundwater.

Although pharmaceuticals concentration is too low to pose an acute risk, it is not known whether other receptors in non-target organisms are sensitive to individual residues, or the pharmaceuticals that share a common mechanism of action exhibit synergetic effects. However, due to the widespread usage of pharmaceuticals in everyday life and because their purpose is to produce specific biological effects on organisms or living tissue, unwanted environmental effects are to be expected. Since pharmaceuticals are continually being introduced into the environment, they do not need to be persistent to cause negative effects.

So far, strategies for wastewater treatment have not been focused on the elimination of organic micropollutants. The precautionary principle with regard to drinking water supply and wastewater treatment implies an efficient removal of all potential harmful constituents. However, pharmaceuticals recently detected in surface water and drinking water are not included in the regulatory list of environmental pollutants. As a consequence the indirect potable water reuse of municipal WWTP discharges leads to an exposure of the environment and ultimately of drinking water to these chemicals. Therefore, the removal efficiency of existing wastewater treatment must be optimized and new technologies need to be developed (Petrović et al., 2013).

AOPs are generally defined as aqueous phase oxidation methods based on the generation of highly reactive oxidative species such as hydroxyl radicals ($OH^{\bullet}$) and the reducing hydrated electrons (e^{-}_{aq}), that are capable to degrade/destruct the target pollutant(s). Key AOPs include heterogeneous and homogeneous photocatalysis based on ultraviolet (UV), solar or visible irradiation; electrolysis; ozonation; the Fenton's reagent; high-power ultrasound and wet air oxidation, (Oppenländer, 2003; Comninellis et al., 2008; Klavariotti et al., 2009).

The main objective of this research work was to study the applicability of different AOPs for the degradation of three pharmaceuticals in model water: photochemical (UV-C, UV-A) and photocatalytic (UV-C or UV-A with TiO_2) degradation process.

The semiconductor photocatalyst TiO_2 can photocatalytically degrade and mineralize a large variety of environmental contaminations, including organic and inorganic materials, to CO_2, H_2O, and harmless inorganic anions (Mills and Le Hunte, 1997; Hoffmann et al., 1995). As TiO_2 is illuminated by UV radiation with wavelengths below 400 nm, the photons excite valence band electrons across the band gap into conduction band, leaving holes in the valence band (Linsebigler, 1995). The holes in TiO_2 will react with water molecules or OH^- ions and then produce hydroxyl radicals or directly oxidize adsorbed organics, so the natural solar radiation could be activator (it consists of 3-5% of UV radiation) of the process (Ljubas, 2005). TiO_2 can be applied in the form of a suspension (slurry) or it can be immobilised by different techniques on different substrates, i.e. reactor walls (Šegota et al., 2011; Ćurković et al., 2014). The use of a slurry TiO_2 system requires an additional process step to be entailed for postseparation of the catalyst. This separation process is crucial to avoid the loss of catalyst particles and to avoid the introduction of TiO_2 in the treated water as the new pollutant (Chong et al., 2010). The catalyst recovery can be achieved nowadays through membrane filtration (Chong, 2010) or through a magnetic separation, if the TiO_2 particles were coupled to a magnetic material (Zhao et al., 2002). Nevertheless, several important operating issues with slurry TiO_2 still remain even with a membrane integration process (types of membrane, pore size, regeneration or backwashing, and fouling (Chong et al., 2010)) or with the magnetic separation process (Beydoun et al., 2000; Ljubas et al., 2014). Coupling with magnetic material causes loosing of the activity of the TiO_2 due to the recombination process between magnetic material and TiO_2, or, if insulation layer is used, the particles dimensions increase and the overall photocatalytic surface area decreases. The main problems with regard to this process relate to the efficiency due to the limited mass transfer and/or technical effort leading to high operational cost.

The photocatalytic oxidation processes in this research will be performed with the immobilized photocatalysts in a form of thin ceramic film using a new approach that has been developed with the aim to avoid the above mentioned problems within catalyst separation step (Šegota et al., 2011).

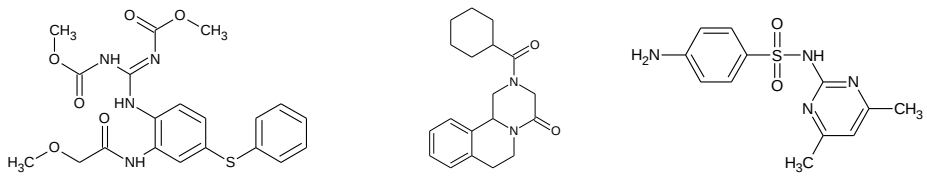
The effectiveness of each AOP and their combinations are examined on the basis of conversion of targeted pharmaceutical(s), which was monitored by HPLC coupled to mass spectrometry.

Materials and methods

Chemicals

Analytical standards (Fig. 1) of febantel (FBT), praziquantel (PZQ) and sulfamethazine (SMT) were obtained from Veterina Animal Health (Kalinovica, Croatia). For chromatographic analysis methanol (J. T. Baker, Deventer, Netherlands), acetonitril (J. T. Baker, Deventer, Netherlands) and formic acid (Merck, Darmstadt, Germany) were used. All solvents used were HPLC-grade. Ultra pure water was prepared by a Millipore

Simplicity UV system (Millipore Corporation, Billerica, MA, USA) and was used for all experiments. Investigated pharmaceuticals were prepared in aqueous solutions in the concentrations of 1 mg/L and 10 mg/L. For FBT and PZQ in the standard solutions 0,01% of organic solvent was added for enhancement of solubility.



Febantel *Praziquantel* *Sulfamethazine*

Fig. 1. Chemical structures of the investigated pharmaceuticals

Photocatalytic experiments

All experiments were carried out in 0.11 L borosilicate glass cylinders as the reactors (Fig. 2):
A - Reactor - a borosilicate glass with a sol-gel TiO_2 film (with the addition of PEG), and
B - Reactor - a borosilicate glass cylinder without coating.
Details about the preparation of the TiO_2 film, with the addition of PEG, can be found elsewhere (Šegota et al., 2011; Ćurković et al., 2014).
Two UV-radiation lamps were used: model Pen-Ray CPQ 7427, with λ_{max} = 365 nm (UV-A) and model Pen Ray 90-0004-07 with λ_{max} = 254 nm (UV-C), both lamps are manufactured by UVP (Upland, CA, USA).

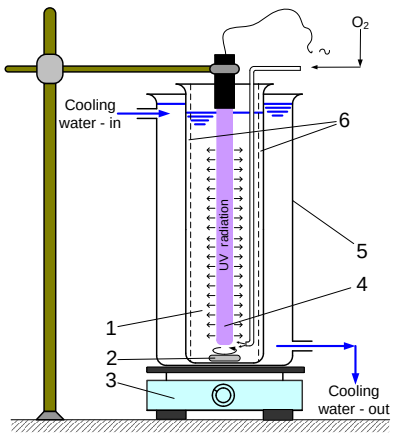


Fig. 2. A scheme of the photoreactor system: 1 – reactor with a solution of the pharmaceuticals, 2 – PTFE magnetic stir bar, 3 – magnetic stirrer, 4 – UV-A or UV-C lamp, 5 – thermostatic bath, 6 – TiO_2 film (in photocatalytic experiments)

The removal/degradation of the pharmaceuticals was ensured with continuous purging with air (O_2) to the solution, using three different conditions, as in (Ljubas, 2015):
(a) under UV illumination in the absence of TiO_2 film (photolysis),
(b) "in the dark" (without UV radiation) with TiO_2 film (adsorption),
(c) under UV illumination in the presence of TiO_2 film (photocatalysis).
The sample aliquots (2 mL) were taken from the reactor, shown in Fig. 2, at certain reaction intervals: usually in 0, 15, 30, 45, 60, 90 and 120 minutes, but in some experiments more often in first 15 minutes.

Analytical procedures

In order to monitor the degradation of all three pharmaceuticals and the formation of their degradation products, sample aliqouts were analyzed using LC-MS/MS. Liquid chromatography analysis was performed using Agilent (Santa Clara, CA, USA) series 1200 coupled to an Agilent 6410 triple-quadrupole mass spectrometer equipped with an ESI interface.
Chromatographic separation was achieved using a Synergy Fusion C18 embedded column for SMT and PZQ (150 mm×2.0 mm, particle size 4 μm) supplied by Phenomenex Co. and the column used for chromatographic separation of the degradation products for FBT was Synergy Polar C18 (100 mm x 2.0 mm, particle size 2.5 μm) supplied by Phenomenex Co, too. The mobile phase consisted of 0.1% formic acid in MilliQ water as eluent A and 0.1% formic acid in acetonitrile as eluent B in gradient elution mode.
For FBT analysis the gradient elution was started with 8% of B which was held for 3 min. During the next 12 min the percentage of B was increased linearly to 95% and was held for 5 min. During 0.01 min it was set to 0% of B and was held for 10 min for equilibration of column.
The flow rate for SMT and PZQ analysis was 0.2 mL/min and the injection volume was 5 μL for all analyses. The gradient elution started with 0% of B, during 2.30 min it rose to 8% of B followed with a rise to 10% of B in the 6th min, to 30% in the 11th min, to 60% in the 15th min and to 95% in the 18th min. During a 10-min period that followed, the content of B was constant at 95%. In the 29th minute (28.10 min), the content of B dropped to 0% and remained that way until the 40th min, which was the end of the run.
Parameters for the mass spectrometer for all the pharmaceuticals were the following: drying gas temperature - 350 °C; capillary voltage - 4.0 kV; drying gas flow - 11 $Lmin^{-1}$, and nebulizer pressure - 35 psi. Positive-mode electrospray ionization (ESI) was used for ionization. Fragmentor voltages were optimized to obtain precursor ions of best abundance for the SMT and degradation products. After the selection of precursor ions, product ions were obtained based on optimized collision energies. Instrument control, data acquisition and evaluation were done using the Agilent MassHunter 2003–2007 Data Acquisition for Triple Quad B.01.04 (B84) software.

Results and discussion

As can be seen on the Fig. 3, for all investigated pharmaceuticals using only UV-A radiation as a degradation mean did not result in degradation.

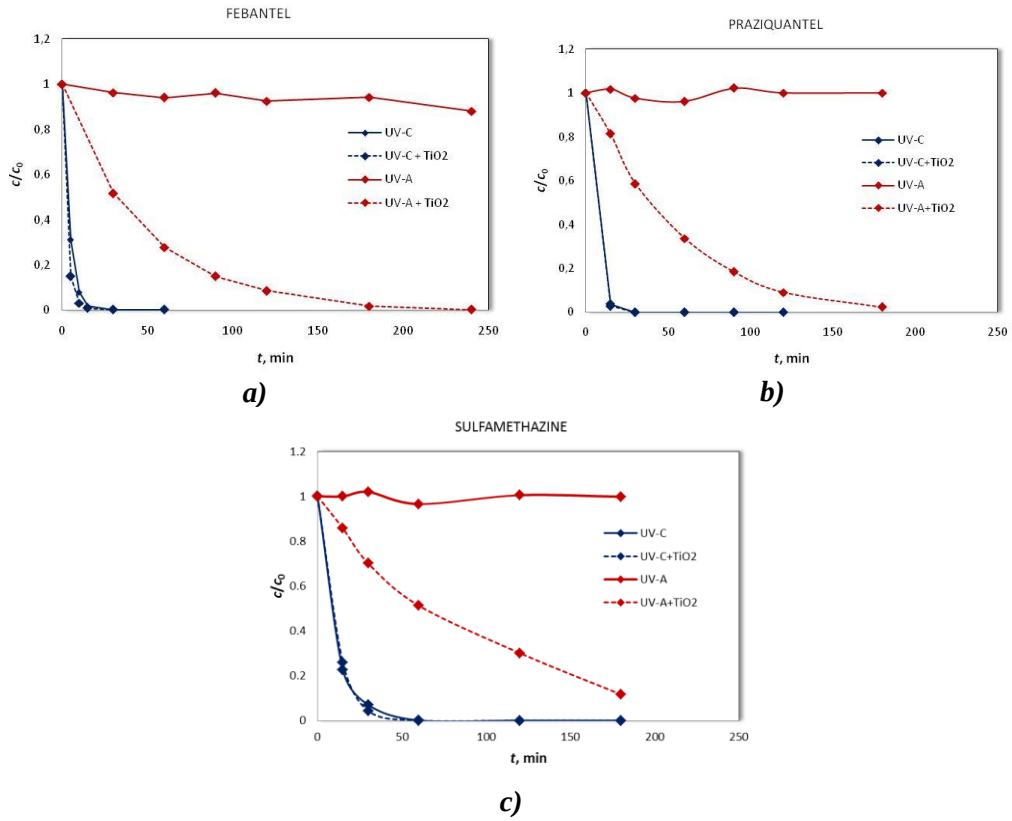


Fig. 3. Degradation of pharmaceuticals: a) febantel, b) praziquantel, c) sulfamethanzine

However, adding TiO_2 film as the catalyst enhanced degradation, so FBT and PZQ were degraded within investigated time (240 min). SMT did not degrade completely during the investigated time of 180 min but 90% of the compound was degraded with the trend of complete degradation. More successful degradation was achieved when the UV-C light was used with and without the catalyst (Čizmić et al., 2016; Babić et al., 2015).

All investigated degradations followed the first order kinetics model which is confirmed with R^2 higher than 0.97 (Table 1). Higher efficiency of UV-C radiation for degradation can be seen when comparing the degradation rates of investigated degradations.

Table 1. Parameters of the first order kinetic models

		k (min^{-1})	R^2	$t_{½}$ (min)
PRAZIQUANTEL	**UV-C**	0.22	1.0000	3.13
	UV-C + TiO_2	0.24	1.0000	2.90
	UV-A +TiO_2	0.02	0.9949	34.48
SULFAMETHAZINE	**UV-C**	0.11	0.9762	6.24
	UV-C + TiO_2	0.10	0.9927	6.86
	UV-A +TiO_2	0.01	0.9991	63.01
FEBANTEL	**UV-C**	0.26	0.9970	2.67
	UV-C + TiO_2	0.32	0.9836	2.15
	UV-A +TiO_2	0.02	0.9900	30.27

From the kinetic model parameters it is obvious that the degradation of all pharmaceuticals is significantly faster when UV-C radiation was applied - almost ten times faster degradation than in the case when UV-A radiation was applied. But, it should be mentioned that the UV-A radiation source for the process of SMT degradation (and of other organic pollutants) could be the UV-A part of solar radiation that reaches the Earth's surface and if solar radiation is used, then the costs of ensuring UV-A radiation could be significantly lowered (it should be considered in future experiments and in the real-scale reactor design) (Babić et al., 2015).

Five photodegradation products of PZQ were identified using MS/MS analysis. Photoproducts reached their maximum concentration after 60 min and none of them was completely degraded in the investigated period of 120 min. Similar formation/degradation profiles were obtained in both processes, i.e. photolysis and photocatalysis (Fig. 4).

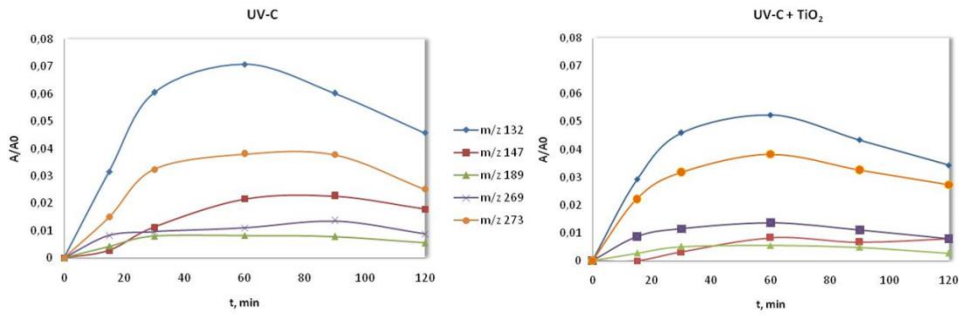


Fig. 4. Formation and degradation of praziquantel degradation products

The formation and degradation profiles of FBT photodegradation products are shown on Fig. 5. In total, five photodegradation products were identified; two of them are present in the reaction solution even after 60 min of degradation and complete degradation of parent compound.

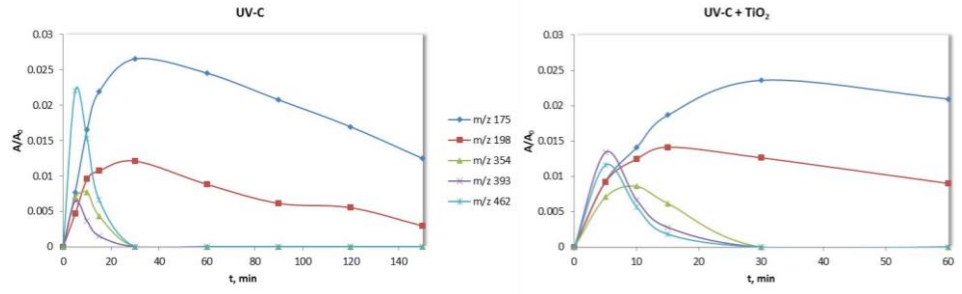


Fig. 5. Evolution and degradation of febantel degradation products

As can be seen on Fig. 6, evolution and degradation of SMT photodegradation products under UV-C radiation are enhanced by presence of TiO_2. In total, five photodegradation products were identified. They reached their maximum concentration after 30 min and 20 min during photolytic and photocatalytic degradation, respectively.

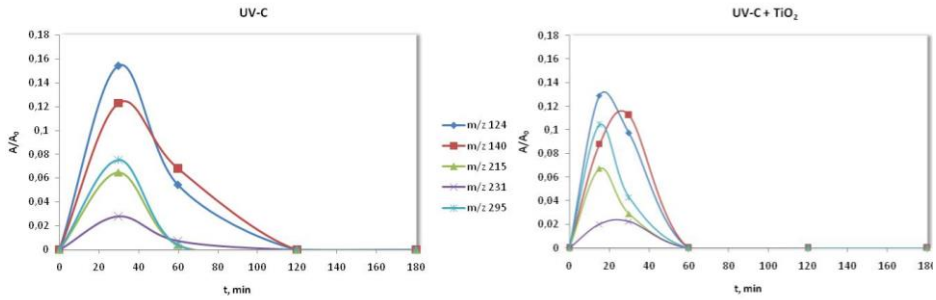


Fig. 6. Evolution and degradation of sulfamethazine degradation products

Conclusions

Based on the experimental results, the following conclusions can be drawn:

- with UV-C radiation both photolytic and photocatalytic degradation processes occur for all three investigated compounds
- for sulfamethazine degradation - presence of the TiO_2 film in the UV-C/TiO_2 photocatalysis system had a positive influence in terms of faster degradation of photoproducts while in the case of degradation of praziquantel and febantel it was not observed
- degradation of all three pharmaceuticals is in average ten times faster when UV-C radiation was applied instead of UV-A radiation
- with UV-A radiation only photocatalytic treatment was driven, photolytic degradation did not occur
- although UV-A photocatalytic experiments need more time than UV-C experiments, they have a potential for practical use since natural UV-A solar radiation could be used here, which lowers the overall cost of the treatment
- for each of the three investigated pharmaceuticals, using HPLC-MS/MS, five degradation products were identified during the degradation process.

Acknowledgments

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