Inżynieria i Ochrona Środowiska 2016, 19(4), 553-560
Engineering and Protection of Environment
https://ios.is.pcz.pl/
p-ISSN 1505-3695
e-ISSN 2391-7253
DOI: 10.17512/ios.2016.4.9

Lidia WOLNY, Marta PRÓBA, Iwona ZAWIEJA, Elżbieta WŁODARCZYK

Czestochowa University of Technology, Faculty of Infrastructure and Environment
Institute of Environmental Engineering
ul. Brzeźnicka 60a, 42-200 Częstochowa
e-mail: wolny@is.pcz.czest.pl

Determination of Ketoprofen and Diclofenac Ultrasonic Removal from Aqueous Solutions

Określenie stopnia usunięcia ketoprofenu i diklofenaku z roztworów wodnych za pomocą ultradźwięków

In the paper the problem of water pollution risks with nonsteroidal anti-inflammatory drugs (NSAIDs) was discussed. The aim of the study was to determine the reduction degree of ketoprofen and diclofenac in solutions exposed to ultrasound. The samples were exposed to ultrasonic field with parameters: power of 750 W and low frequency of 20 kHz (for 240 seconds). In all samples treated with the ultrasounds, a decrease of concentration of the studied drugs was observed. For example reduction of ketoprofen concentration from 40.5 to 10.5 mg/L was noticed. In the sludge water extracts the presence of both drug was proved.

Keywords: **diclofenac, ketoprofen, water extract, sewage sludge, ultrasound**

Introduction

In the last years, pharmaceuticals and their metabolites have been reported in the aquatic environment: surface waters, wastewater, groundwater and even in drinking-water. Medicines were present at levels from the nanograms to low micrograms per litre range usually (concentration continues to increase through years). The progress in analytical technology has been a major factor driving their increased detection. Drugs presence in water, even at these very low concentrations, has raised concerns among drinking-water regulators, governments, water suppliers and the public [1].

The presence of toxic contaminants found in the environment, even at low levels, can cause a potential threat to the proper functioning of the natural environment and human health [2, 3]. One of the occurring micro pollutants are pharmaceuticals, including nonsteroidal anti-inflammatory drugs (NSAIDs) [4]. NSAIDs are widely used medicines without a prescription. The group of NSAID includes so popular drugs as: aspirin, indomethacin, ibuprofen, naproxen, ketoprofen, diclofenac, piroxicam and nabumetone. People who take this pharmaceuticals may have a higher risk of having a stroke and a heart attack than people who do not take NSAIDs.

This risk may be higher for patients who consume NSAIDs for a long period of time. Additional side effects of NSAIDs are digestion problems: abdominal pain, diarrhoea, bloating, heartburn, and upset stomach (for 10÷50% of patients).

Widespread use of these drugs can lead to the penetration of their residues into wastewater as well as the natural environment [5]. Numerous studies have confirmed NSAIDs presence in effluents from sewage treatment plant [6]. Later investigations show that for some pharmaceuticals there was poor or no elimination in many of the WWTPs (antibiotics, benzodiazepines). Relatively good treatment was observed for large group of pharmaceuticals with removal level 40÷70% (lipid regulators, beta-blockers, some NSAIDs). NSAIDs were treated efficiently, with removal roughly equal 80÷90%. The pharmaceuticals detected more often in river waters tended to be those that were not removed successfully during wastewater treatment processes. Despite quite good removal levels NSAIDs were present at high concentrations in rivers. This was because their concentration in the influent was so high that significant levels remain in the effluent and next reach rivers.

Because of mentioned disadvantages and health risks of NSAIDs, their propagation in natural environment may be very dangerous to human health. For last two decades scientists initiated numerous research to increase the efficiency of wastewater treatment level. One of the method of wastewater purification for chosen NSAIDs may be an ultrasonic field treatment [7]. This technology uses ultrasound to destroy contaminants or to assist in accelerating mineralization reactions in liquid phase. The technique of sonolysis has been found effective in various industries such as cleaning, sterilization in biological and food processes, floatation, drying, degassing, defoaming, filtration, homogenization, emulsification, dissolution, disaggregation of powder and catalyst, and biological cell destruction [3].

The aim of this study was to determine the concentration changes of selected pharmaceuticals under the influence of ultrasonic field. Additionally the water extracts of sludge were investigated on the presence of some NSAIDs (diclofenac and ketoprofen) [8-10].

1. Materials and methods

1.1. Investigated substances

Two pharmaceuticals were selected to study (from whole NSAID group): ketoprofen (CAS 22071-15-4) and diclofenac (CAS 15307-79-6). Both substances are frequently present in municipal wastewater, which may indicate an excessive consumption. Many authors have confirmed that both substances can affect several metabolic pathways in the human body including the endocrine system. Mentioned pharmaceuticals have a toxic effect on aquatic organisms and the environment [2]. The degree of removal of diclofenac in the treatment process varies considerably between individual wastewater treatment plants, depending on the used method and the treatment conditions such as season and temperature [4]. Major differences are present also in the results of research on methods of disposal, the degree of elimination of diclofenac ranging from 17 to 75% [5, 6]. Ketoprofen is susceptible to photodegradation and other methods of treatment, nevertheless several studies indicate that the degree of ketoprofen removal is also highly volatile. The degree of elimination of ketoprofen was determined at 98% [11]. In further research elimination of ketoprofen was varied in the range of 8 to 53% [12]. Figure 1 present structural formulas of diclofenac and ketoprofen.

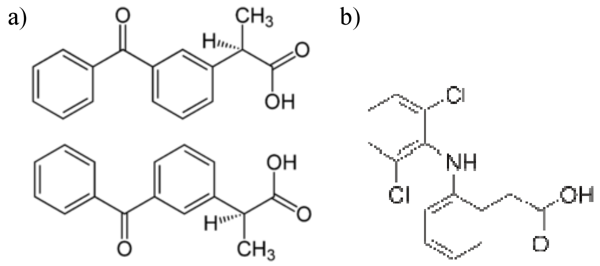

Fig. 1. The structural formulas of selected NSAID: a) ketoprofen, b) diclofenac [8, 9]

1.2. Preparation of samples

The two types of solutions were selected for tests, model solutions of pharmaceuticals, prepared under laboratory conditions, and aqueous extracts of sewage sludge. Into solutions were added: 50 mg/L diclofenac and 50 mg/L of ketoprofen. The water extract from the wet sewage sludge was made by dilution of 100 g sample with ratio 1:10 (distilled water) and filtered for analysis. The resulting aqueous solution was transferred to a chromatographic investigations.

1.3. Sonication of samples

In order to prepare the sonicated samples, pharmaceutical solutions with a concentration of 50 mg/L were treated with ultrasonic field with the following parameters: power of 750 W and frequency of 20 kHz. Sonication time was 4 minutes and was chosen based on previous studies assessing the impact of ultrasonic field on the removal of pharmaceuticals from wastewater [7, 13]. Water extracts from the sewage sludge were treated with ultrasonic field of the same parameters. Samples were tested according to parameters presented in Table 1.

Table 1. **Sonication process parameters**

Process parameters	Value
Power P, W	750
Frequency f, kHz	20
Time t_s, sec	240
Cross-section area of vessel S, m^2	0.0176
Energy E, J	750
Intensity of ultrasonic wave I_s, W/m^2	176.84

1.4. Chromatography GC-MS

A 1000 mL volume sample was connected with a column using plastic tubing. Then started the whole extraction system. Dried sample was desorbed with 10 mL of hexane, and then the solution was collected in a tube intended to condense. The extract was concentrated to 1 mL in concentration apparatus [11]. Next sample was tested according to parameters placed in Table 2. Gas chromatography was selected as a research method based on literature review. In chosen articles GC-MS analysis were applied for pharmaceuticals detection (including diclofenac) in river water and sewage water [12-14].

Table 2. **Instrument parameters and GC/MS conditions**

GC Conditions		MS Conditions (Full Scan Mode)	
Column:	Agilent DB5-MS325°C (30 m/0.32 mm id/1μm d_f)	Acquisition Mode:	Scan/SIM
Initial Temp:	100°C	Scan Range:	100÷350 amu
Transfer Line Temp:	290°C	Sampling Rate:	2 (Scan Rate of about 4 scans/sec)
Injection Mode:	Split (split ratio 2:1)	Solvent Delay:	3.50 minutes
Injection Vol:	2 μL	MS Temp	230°C (Source) 150°C (Quad)
Carrier Gas Flow:	He at 1.5 mL/min		
Pressure:	4.3174 psi		
Oven Program:	100°C (0 min) to 260°C at 15°C/min for a total run time of 15.667 min		

1.5. Equipment

Instruments used for GC-MS investigations are listed below:

1. Gas chromatograph equipped with a split-splitless injector
2. Capillary column: Agilent column of a 30 m in length, internal diameter equal 0.32 mm, coated with film phase of 1 μm in thickness
3. Microliter syringes with scale intervals of 0.05 and 1 mm^3, measuring flask and pipettes.

1.6. Standards

The used standards were chromatographically pure. The chosen diluent was hexane with no impurities interfering in the analysis. Use of 50% aqueous acetonitrile for cleaning the syringe between injections removed sample residue (which might not be soluble in other wash solvents). That additional flushing reduced injector errors.

2. Results

Test specimens were divided into two groups: the pharmaceutical solutions and aqueous extracts which were not exposed to the ultrasound field, and solutions and extracts after sonication process.

Table 3 shows the values obtained for the different concentrations of pharmaceuticals and water extracts. In the case of pharmaceuticals solutions initial concentration was 50 mg/L. Aqueous extracts of sludge were drawn from environmental samples, therefore their initial concentration has not been determined. The concentration values in the solution not subjected to sonication were approximately equal 40 mg/L for both pharmaceuticals (samples A and B). For sonicated samples a decrease in the concentration was observed at levels: 12.0 mg/L (sample A), 10.5 mg/L (sample B) for ketoprofen and 14.2 mg/L (sample A), 12.1 mg/L (sample B) for diclofenac.

Not sonicated drug concentration in aqueous extracts was about: 4.3 mg/L (sample A), 3.9 mg/L (sample B), whereas in the case of samples sonicated the concentration decreased below 0.1 mg/L (both samples) or less than the detection range of the selected method.

Table 3. **Concentration of pharmaceuticals in test solutions and water extracts of sewage sludge**

Sample	Initial concentration	Not sonicated solutions		Sonicated solutions		Used method	Method range
		A	B	A	B		
Detection in prepared solutions							
Ketoprofen, mg/L	50.0	40.5	39.8	12.0	10.5	PB/I/27/C: 01.08.2014	0.1-1.0
Diclofenac, mg/L	50.0	42.1	40.0	14.2	12.1	PB/I/27/C: 01.08.2014	0.1-1.0
Detection in water extracts from sewage sludge							
Ketoprofen, mg/L	–	4.1	3.9	< 0.1	< 0.1	PB/I/27/C: 01.08.2014	0.1-1.0
Diclofenac, mg/L	–	4.3	4.0	< 0.1	< 0.1	PB/I/27/C: 01.08.2014	0.1-1.0

3. Discussion

Ultrasonic degradation of molecules in solution is an interesting case of disintegration reaction of the molecules (and macromolecules) induced by a complicated action in with hydrodynamic forces are of primary importance. Ultrasonic field action is known to influence on the physicochemical properties of chemical compounds. One of ultrasound degradation processes is depolymerization. By the action of ultrasound on the polymer solutions bigger molecules are more easily degraded than smaller one. This process allows to elimination of large molecular parts present in technically produced polymers [15, 16].

Next were the attempts of other organic compounds degradation [17] and research on removal of smaller molecules like pharmaceuticals [18]. It has been shown that sonication treatment may enhance degradation, increase solubility and decrease the particle sizes of pharmaceuticals including NSAIDs.

During sonication tests, the effect of the ultrasonic degradation efficiency and physicochemical properties of tested solutions have been analyzed. In investigated samples pH value and redox potential were reduced by the sonication treatment process. However, the changes of these parameters were strongly influenced by the ultrasounds power [19].

Because the diclofenac salt is significantly soluble in water, degradation inside the cavitation bubble was insignificant, so, hydroxyl radical-induced reactions were probably to be the main diclofenac degradation mechanism. Hydroxyl radicals are formed in water sonication process. Consequently, the presented results are, possibly, directly connected to the hydroxyl radicals formation, which rise while ultrasound power is getting higher, and formation of cavitation bubbles is greater. Ketoprofen is poorly aqueous soluble, its water solubility equals 51 mg/L (at 22°C) [8, 9]. Problem associated with weak solubility is poor dissolution rate. In this case degradation inside cavitation bubble may be more significant than hydroxyl radical action.

Still, the explanation of the influence of the ultrasonic treatment on the aqueous phase remains complex, considering thermal properties, organic compounds degradation and synchronous phenomena occurring such as depolymerization.

Conclusions

Presented in the article correlation between the concentration of pharmaceuticals and ultrasonic field may lead to the following conclusions:

- physicochemical phenomena occurring in the tested samples placed in an ultrasonic field affect on the concentration decrease of selected non-steroidal anti-inflammatory drugs,
- sonication proved to be relatively effective method of wastewater conditioning, all samples showed a decrease in the concentration of pharmaceuticals,
- investigation of water extracts of sewage sludge on the presence of some NSAIDs confirmed the presence of ketoprofen and diclofenac in sewage sludge coming from municipal wastewater treatment plant placed in Silesia region.

The results obtained through this investigation can be next improved through the examination of the by-products formation using chromatography, in order to better determine and estimate the removal kinetics of the formed products. It is also necessary to implement the combined processes at a real scale to better assess the pharmaceuticals degradation in the operated wastewater treatment plant.

Acknowledgements

The financial support by Czestochowa University of Technology, Institute of Environmental Engineering (BS/MN-401-306/14 and BS/PB-401-303/12) is gratefully acknowledged.

References

[1] Szymonik A., Lach J., Zagrożenie środowiska wodnego obecnością środków farmaceutycznych, Inż. Ochr. Środ. 2012, 3, 249-263.

[2] Mehinto A.C., Impacts of the Human Pharmaceutical Diclofenac in the Aquatic Environment, PhD Thesis, University of Exeter 2009.

[3] Mason T.J., Sonochemistry, Oxford University Press, Primer Series 1999, 70, Oxford, UK.

[4] Andreozzi R., Raffaele M., Nicklas P., Pharmaceuticals in STP effluents and their photodegradation in aquatic environment, Chemosphere 2003, 50, 1319-1330.

[5] Heberer T., Reddersen K., Melchinski A., From municipal sewage to drinking water: fate and removal of pharmaceutical residues in the aquatic environment in urban areas, Water Sci. Technol. 2002, 46, 81-88.

[6] Ternes T.A., Occurrence of drugs in German sewage treatment plants and rivers, Water Res. 1998, 32, 3245-3260.

[7] Próba M., Wolny L., Zawieja I., Ultrasonic aiding of selected pharmaceuticals removal from wastewater, Desalin. Water Treat. 2014, 52, 3832-3836.

[8] Material Safety Data Sheet of ketoprofen, 2006. MP Biomedicals.

[9] Material Safety Data Sheet of diclofenac, 2006. MP Biomedicals.

[10] Zawieja I., Wolski P., Wolny L., Influence of chemical conditioning on the physicochemical parameters of digested sewage sludge, Eng. Protection. Environ. 2008, 11(3), 387-396.

[11] Thomas P.M., Foster G.D., Determination of nonsteroidal anti-inflammatory drugs, caffeine, and triclosan in wastewater by gas chromatography-mass spectrometry. J. Environ. Sci. Health A 2004, 39, 1969-1978.

[12] Koutsouba V., Heberer T., Fuhrmann B., Schmidt-Baumler K., Tsipi D., Hiskia A., Determination of polar pharmaceuticals in sewage water of Greece by gas chromatography-mass spectrometry, Chemosphere 2003, 51(2), 69-75.

[13] Zhao J.L., Ying G.G., Wang L., Yang J.F., Yang X.B., Yang L.H., Li X., Determination of phenolic endocrine disrupting chemicals and acidic pharmaceuticals in surface water of the Pearl Rivers in South China by gas chromatography-negative chemical ionization-mass spectrometry, Sci. Total Environ. 2009, 407(2), 962-974.

[14] Tauxe-Wuersch A., De Alencastro L.F., Grandjean D., Tarradellas J., Occurrence of several acidic drugs in sewage treatment plants in Switzerland and risk assessment, Water Res. 2005, 39, 1761-1772.

[15] Próba M., Ultradźwiękowe wspomaganie degradacji wybranych niesteroidowych leków przeciwzapalnych w ściekach, Technol. Wody 2013, 7/8, 24-42.

[16] Basedow M.A., Ebert K.E., Ultrasonic degradation of polymers in solution, Adv. Polymer Sci. 2005, 22, 83-148.

[17] Bremner H.D., Burgess E.C., Chand R., The chemistry of ultrasonic degradation of organic compounds, Curr. Organ. Chem. 2011, 15(2), 168-177.

[18] Naddeo V., Ricco D., Scannapieco D., Belgiorno V., Degradation of antibiotics in wastewater during sonolysis, ozonation, and their simultaneous application: operating conditions effects and processes evaluation, Inter. J. Photoener. 2012, 2012, article ID 624270, 7 pages, DOI: 10.1155/2012/624270.

[19] Naddeo V., Belgiorno V., Napoli R.M.A., Behaviour of natural organic matter during ultrasonic irradiation, Desalination 2007, 210, 175-182.

Streszczenie

W artykule przedstawiono problem zanieczyszczenia wód niesteroidowymi lekami przeciwzapalnymi (NLPZ). Celem badania było wyznaczenie stopnia redukcji ketoprofenu i diklofenaku w roztworach wystawionych na działanie pola ultradźwiękowego. Próbki poddano działaniu pola ultradźwiękowego o następujących parametrach: moc 750 W i niska częstotliwość 20 kHz (dla czasu sonikacji równego 240 sekund). We wszystkich próbkach poddanych działaniu ultradźwięków zaobserwowano spadek stężenia badanych leków. Na przykład zaobserwowano zmniejszenie stężenia ketoprofenu z 40,5 do 10,5 mg/L. Potwierdzono obecność obu farmaceutyków w ekstraktach wodnych osadów ściekowych.

Słowa kluczowe: **diklofenak, ketoprofen, wodny ekstrakt, osady ściekowe, ultradźwięki**