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OCCURRENCE OF ANTIDEPRESSANTS – FROM WASTEWATER TO DRINKING WATER

WYSTĘPOWANIE LEKÓW PRZECIWDEPRESYJNYCH – ZE ŚCIEKÓW DO WODY UZDATNIONEJ

Abstract

The article's subject is the presence of antidepressants in the wastewater and aquatic environment. The basic characteristics of selected antidepressants were presented. A review of the literature on the occurrence of these compounds in sewage influents and effluents, surface waters and sludge was made. As a general rule, drinking water should be free of any organic, especially pharmaceutical, contaminants. But according to data, the presence of antidepressants in source water for water purification plants poses a threat to their penetration to the water supply system and, eventually, to consumers of water intended for human consumption.

Keywords: *Selective Serotonin Reuptake Inhibitors, SSRI, wastewater, surface water, drinking water, sewage sludge*

Streszczenie

W artykule omówiono zagadnienie występowania leków przeciwdepresyjnych w ściekach i środowisku wodnym. Dokonano przeglądu literatury dotyczącej występowania tych związków w ściekach surowych i oczyszczonych oraz wodach powierzchniowych, a także w osadach z oczyszczalni. Jak wynika z danych literaturowych, obecność antydepresantów w wodzie surowej ujmowanej przez stacje uzdatniania wody stwarza realne zagrożenie dla systemów wodociągowych, a w następstwie dla odbiorców wody przeznaczonej do spożycia.

Słowa kluczowe: *selektywne inhibitory zwrotnego wychwytu serotoniny, ścieki, wody powierzchniowe, wody, woda do picia, osady ściekowe*

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1. Introduction

The subject of pharmaceuticals and their presence in the wastewater or the environment has become one of the most analyzed problems over the years. Despite the passing years since the first mention of drug pollution of the aquatic environment, treatment technologies that can completely eliminate the issue of their emissions still have not been implemented. On the one hand, the difficulty lies in the variability of the composition of the wastewater supplied to the treatment plant and various properties of the impurities in them, such as low adsorbability and biodegradability of cytostatic drugs [5]. On the other hand, economic considerations are the ones that restrict the implementation of advanced and modern methods of wastewater treatment, which will most likely entail a significant increase in the costs and an increase in the prices of sewage management. Insufficient elimination and degradation of pharmaceutical pollutants during wastewater treatment poses a risk of emission of these substances into the aquatic environment. One group of pharmaceuticals widely used in medicine is antidepressants. They are found in the environmental samples in one of the largest quantities (8%) out of all the detected pharmaceuticals [49].

2. Characteristics of antidepressants

Drugs for depression are a type of psychotropic drugs, which are substances that affect the mental processes of humans that refer to, among other things, affecting mood, sedation, stimulation, thinking and behavior [53]. Most antidepressants in use are Selective Serotonin Reuptake Inhibitors (SSRIs), which act to regulate the levels of serotonin, which is a neurotransmitter (a chemical compound of transmitting signals between neurons). Antidepressants are used to treat depression, anxiety, panic disorder, eating disorder, obsessive compulsive disorder and social phobia [11]. The most commonly used antidepressants and fluoxetine metabolite norfluoxetine as well as their basic characteristics (e.g. Chemical Abstracts Service (CAS) number and half-life) are presented in Table 1.

3. Occurrence of antidepressants

Antidepressant pharmaceuticals are typical anthropogenic pollutants because those are not the type of substances naturally occurring in the environment. For this reason, the main sources of these drugs in wastewater and natural waters are households and hospitals. Fig. 1 presents the sources and paths of emission of pharmaceutical impurities in the environment. Hospital wastewater has a much higher concentration range of antidepressants, but in their case, there is a possibility for pre-treatment prior to their transport to the treatment plant. In the case of municipal wastewater produced by people in their homes, there is no possibility for pre-treatment. Metabolized, or in the form of primary, antidepressants are transported via a sewer system to municipal wastewater treatment plants, where they should be removed from the wastewater during treatment processes.

Table 1

Characteristics of selected antidepressants [13]

Name	Formula	Molecular mass [g/mol]	CAS No.	Half-life
Amitriptyline	$C_{20}H_{23}N$	277.4	50-48-6	10–50 h
Bupropion	$C_{13}H_{18}ClNO$	239.7	34841-39-9	24 h
Citalopram	$C_{20}H_{21}FN_2O$	324.4	59729-33-8	35 h
Dosulepin	$C_{19}H_{21}NS$	295.4	113-53-1	14–54 h
Fluoxetine	$C_{17}H_{18}F_3NO$	309.3	54910-89-3	1–6 d
Fluvoxamine	$C_{15}H_{21}F_3N_2O_2$	318.3	54739-18-3	15.6 h
Norfluoxetine(m)	$C_{16}H_{16}F_3NO$	295.3	126924-38-7	4–16 d
Nortriptyline	$C_{19}H_{21}N$	263.4	72-69-5	16–90 h
Paroxetine	$C_{19}H_{20}FNO_3$	329.4	61869-08-7	21–24 h
Risperidone	$C_{23}H_{27}FN_4O_2$	410.5	106266-06-2	20–24 h
Sertraline	$C_{17}H_{17}Cl_2N$	306.2	79617-96-2	25–26 h
Venlafaxine	$C_{17}H_{27}NO_2$	277.4	93413-69-5	5 h

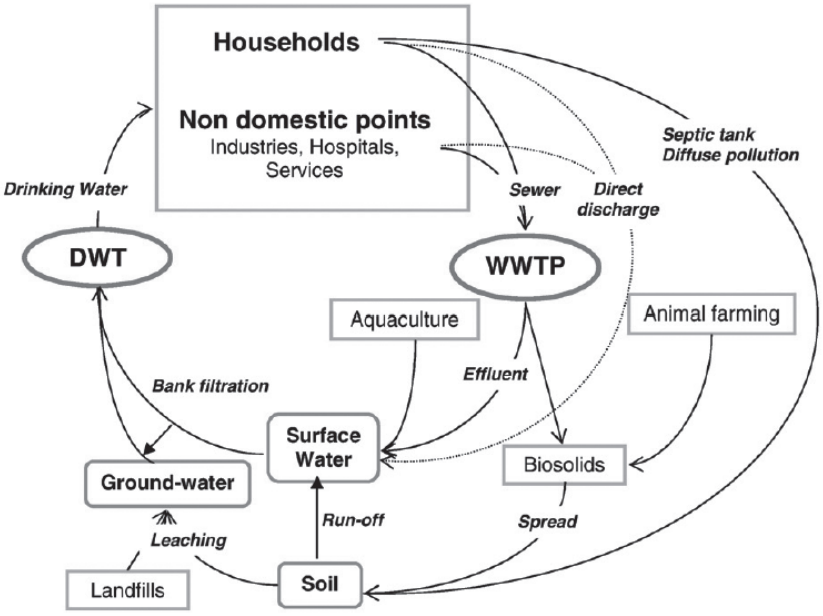

Fig. 1. Potential sources of pharmaceuticals in aquatic environment [32]

Table 2

Concentrations (min-max or mean) of detected antidepressants

Compound	Influent (ng/l)	Effluent (ng/l)	Surface water (ng/l)
Amitriptyline	341-5143[24] 106-2092[33] 35.8-1055.5[4] 3100[48] 659[3] 138[28]	53-357[24] 18.2-243.0[4] 66-207[33] 140[48] 129.8[3] 83[47] 71[28]	0.5-72[33] 1.0-2.0[20] 29.5[3]
Bupropion	17.1-378[41] 74[35]	28-4300[50] 7.3-264[41] 57[35]	–
Citalopram	27-180[19] 35.1-170[41] 99.2-213.6[38] 650.0[14] 236[28] 180[35] 4.0[52]	21-520[50] 104-404[41] 30-120[19] 82.8-95.6[38] 173[28] 120[35] 53.0[14] 5.0[52]	40-8000[16] 0.5-219[37] 4-206[30] 26-160[44] 3-120[1] 2-95[35] 40-90[36] 4-17[18] 3.4-11.5[27]
Dosulepin	17.2-673.3[4] 227.6[3]	3.1-125.1[4] 57.2[3]	0.5-32[33] 9.7[3]
Fluoxetine	17-3645[34] 4.9-175.9[4] 20-91[30] 105.8-157.4[38] 8.0-30.0[42] 1.1-18.7[45] 3.1-3.5[27] 0.4-2.4[46] 540[48] 86.1[3] 51.0[14] 26[22] 24[35] 18.0[28] 18.0[29]	19-929[10] 11-76[50] 50-99[31] 40-73[7] 5.6-44.9[4] 0.6-8.4[45] 2.0-3.7[27] 0.12-1.3[46] 240[48] 29.3[3] 26.0[14] 16[22] 14[29] 11.0[28] 1.7[25] 8[35]	4-141[30] 0.6-66.1[15] 8.0-44.0[1] 0.5-43.2[37] 12.0-20.0[36] 5.8-14[33] 3.2-5.5[18] 1.0-2.0[20] 0.42-1.3[27] 12.0[26] 9.0[3] 3.0[22]
Fluvoxamine	0.4-3.9[46] 0.8-1.7[45] 5.2[28]	0.49-0.8[45] 0.15-0.8[46] 3.4[28]	0.5-4.6[37] 0.5-0.8[45]

Continue Table 2

Compound	Influent (ng/l)	Effluent (ng/l)	Surface water (ng/l)
Norfluoxetine(m)	3.4-118.0[4] 1.8-4.2[27] 62.8[3] 13[35] 12.0[48] 11.0[30] 9.1[28]	1.1-20.2[4] 1.7-1.8[27] 13.2[3] 10.0[48] 7.4[28] 1.0[35]	0.5-13.6[37] 1.2-1.3[27] 0.83-1.0[36] 4.0[30] 3.5[33]
Nortriptyline	6.9-185.8[4] 114.1[3] 18.0[28]	0.9-53.8[4] 32.9[3] 11.0[28]	0.8-19[33] 6.8[3]
Paroxetine	14-32228[34] 137.9-186.4[38] 45-105[39] 2.9-12.9[45] 4.6-5.3[27] 16.0[48] 9.1[35] 8.0[28]	60-240[39] 1.0-11.7[45] 4.3-5.2[27] 1141[10] 81.1[38] 13.0[7] 5.6[28] 7.0[48] 2.3[35]	2.1-3.0[36] 1.3-3.0[27] 0.5-5.8[37] 0.6-1.4[45] 90[51]
Risperidone	364[47]	154[47]	–
Sertraline	31.6-114[41] 14.0-34.0[30] 7-27[19] 6.0-6.1[27] 8.4-19.8[45] 100.4[38] 49[35] 20.0[28]	15.7-88.3[41] 57-87[7] 3-6[19] 3.7-14.6[45] 5.1-5.8[27] 12.0[28] 9.0[35]	0.5-37.5[37] 33-49[36] 6.0-17.0[30] 0.84-2.4[27] 11.0[23]
Venlafaxine	40-980[21] 120-800[19] 169-609[41] 28.8-446.1[4] 121-529[42] 1343[28] 403[47] 352.7[14] 260[35] 249[3]	12-5500[50] 120-1110[19] 60-550[21] 209-553[41] 21.4-285.1[4] 1087[28] 365[47] 220.3[14] 220[35] 187.5[3]	100-1003[44] 0.8-250[18] 1-202[2] 11-180[35] 1.1-85[33] 35.1[3]

However, the efficiency of antidepressant removal in municipal sewage treatment plants is not high enough. Despite the relatively high efficiency of paroxetine elimination (over 90%), most anti-depression drugs are eliminated in an average degree: more than 25% for

venlafaxine, 40–90% for fluoxetine, 60–80% for amitriptyline; also in the case of metabolite norfluoxetine, 40–50% is eliminated [4, 24, 48]. It should be taken into consideration that, in some wastewater treatment plants, the removal efficiencies can be drastically lower.

Insufficient efficiency of processes used in wastewater treatment poses a risk of the emission of pharmaceuticals into the recipient rivers, which was confirmed by the analysis results by Baker and Kasprzyk-Hordern, showing an increase in the concentration of the analyzed antidepressants in water samples collected from rivers upstream and downstream from the point of effluent discharge [4]. Some substances (fluoxetine and its metabolite) were present only in downstream samples taken after effluent discharge (lack of detection in upstream samples). In most cases, the increase in the concentration range of a few to several ng/l, whereas the sample obtained in the vicinity of one of the treatment plants showed significant increases in the concentration of dosulepin (increase from 1.7 to 32.2 ng/l), venlafaxine (3.6 to 47.3 ng/l) and amitriptyline (4.9 to 71.0 ng/l). Table 2 presents a wide review of analysis results that confirm the presence of antidepressants in raw and treated wastewater and surface waters.

Regular emission of pharmaceuticals from wastewater treatment plants into rivers results in the contamination of water and exposure of aquatic organisms to these substances and their potential storage in the tissues of fish. Studies conducted in the USA on fish living in an effluent-impacted river showed the presence of fluoxetine, norfluoxetine, paroxetine and sertraline in the meat, brain and liver of the fish in quantities of 0.1–10 mg/kg [9]. Antidepressants in the fish meat have also been detected in Canada, where the analysis showed 0.14–1.02 mg/kg of fluoxetine, 0.15–1.08 mg/kg norfluoxetine and 0.48–0.58 mg/kg paroxetine [12]. Consumption of contaminated fish by humans may pose a risk to their health, especially in the case of allergy to the drug. In addition, the potential impact of even low concentrations of antidepressants on the human body should not be underestimated. These results allow to presume that frequent consumption of fish caught in effluent-impacted rivers is at least risky from the human health point of view.

The tendency to the accumulation of the organic contamination in sediments and soils poses a risk of contamination in agricultural use of sludge produced in the wastewater treatment plants. In addition, antidepressants that are present in surface waters can accumulate in sediments, which is confirmed by the analysis of sludge from wastewater treatment showing (per kg dry weight) concentrations of fluoxetine 170 ng/kg [17]; amitriptyline 263–583 μg/kg, citalopram 95–1381 μg/kg, fluoxetine 34–152 μg/kg, norfluoxetine 8.9–60 μg/kg, nortriptyline 22–61 μg/kg, paroxetine 11–70 μg/kg, sertraline 203–528 μg/kg and venlafaxine 289–499 μg/kg [28]; fluoxetine and venlafaxine less than 90 μg/kg [14]; bupropion 7.07–46.2 μg/kg, citalopram 131–429 μg/kg, sertraline 788–1993 μg/kg and venlafaxine 66.6–162 μg/kg [41]. The use of sludge of such quality in agriculture could result in soil pollution, which in combination with the possible migration of antidepressants from surface water, may result in their presence in groundwater, like in United States – 56 ng/l of fluoxetine in groundwater [6].

4. Antidepressants in drinking water

The presence of pharmaceuticals in surface and groundwater sources of raw water for drinking water treatment pose a risk of these compounds penetrating to water intended for human consumption. The use of advanced methods of purifying water should result in the

total removal of pharmaceutical impurities. However, an analysis of the finished water shows possible exposure to the effects of antidepressant for drinking water recipients. In the Polish capital, Warsaw, citalopram (1.5 ng/l) and venlafaxine (0.5–1.9 ng/l) were detected in tap water [18]; in USA, risperidone 0.34 ng/l in finished water (Snyder 2008) and fluoxetine 0.64 ng/l with norfluoxetine 0.77 ng/l in tap water (Benotti et al. 2009); in France amitriptyline 1.4 ng/l [43] and in Spain venlafaxine 9 ng/l also in tap water [44].

5. Conclusions

Extensive review of the literature confirms that the pharmaceuticals used, among others, to treat depression commonly occur in the aquatic environment. High, in some cases, concentrations of these compounds in the raw sewage indicate that these drugs are frequently prescribed. The effectiveness of the removal of these compounds during wastewater treatment is not satisfactory due to their continuous emission into the aqueous environment, especially recipient rivers. In addition, a clear tendency to accumulate in sludge and sediments means that using sludge from wastewater treatment in agriculture can pose a risk of soil pollution. This kind of sludge management should be approached with caution and thermal treatment seems advisable prior to using sludge for agricultural purposes.

Quoted analysis results of drinking water confirm that the phenomenon of antidepressant penetration to water intended for human consumption is not the domain of the underdeveloped countries or countries with low-advanced technologies for water treatment. As of today, it has not been clearly confirmed that the consumption of water containing low or very low amounts of antidepressants can affect the organisms of humans, especially people who are allergic to specific pharmaceuticals. Perhaps, there will be no serious allergic reaction, but there can be other unwanted side effects from the continuous supply of allergens. The best solution seems to be further work on the development of new or an improvement of the existing wastewater treatment technology, so that there is no pharmaceuticals emission into the aquatic environment.

References

[1] Alonso S.G., Catala M., Maroto R.R., Rodriguez J.L.G., Miguel A.G., Valvarcel Y., *Pollution by psychoactive pharmaceuticals in the rivers of Madrid metropolitan area (Spain)*, Environment International, Vol. 36, 2010, 195–201.

[2] Arlos M.J., Bragg L.M., Parker W.J., Servos M.R., *Distribution of selected antiandrogens and pharmaceuticals in a highly impacted watershed*, Water Research, Vol. 72, 2015, 40–50.

[3] Baker D.R., Kasprzyk-Hordern B., *Multi-residue analysis of drugs of abuse in wastewater and surface water by solid-phase extraction and liquid chromatography-positive electrospray ionization tandem mass spectrometry*, Journal of Chromatography A, Vol. 1218, 2011, 1620–1631.

[4] Baker D.R., Kasprzyk-Hordern B., *Spatial and temporal occurrence of pharmaceuticals and illicit drugs in the aqueous environment and during wastewater treatment: New developments*, Science of the Total Environment, Vol. 454-455, 2013, 442–456.

[5] Balcerzak W., Rezka P., *Occurrence of anti–cancer drugs in the aquatic environment and efficiency of their removal – the selected issues*, Technical Transactions, vol. 1–Ś/2014, 11–18.

[6] Barnes K.K., Kolpin D.W., Furlong E.T., Zaugg S.D., Meyer M.T., Barber L.B., *A national reconnaissance of pharmaceuticals and other organic wastewater contaminants in the United States-I) Groundwater*, Science of the Total Environment, Vol. 402, 2008, 192–200.

[7] Batt A.L., Kostich M.S., Lazorchak J.M., *Analysis of ecologically relevant pharmaceuticals in wastewater and surface water using selective solid-phase extraction and UPLC/MS/MS*, Analytical Chemistry, Vol. 80, 2008, 5021–5030.

[8] Benotti M.J., Trenholm R.A., Vanderford B.J., Holady J.C., Stanford B.D., Snyder S.A., *Pharmaceuticals and endocrine disrupting compunds in U.S. drinking water*, Environmental Science and Technology, Vol. 43, 2009, 597–603.

[9] Brooks B.W., Chambliss C.K., Stanley J.K., Ramirez A., Banks K.E., Johnson R.D., Lewis R.J., *Determination of select antidepressants in fish from an effluent-dominated stream*, Environmental Toxicology and Chemistry, Vol. 24, 2005, 464–469.

[10] Bueno M.J.M., Aguera A., Gomez M.J., Hernando M.D., Reyes J.F.G., Alba A.R.F., *Application of liquid chromatography/quadrupole-linear ion trap mass spectrometry and time-of-flight mass spectrometry to the determination of pharmaceuticals and related contaminants in wastewater*, Analytical Chemistry, Vol. 79, 2007, 9372–84.

[11] Caracciolo A.B., Topp E., Grenni P., *Pharmaceuticals in the environment: Biodegradation and effects on natural microbial communities. A review*, Journal of Pharmaceutical and Biomedical Analysis, Vol. 106, 2015, 25–36.

[12] Chu S., Metcalfe C.D., *Analysis of paroxetine, fluoxetine and norfluoxetine in fish tissues using pressurized liquid extraction, mixed mode solid phase extraction cleanup and liquid chromatography-tandem mass spectrometry*, Journal of Chromatography A, Vol. 1163, 2007, 112–118.

[13] Drugbank database (http://www.drugbank.ca) – online 27.04.2016.

[14] Evans S.E., Davies P., Lubben A., Kasprzyk-Hordern B., *Determination of chiral pharmaceuticals and illicit drugs in wastewater and sludge using microwave assisted extraction, solid-phase extraction and chiral liquid chromatography coupled with tandem mass spectrometry*, Analytica Chimica Acta, Vol. 882, 2015, 112–126.

[15] Fernandez C., Gonzalez-Doncel M., Pro J., Carbonell G., Tarazona J.V., *Occurrence of pharmaceutically active compounds in surface waters of the Henares-Jarama-Tajo river system (Madrid, Spain) and a potential risk characterization*, Science of the Total Environment, Vol. 408, 2010, 543–551.

[16] Fick J., Soderstrom H., Lindberg R.H., Phan C., Tysklind M., Larsson D.G.J., *Contamination of surface ground and drinking water from pharmaceutical production*, Environmental Toxicology and Chemistry, Vol. 28, 2009, 2522–2527.

[17] Gardner M., Jones V., Comber S., Scrimshaw M.D., Coello-Garcia T., Cartmell E., Lester J., Ellor B., *Performance of UK wastewater treatment works with respect to trace contaminants*, Science of the Total Environment, Vol. 456-457, 2013, 359–369.

[18] Giebułtowicz J., Nałęcz-Jawecki G., *Occurrence of antidepressant residues in the sewage-impacted Vistula and Utrata rivers and in tap water in Warsaw (Poland)*, Ecotoxicology and Environmental Safety, Vol. 104, 2014, 103–109.

[19] Golovko O., Kumar V., Fedorova G., Randak T., Grabic R., *Seasonal changes in antibiotics, antidepressants/psychiatric drugs, antihistamines and lipid regulators in a wastewater treatment plant*, Chemosphere, Vol. 111, 2014, 418–426.

[20] Gonzalez-Rey M., Tapie N., Le Menach K., Devier M.-H., Budzinski H., Bebianno M.J., *Occurrence of pharmaceutical compounds and pesticides in aquatic systems*, Marine Pollution Bulletin, Vol. 96 (1–2), 2015, 384–400.

[21] Gracia-Lor E., Sancho J.V., Serrano R., Hernandez F., *Occurrence and removal of pharmaceuticals in wastewater treatment plants at the Spanish Mediterranean area of Valencia*, Chemosphere, Vol. 87, 2012, 453–462.

[22] Gros M., Petrovic M., Barcelo D., *Tracing pharmaceutical residues of different therapeutic classes in environmental waters by using liquid chromatography/ quadrupole-linear ion trap mass spectrometry and automated library searching*, Analytical Chemistry, Vol. 81, 2009, 898–912.

[23] Huerta-Fontela M., Galceran M.T., Ventura F., *Occurrence and removal of pharmaceuticals and hormones through drinking water treatment*, Water Research, Vol. 45, 2011, 1432–1442.

[24] Kasprzyk-Hordern B., Dinsdale R.M., Guwy A.J., *The removal of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs during wastewater treatment and its impacts on the quality of receiving waters*, Water Research, Vol. 43, 2009, 363–380.

[25] Kim S.D., Cho J., Kim I.S., Vanderford B.J., Snyder S.A., *Occurrence and removal of pharmaceuticals and endocrine disruptors in South Korean surface, drinking and waste waters*, Water Research, Vol. 41, 2007, 1013–1021.

[26] Kolpin D.W., Furlong E.T., Meyer M.T., Thurman E.M., Zaugg S.D., Barber L.B., Buxton H.T., *Pharmaceuticals, hormones and other organic wastewater contaminants in US streams, 1999–2000: a national reconnaissance*, Environmental Science and Technology, Vol. 36, 2002, 1202–1211.

[27] Lajeunesse A., Gagnon C., Sauve S., *Determination of basic antidepressants and their N-desmethyl metabolites in raw sewage and wastewater using solid-phase extraction and liquid chromatography-tandem mass spectrometry*, Analytical Chemistry, Vol. 80, 2008, 5325–5333.

[28] Lajuenesse A., Smyth S.A., Barclay K., Sauve S., Gagnon C., *Distribution of antidepressant residues in wastewater and biosolids following different treatment processes by municipal wastewater treatment plants in Canada*, Water Research, Vol. 46, 2012, 5600–5612.

[29] MacLeod S.L., Sudhir P., Wong C.S., *Stereoisomer analysis of wastewater-derived β-blockers, selective serotonin re-uptake inhibitors and salbutamol by high-performance liquid chromatography-tandem mass spectrometry*, Journal of Chromatography A, Vol. 1170, 2007, 23–33.

[30] Metcalfe C.D., Chu S., Judt C., Li H., Ken D.O., Servos M.R., Andrews D.M., *Antidepressants and their metabolites in municipal wastewater and downstream exposure in an urban watershed*, Environmental Toxicology and Chemistry, Vol. 29, 2010, 79–89.

[31] Metcalfe C.D., Miao X.S., Koenig B.G., Struger J., *Distribution of acidic and neutral drugs in surface waters near sewage treatment plants in the lower Great Lakes, Canada*, Environmental Toxicology and Chemistry, Vol. 22, 2003, 2881–2889.

[32] Mompelat S., Le Bot B., Thomas O., *Occurrence and fate of pharmaceutical products and by-products, from resource to drinking water*, Environment International, Vol. 35, 2009, 803–814.

[33] Petrie B., Barden R., Kasprzyk-Hordern B., *A review on emerging contaminants in wastewaters and the environment: Current knowledge, understudied areas and recommendations for future monitoring*, Water Research, Vol. 72, 2015, 3–27.

[34] Salgado R., Marques R., Noronha J.P., Mexia J.T., Carvalho G., Oehmen A., Reis M.A.M., *Assessing the diurnal variability of pharmaceutical and personal care products in a full-scale activated sludge plant*, Environmental Pollution, Vol. 159, 2011, 2359–2367.

[35] Schlusener M.P., Hardenbicker P., Nilson E., Schulz M., Viergutz C., Ternes T.A., *Occurrence of venlafaxine, other antidepressants and selected metabolites in the Rhine catchment in the face of climate change*, Environmental Pollution, Vol. 196, 2015, 247–256.

[36] Schultz M.M., Furlong E.T., *Trace analysis of antidepressant pharmaceuticals and their select degradates in aquatic matrixes by LC/ESI/MS/MS*, Analytical Chemistry, Vol. 80, 2008, 1756–1762.

[37] Schultz M.M., Furlong E.T., Kolpin D.W., Werner S.L., Schoenfuss H.L., Barber L.B., Blazer V.S., Norris D.O., Vajda A.M., *Antidepressant pharmaceuticals in two U.S. effluent-impacted streams: occurrence and fate in water and sediment and selective uptake in fish neural tissue*, Environmental Science and Technology, Vol. 44, 2010, 1918–1925.

[38] Silva L.J.G., Pereira A.M.P.T., Meisel L.M., Lino C.M., Pena A., *A one-year follow-up analysis of antidepressants in Portuguese wastewaters: Occurrence and fate, seasonal influence and risk assessment*, Science of the Total Environment, Vol. 490, 2014, 279–287.

[39] Sousa M.A., Goncalves C., Cunha E., Hajslova J., Alpendurada M.F., *Cleanup strategies and advantages in the determination of several therapeutic classes of pharmaceuticals in wastewater samples by SPE-LC-MS/MS*, Analytical and Bioanalytical Chemistry, Vol. 399, 2011, 807–822.

[40] Snyder S.A., *Occurrence, treatment and toxicological relevance of EDCs and pharmaceuticals in water*, Ozone: Science & Engineering Vol. 30, 2008, 65–69.

[41] Subedi B., Kannan K., *Occurrence and fate of select psychoactive pharmaceuticals and antihypertensives in two wastewater treatment plants in New York State, USA*, Science of the Total Environment, Vol. 514, 2015, 273–280.

[42] Tarcomnicu I., van Nuijs A.L.N., Simons W., Bervoets L., Blust R., Jorens P.G., Neels H., Covaci A., *Simultaneous determination of 15 top-prescribed pharmaceuticals and their metabolites in influent wastewater by reversed-phase liquid chromatography coupled to tandem mass spectrometry*, Talanta, Vol. 83, 2011, 795–803.

[43] Togola A., Budzinski H., *Multi-residue analysis of pharmaceutical compounds in aqueous samples*, Journal of Chromatography A, Vol. 1177, 2008, 150–158.

[44] Valcarcel Y., Alonso S.G., Rodriguez-Gil J.L., Gil A., Catala M., *Detection of pharmaceutically active compounds in the rivers and tap water of the Madrid*

Region (Spain) and potential ecotoxicological risk, Chemosphere, Vol. 84, 2011, 1336–1348.

[45] Vasskog T., Anderssen T., Pedersen-Bjergaard S., Kallenborn R., Jensen E., *Occurrence of selective serotonin reuptake inhibitors in sewage and receiving waters at Spitsbergen and in Norway*, Journal of Chromatography A, Vol. 1185, 2008, 194–205.

[46] Vasskog T., Berger U., Samuelsen P.J., Kallenborn R., Jensen R., *Selective serotonin reuptake inhibitors in sewage influents and effluents from TromsØ, Norway*, Journal of Chromatography A, Vol. 1115, 2006, 187–195.

[47] Vergeynst L., Haeck A., De Wispelaere P., Van Langenhove H., Demeestere K., *Multi-residue analysis of pharmaceuticals in wastewater by liquid chromatography-magnetic sector mass spectrometry: Method quality assessment and application in a Belgian case study*, Chemosphere, Vol. 119, 2015, S2–S8.

[48] Verlicchi P., Al. Aukidy M., Zambello E., *Occurrence of pharmaceutical compounds in urban wastewater: Removal, mass load and environmental risk after a secondary treatment-A review*, Science of the Total Environment, Vol. 429, 2012, 123–155.

[49] Węgrzyn A., Machura M., Żabczyk S., *Possibilities for Removal of Contrast Agents from Wastewater*, Ochrona Srodowiska, Vol. 37(1), 2015, 55–63.

[50] Writer J.H., Ferrer I., Barber L.B., Thurman E.M., *Widespread occurrence of neuro-active pharmaceuticals and metabolites in 24 Minnesota rivers and wastewaters*, Science of the Total Environment, Vol. 461–462, 2013, 519–527.

[51] Wu C., Witter J.D., Spongberg A.L., Czajkowski K.P., *Occurrence of selected pharmaceuticals in an agricultural landscape, western Lake Erie basin*, Water Research, Vol. 43, 2009, 3407–3416.

[52] Yuan S., Jiang X., Xia X., Zhang H., Zheng S., *Detection, occurrence and fate of 22 psychiatric pharmaceuticals in psychiatric hospital and municipal wastewater treatment plants in Beijing*, Chemosphere, Vol. 90, 2013, 2520–2525.

[53] Zejc A., Gorczyca M., *Chemia Leków*, Warszawa, PZWL, 2009.

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