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PHARMACEUTICALS IN WATER AND WASTEWATER – OVERVIEW

FARMACEUTYKI W WODACH I ŚCIEKACH

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Abstract

The paper presents concentrations of pharmaceuticals in surface water and sewage. Special attention was paid to the content of estrogens in municipal sewage and the method of their disposal. Concentrations of various pharmaceuticals in raw and treated wastewater were compared and the pharmaceuticals in different countries and waters were presented in tables. The most frequently identified drugs in sewage are sex hormones (etradiol, ester, ethinylestradiol, 17 β-estradiol) and the antiepileptic drug Carbamazepine. These drugs are difficult to remove from water and therefore appropriate treatment processes are used, such as: adsorption on active carbon, UV irradiation, etc. Contamination of water with pharmaceuticals has a negative impact on the development of aquatic organisms and can lead to serious human health problems.

Keywords: surface waters, pharmaceuticals, estrogens, wastewater, pollution

Streszczenie

W pracy przedstawiono stężenia farmaceutyków w wodach powierzchniowych oraz ściekach. Szczególną uwagę skupiono na zawartości estrogenów w ściekach komunalnych oraz na sposobie ich usuwania. Porównano stężenia różnych farmaceutyków w ściekach surowych oraz ściekach oczyszczonych, a także zostały przedstawione tabelarycznie farmaceutyki występujące w różnych państwach oraz wodach. Najczęściej identyfikowanymi lekami w ściekach są: hormony płciowe (etradiol, estron, etinyloestradiol, 17 β-estradiol) oraz lek przeciwpadaczkowy – Karbamazepina. Leki te są ciężko usuwalne z wód, dlatego też stosuje się odpowiednie procesy ich oczyszczania, takie jak: adsorpcje na węglu aktywnym, naświetlanie promieniami UV itp. Zanieczyszczenia wód farmaceutykami wpływa negatywnie na rozwój organizmów wodnych, a także może prowadzić do poważnych problemów zdrowia ludzkiego.

Słowa kluczowe: wody powierzchniowe, farmaceutyki, estrogeny, ścieki, zanieczyszczenia

1. INTRODUCTION

The pharmaceutical industry is an ever-growing economic sector worldwide. Due to the spread of various diseases, infections and infections both in humans and animals, the most commonly prescribed pharmaceuticals are antibiotics, anti-inflammatory and antiepileptic drugs as well as hormonal agents, which have a huge impact on the quality of drinking water, human health but also the development of aquatic organisms [1]. The antibiotics prescribed worldwide every year exceed 12.000 Mg, of which 65% are used in the treatment, 29% in veterinary medicine and 6% are used in veterinary medicine as growth inhibitors [2]. The consumed drugs undergo the metabolic process in the body. The metabolism of drugs, however, never occurs in 100%, thus the free and metabolized form is expelled from the body and then seeped into sewage. Moreover, a big problem is the introduction of overdue, poorly disposed drugs into sewage, which are simply thrown into the sewage system [2]. At present, sewage treatment plants are not obliged to check the effectiveness of treatment for pharmaceuticals. Through studies carried out over the last few years in various countries over 80 different pharmaceuticals present in the aquatic environment were found. The exposure of organisms even to low concentrations of drugs may cause endocrine disorders, resistance to pathogens and toxic effects [3].

This article presents the role of pharmaceuticals in the aquatic environment and the detailed influence of estrogens on water quality and human health.

2. SOURCE OF ESTROGEN IN MUNICIPAL WASTEWATER

Oestrogen is an important problem of water environment pollution. They deserve special attention, as only a small number of people are aware of the huge impact they have on human health and functioning. Estrogens are steroid female sex hormones. For a long time this aspect has been ignored because estrogens are natural substances formed in the human body, however they are divided into natural and synthetic. The first group includes progesterone, testosterone, ester, oestradiol, phytoestrogens; synthetic hormones are components of pharmaceutical preparations and may include gestagens, ethinylestradiol, diethylstylbestrol [4]. In recent years, estrogens are more and more often used in veterinary animal treatment and hormone replacement therapy, and most of all estrogens can be found in contraception, which is very popular nowadays [5]. The hormones taken by humans are excreted from the body through urine, then they are introduced into the aquatic environment by discharging raw and treated sewage [6]. Estrogens are divided into three types: ester (E1), estradiol (E2), estriol (E3) and the natural hormone produced during pregnancy, estrol (E4) [4]. The content of this hormone in wastewater depends on the population of people living in a given area as well as the number of women in the reproductive and menopausal period and pregnant women. A pregnant woman's organism produces even 120 times more hormone 17-estradiol than a woman's organism during the menopause [3]. Table 1 presents the mean daily production of estrogens by humans.

The most hormones are produced by pregnant women, where the level of ester during the day is 787 µg/day and estriol is almost 10 thousand. Considering that the pregnancy lasts 9 months it is a lot and even though these are natural hormones they can adversely affect water quality. In contrast, women in the menopausal period are in second place but produce much lower hormone values, however, it should be noted that estriol, which is 90.70 µg/day and 59.20 µg/day 17 β-estradiol prevails. Subsequent groups produce hormones in the range 0 to 10 µg/day except for women in menstruation where they produce 17.40 µg/day oestriol.

Table 1. Average steroid estrogen excretion by humans (per person) µg/day [7]

	Estrone, µg/day	17 β-estradiol, µg/day	Estriol, µg/day
Pregnant women	787	277	9850
Menopausal, with HRT	31.50	59.20	90.70
Menstruating woman	9.32	6.14	17.40
Women	7.00	2.40	4.40
Menstruating females	3.50	8.00	4.80
Adult male	3.50	1.83	3.21
Menopausal, no HRT	2.93	1.49	3.90
Menopausal females	2.30	4.00	1.00
Males	1.60	3.90	1.50
Female child	0.60	2.50	0.918

Oestrogens in water are usually detected in low concentrations, but they can nevertheless affect the proper functioning of organisms, causing quite serious disturbances in the development of organisms and reproductive processes such as, for example, reduced fertility in animals or development of testicular cancer [6].

Steroid sex hormones can be eliminated from sewage by adsorption on the activated sludge, ozonization, ozonization/H_2O_2 and by using biological filters [8]. The method of elimination is chosen according to what hormone and to what extent we want to remove it from the sewage. For example, using the adsorption method on activated sludge, about 70-90% of ester can be removed from sewage [1].

Table 2 presents the hormone content in Polish rivers. The analysis of water samples taken from these rivers shows that ester is present in two rivers with concentrations of 1.3 µg/dm^3 and 1.1 µg/dm^3, whereas in the Vistula River estradiol with concentration of 1.3 µg/dm^3 was detected. The remaining oestrogens entered the amount below 1 ng/l, i.e. at the method determination limit in the range of 0.5÷1 µg/dm^3 [3].

Table 2. Hormone content in Polish rivers [9]

Polish rivers	Hormone content, μg/dm^3		
	estron	estradiol	etinyloestradiol
Odra	1.3	gom.	gom.
Kanał Gliwicki	1.1	gom.	gom.
Wisła	gom.	1.3	gom.

gom. – limit of determination of the method

Concentrations of these hormones in Polish rivers are relatively low compared to other countries such as Germany, Italy, the Czech Republic or Japan, where hormone concentrations in surface waters are several times higher than in Poland, as shown in Table 3.

Table 3. Occurrence and concentration of hormones in water [10]

Hormone	Occurrence	Concentration, μg/dm^3	Country
Estradiol	surface waters	0.0006	Germany
	drinking water	0.0003	Germany
	surface waters	0.0021	Japan
Estron	surface waters	0.0007	Germany
	drinking water	0.0004	Germany
	surface waters	0.0015	Italy
Etinyloestradiol	surface waters	0.0001÷0.0051	Germany
	surface waters	0.00004	Italy
	surface waters	0.0046	Czech Republic
17 β-estradiol	drinking water	0.0003÷0.0021	Germany

Oestrogen concentrations in water reach values below 1 μg/dm^3, but are nevertheless of great concern. Low estrogen content in water is caused by accumulation of compounds in bottom sediments, which may cause a secondary source of water supply with steroid hormones. The following oestrogen values at levels have been recorded in bottom sediments: E1-1.5÷33.0 (11.43) μg/kg and E2-0.71÷16.0 (5.43) μg/kg, while as far as ethinylestradiol EE2-8.43 μg/kg is concerned. The accumulation of estrogenic compounds in bottom sediments may be caused by their physicochemical composition and specific local conditions [11]. Identification of the decomposition of these compounds in water is not easy as their half-life in bottom sediments and water is about 2÷6 days with simultaneous observation of changes in the water environment under the influence of microorganisms [12]. In adipose tissues of aquatic organisms, overestimation of estrogen levels is observed. This level is expressed on the basis of the logarithm of the so-called bioaccumulation factor as the ratio of compounds in aquatic organisms to their content in water. An example is fish, where their level ranges from 2.22 (E1) to 2.83 (EE2). In this case, we can say that this is a growing threat to the aquatic environment [13].

After the analysis of samples in water in Poland, the presence of hormonal compounds was detected, which may contribute to the degradation of the aquatic environment. Moreover, it was shown that they may have a negative impact on the development of animal organisms as well as on human reproductive processes, especially on the foetus, which can be observed at a later stage of human maturation. Therefore, the level of estrogens in water should be constantly controlled and the purification process should ensure complete removal of these compounds [5].

3. OESTROGEN REMOVAL FROM WASTE WATER

According to various sources of hormonal pollution can be removed from the wastewater by accumulation on suspended solids, however, the degree of treatment is not very effective and therefore ancillary processes are used. These include: active carbon adsorption, UV irradiation, advanced catalytic oxidation and the use of membrane reactors. The Table 4 presents data from the course of wastewater treatment in terms of estrogen presence [3].

Table 4. Concentration of hormones at the input and output of the plant and the degree of purification [3]

Hormone	Concentration in raw sewage, μg/dm^3	Concentration in treated wastewater, μg/dm^3	Degree of purification, %
Estradiol	0.003	0.0004	85
Estron	0.0024	0.0044	0

Aerobic microorganisms can convert one estrogen into another as shown in Figure 1. For example, some microorganisms (e.g. nitrifying bacteria) can convert E1 to E3 and others decompose E1, E2 and EE2 (e.g. Novosphingobium sp. in active sediment). Moreover, synthetic EE2 can be converted to E1 by Sphingobacterium sp [14]. There are also many strains of anaerobic bacteria, which can convert one estrogen into another. For example, in lake water and sediments under anaerobic conditions, E2 was chemically converted to E1 under methanogenic,

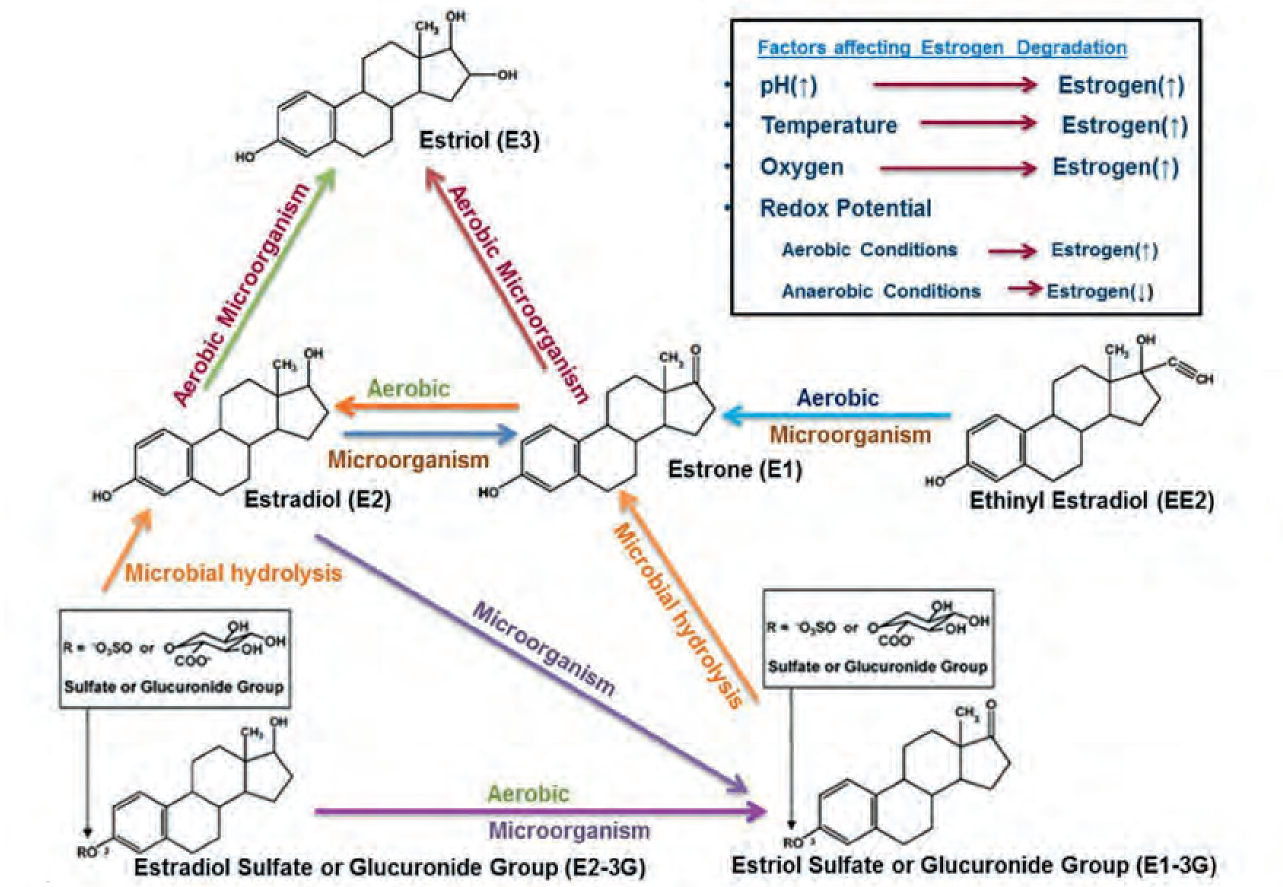

Fig. 1. Interconversion pathways of natural and synthetic estrogens [7]

sulphate, ferric and nitrate reducing conditions; however, no degradation of EE2 was observed [15].

4. CONTENT OF OTHER PHARMACEUTICALS IN AN AQUATIC ENVIRONMENT

Estrogens are not the only pharmaceuticals that pollute the water environment. Carbamazepine should be mentioned here, it is the most commonly used antiepileptic drug, which is absorbed very slowly from the gastrointestinal tract, while the maximum concentration is observed from 4÷6 days. This drug is excreted in urine, earlier metabolism takes place in the liver. Carbamazepine is usually detected in surface water, although it is also found in drinking water. This drug is difficult to remove from waste water during treatment processes and is resistant to biodegradation processes. To remove this drug from the waste water, ozone treatment can be used, which treats the waste water from carbamazepine up to 90%, another process is adsorption on active carbon, where the effectiveness of removing this drug is up to 90%, and phytolysis is an equally effective process. The Table 5 presents the occurrence and concentration of carbamazepine in comparison to other compact pharmaceuticals in waters of different countries [3].

Table 5. Presence and concentration of pharmaceuticals in water [3]

Substance	Presence	Concentration, µg/dm^3	Country
Carbamazepine	surface waters	0.025÷1.07	Germany
	drinking water	0.258	USA
	surface waters	0.001÷0.009	United Kingdom
Diazepam	surface waters	0.88	Germany
Clofiberic acid	surface waters	below 0.45	Germany
	drinking water	0.07÷0.27	Italy
Bezafibrat	drinking water	0.0027	Germany
Metoprolol	surface waters	0.05÷0.15	Poland
Propanolol	surface waters	0.005÷0.007	United Kingdom
	surface waters	0.015÷0.178	Spain
Athensolol	surface waters	0.318÷6.167	Spain

Compared to other pharmaceuticals, carbamazepine has a fairly high concentration, but not the highest. In Germany, the concentration of this drug in water can reach up to 1.07 μg/dm^3 in surface water, while in drinking water in the USA the concentration is much lower at 0.258 μg/dm^3. Nevertheless, this drug has an adverse effect on the aquatic environment and the organisms living in it.

Table 6 shows the concentration at the exit and entry of the pharmaceuticals in question. Carbamazepine is removed from wastewater only 8%, a very small percentage compared to Bezafibrate, which has a treatment rate of 91%, while clofiberic acid is not removed at all in wastewater treatment processes.

Table 6. Concentrations at the input and output of the plant and the degree of purification [3]

Medicine	Concentration in raw sewage, μg/dm^3	Concentration in treated wastewater, μg/dm^3	Degree of purification, %
Carbamazepine	1.78	1.63	8
Bezafibrat	2.6	0.24	91
Clofiberic acid	0.15÷0.25	0.15÷0.25	0

Carbamazepine contributes to the growth inhibition of green algae of the species S. capricornutum in concentrations from 2.1 to 20 000 mg/dm^3, whereas for D. magna EC50 = 157 000 mg/dm^3 and for D. subspicatus EC50 = 85 000 mg/dm^3 [9].

In addition to the above mentioned in the table of pharmaceuticals, surface waters have high levels of caffeine, which is found in coffee, energy drinks, medicines and supplements. However, it was found that this substance does not pose a risk to the human body. In contrast, the concentrations of drugs such as cocaine and matamfetamine iecstasy detected in water have very strong pharmacological effects and may be toxic to aquatic organisms [3].

There are many ways to remove or minimize pharmaceuticals in water and wastewater. These include biological methods, membrane processes using bioreactors, the use of active carbon, UV radiation, chlorination and ozone. According to research on the effectiveness of pharmaceutical removal, only about one fifth of the compounds are removed in a classic two-stage treatment plant. The removal of carbamazapine and diazepam in 85% can be achieved by using powdered activated carbon in a membrane bioreactor to absorb pharmaceuticals from urban wastewater.

5. SUMMARY AND CONCLUSIONS

Pollution of water and wastewater with various types of pharmaceuticals creates quite serious problems in the aquatic environment, however, Polish and European law has so far not set a limit for water pollution with drugs and hormones. In Europe, on 31 January 2012, the European Commission established the addition of 15 chemical compounds to the list of 33 polluting compounds whose concentration should be monitored in EU waters. The added compounds include diclofenac, ethinylestradiol, 17 β-estradiol [16].

Pharmaceuticals contained in water adversely affect aquatic organisms, and the presence of drugs in drinking water can lead to serious problems for human health, infants and young children. Also, great attention should be paid to the content of estrogens in water, as they may contribute to the incidence of pedestrian and testicular cancer [1].

However, there are serious gaps in our knowledge of estrogen levels in the environment, and there is a need to call for more data on many other sampling sites worldwide. Among the available data, synthetic oestrogen, ethinylestradiol, is more persistent in the environment than natural oestrogens and may be of greater concern for the environment. Oestrogens should be listed as a toxic organic pollutant, which is confirmed by several studies.

Oestrogen contamination is becoming a significant environmental problem and has harmful effects on the growth and development of humans, animals and plants at significant levels. Attention to this issue is essential and requires further in-depth research. The issue of estrogen in waste water will continue in subsequent publications, after appropriate research by the authors.

REFERENCES

[1] Szymonik A., Lach J., *Obecność farmaceutyków w wodach powierzchniowych i przeznaczonych do spożycia,* ECOpole'13 Conference (23-26.10.2013), Jarnołtówek, Poland.

[2] Wanot B., Domagała M., *Antybiotyki w wodach -źródła zanieczyszczeń, degradacja antybiotyków,* Technologia Wody, 2019, Vol 3 (65), pp. 44-47.

[3] Wanot B., Domagała M., *Zanieczyszczenie wody hormonami i innymi farmaceutykami oraz ich degradacja,* Technologia Wody, 2019, Vol 4 (66), pp. 30-34.

[4] https://parenting.pl/estrogen-charakterystyka-poziomy-wskazania-do-badania-opis-badania-wysoki-i-niski-poziom [dostęp: 13.04.2020].

[5] Hanselman, T.A., Graetz, D.A., Wilkie, A.C., 2003. Manure-borne estrogens as potential en-vironmental contaminants: a review. Environ. Sci. Technol. 37, 5471–5478.

[6] Dudziak M., Luks-Betlej K., *Ocena obecności estrogenów –steroidowych hormonów płciowych w wybranych wodach rzecznych w Polsce*, Ochrona Środowiska, Vol. 1, 2004.

[7] Muhammad A., Xiaoming S., Yuanyuan W., Dennis F., Yuesuo Y., *Environmental impact of estrogens on human, animal and plant life: A critical review*, Environment International, 99, 2017, pp. 107–119.

[8] Avberšek, M., Šömen, J., Heath, E., *Dynamics of steroid estrogen daily concentra-tions in hospital effluent and connected waste water treatment plant.* J. Environ. Monit. 13,2-11, pp. 2221–2226.

[9] Włodarczyk-Makuła M., *Wybrane Związki Endokrynnie aktywne EDC w środowisku wodnym.* LAB Laboratoria, Aparatura, Badania, 2014, 19, pp. 20-25.

[10] Czech B., *Usuwanie farmaceutyków z wód i ścieków z wykorzystaniem metod adsorpcyjnych i fotokatalitycznych. Adsorbenty i katalizatory: wybrane technologie, a środowisko*, Uniwersytet Rzeszowski, 2012, pp. 443-452.

[11] Pessoa, G.P., de Souza, N.C., Vidal, C.B., Alves, J.A., Firmino, P.I.M., Nascimento, R.F., dos Santos, A.B., *Occurrence and removal of estrogens in Brazilian wastewater treatment plants.* Sci. Total Environ. 490, 2014, pp. 288–295.

[12] Arnon, S., Dahan, O., Elhanany, S., Cohen, K., Pankratov, I., Gross, A., Ronen, Z., Baram, S., Shore, L.S., *Transport of testosterone and estrogen from dairy-farm waste la-goons to groundwater.* Environ. Sci. Technol. 42, 2008, pp. 5521–5526.

[13] Czajka, C.P., Londry, K.L., A*naerobic biotransformation of estrogens.* Sci. Total Envi-ron. 367, 2006, pp. 932–941.

[14] Goeppert, N., Dror, I., Berkowitz, B., *Detection, fate and transport of estrogen family hormones in soil.* Chemosphere 95, 2014, pp. 336–345.

[15] Ma C., Qin D., Sun Q., Zhang F., Liu H., Yu C.-P., 2016. *Removal of environmental estro-gens by bacterial cell immobilization technique.* Chemosphere 144, 2016, pp. 607–614.

[16] Szymonik A., Lach J., *Zagrożenie środowiska wodnego obecnością środków farmaceutycznych.* Inżynieria i Ochrona Środowiska, Vol. 15, 3, 2012, pp. 249-263.

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