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PHENOLIC COMPOUNDS IN THE ENVIRONMENT - OCCURRENCE AND EFFECT ON LIVING ORGANISMS

ZWIĄZKI FENOLOWE W ŚRODOWISKU - WYSTĘPOWANIE I WPŁYW NA ORGANIZMY ŻYWE

Abstract: Many of organic compounds used as preservatives in cosmetics, drugs and foods have adverse impact on human and animal health. In recent years, special attention has been paid on substances which interferes with endocrine system of living organisms. The group of this substances is called endocrine disrupting compounds (EDCs) and include wide range of chemicals *eg* phenolic compounds (parabens, phenylphenols, alkylphenols, bisphenol A etc.). EDCs can mimic or block the action of natural hormones causing changes mainly in the reproductive and immune systems, as well tumours formation. Similar to the natural hormones, EDCs are biologically active at very low concentration (pg/g - ng/g), it is the level comparable with their presence in wastewater effluents. Wastewater treatment plants using conventional treatment methods are not effective in removing most of EDCs, therefore, these compounds are present in the environment for example in marine and riverine sediments and surface water, which is often a drinking water reservoir.

Keywords: phenolic compounds, endocrine disrupting compounds, EDCs, parabens, alkylphenols, bisphenol A, phenylphenols

Introduction

In recent years, there has been growing concern about occurrence of commonly used preservatives in aquatic environment and their effect on human and animal health. Special attention has been paid on substances which interfere with endocrine system of living organisms. Group of these compounds is called as *endocrine disrupting compounds* (EDCs). The US Environmental Protection Agency defines EDCs as "an exogenous agent that interferes with the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development, and/or behavior" [1]. The list of organic contaminants showing reproductive and endocrine disrupting effects contains: organohalogens, pesticides, phthalates, synthetic steroids, alkylphenols and phytoestrogens [2].

The first cases of the adverse impact of EDCs on living organisms have been observed in the second half of the 20th century, when the declines in seal population occurred in the Baltic Sea and western part of the Wadden Sea were take place. Both of these areas were strongly contaminated with organochlorines. In the next decades the declines in population of many birds species, feminization and intersexuality in fish as well changes in the immune system at marine mammals were reported. EDCs have got ability to bioacumulation and bioconcentration in the food chain, therefore, also people are exposed to their adverse effects. These compounds may cause disturbance in male and female reproduction system *eg* formation of breast and prostate tumours and the endometriosis [3, 4].

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The first action on the issue of EDCs taken by European Union was the workshop "The impact of endocrine disrupters on human health and wildlife", that was held on 2-4 December 1996 in Weybridge. During this workshop a definition of endocrine disrupting compounds was endorsed and the several groups of chemicals which show endocrine properties were identified. Two major group of substances: natural hormones (progesterone, testosterone, phytoestrogens) and synthetically produced hormones (oral contraceptives and synthetic chemicals designed for industrial use) were identified as the most important chemicals causing endocrine disruption [2].

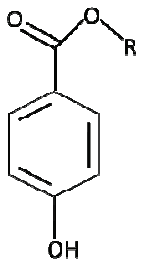
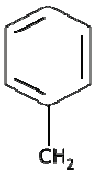
This work is focused on the occurrence of selected phenolic endocrine disrupting compounds in the environment and their effect on living organisms.

Parabens

Parabens (methyl-, propyl-, ethyl-, butylparaben etc.), alkyl esters of *p*-hydroxybenzoic acid (Tab. 1), are commonly used as preservatives in cosmetics, food, pharmaceutical products and personal care products. With the increase of the chain length of the ester groups, antioxidant and antimicrobial activity of parabens increases, while their solubility in water decreases, therefore esters with shorter chain are usually employed [5, 6]. Analysis of cosmetics on the Danish market showed the presence of parabens in 77% of the products at concentration from 0.01 to 0.87%. The maximum concentrations of metyl-, propyl-, etyl-, butyl- and benzylparaben were equal to 0.32, 0.32, 0.19, 0.07 and 0.32%, respectively [7]. Reports of adverse effects of parabens on living organisms caused that use of this preservatives has declined significantly over time. The European Economic Community (EEC) Directive permits the use of parabens in cosmetics with a maximum concentration for each one of 0.4% w/w and a total maximum concentration of 0.8% w/w [8].

Table 1

Chemical structures of selected parabens

Core structure	R	Name
	CH_3	Methylparaben
	CH_2CH_3	Ethylparaben
	$CH_2CH_2CH_2CH_3$	Butylparaben
		Benzylparaben

Widespread use of products containing parabens results in their occurrence in the environment. Many studies have reported the presence of parabens in aquatic environment. These compounds were found in the influent and effluent wastewaters of *Waste Water Treatment Plants* (WWTP) and river waters [9]. The effluents and wastewaters from hospitals and industries (textile manufactures, tanneries, etc.) are considered as the main sources of parabens in the aquatic environment. Parabens concentration in Swedish wastewater is approximately equal to 1 μg/dm^3 [10]. According to the literature, total

concentrations of parabens in river waters are diversified from 6 ng/dm^3 [11] to 3204 ng/dm^3 [12], for Glatt River (Switzerland) and Pearl River (China), respectively.

Several *in vivo* and *in vitro* studies have shown that these compounds can mimic the action of natural estrogens such as 17β-estradiol, by binding to the estrogen receptors and influencing the expression of estrogen-dependent genes. The estrogenic activity of parabens increases with the length of alkyl chain [13, 14]. Exposure to *n*-butyl-, *iso*-butyl- and benzylparaben causes increases uterine weights in immature mice [15, 16]. Rodent exposure to butylparaben and propylparaben adversely affected synthesis of the testosterone and male reproductive function [17, 18]. Data on the effects of parabens on human health are limited, and their toxic effects are mostly unknown. Based on the available literature it can be affirm that parabens have got ability to bioaccumulation in the human body. The presence of parabens was confirmed in milk [19], serum [20] and in placental tissue [21]. Moreover, these compounds have been detected in human breast tumor tissue at the ng/g level [22], which may suggest that the use of parabens in deodorants and antiperspirants can increase the incidence of breast cancer.

Alkylphenols

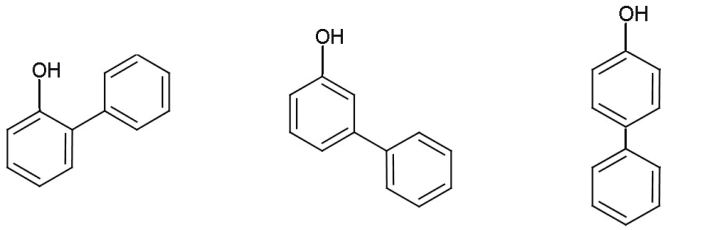
Alkylphenols (octylphenols, nonylphenols etc.) are the main components of *alkylphenol ethoxylates* (APEs), which are nonionic surfactants commonly used as detergents, emulsifiers, wetting agents, plasticizers, UV stabilizers in the herbicides, paints, industrial cleaning and degreasing agents. *Alkylphenols* (APs) are also used as antioxidant and stabilizer of plastics by some industries. The most commercially important alkylphenols are *nonylphenol* (NP) and *octylphenol* (OP) which occur in different forms or isomers [23].

APEs are degraded into APs in wastewater treatment plants, therefore municipal and industrial wastewater treatment plants are main sources of alkylphenols in surface water. The surface water samples contained nonylphenol and octylphenol at concentration equal to 26.4 and 0.68 μg/dm^3 [23], respectively. These compounds were widely detected in sediments [23], as well as in drinking water and food [24]. Amiridou and Voutsa confirmed [25] presence of APs in bottled water. Studies performed on a group of Italians confirmed the presence of seven alkylphenol compounds in the subcutaneous adipose tissue. Nonylphenol was the compound found at the highest level [26]. These compounds were also detected in human milk [27].

APs are persistent environmental pollutants which have been described by European Commission as endocrine disruptors and several of them have been included in the priority list of 33 substances of the *Water Framework European Directive* (WFD) 2000/60/EC [28]. They mimic the action of natural hormones and may interfere with estrogen functions at various reproductive and developmental stages. The highest affinity to the estrogen receptors have been exhibited by mono-substituted alkylphenols with moderate (C4-C6) and long (C8 and C12) alkyl chain length. However, substitution with multiple alkyl groups or presence of substituents in *ortho*- and *meta*- position or lack of hydroxyl group on the benzene ring reduce the binding affinity. APs are known to bioaccumulate and cause cytotoxicity and acute toxicity to aquatic organisms. The cytotoxicity of these compounds increased with their hydrophobicity [29].

Phenylphenols

Phenylphenols (*ortho*-, *meta*- and *para*-phenylphenol), hydroxylated derivates of biphenyl (Fig. 1), have got antimicrobial activity in broad spectrum (efficiency as biocide against bacteria, mold and yeast). *ortho*-phenylphenol has been widely used as a preservative agent for citrus fruits and vegetables, as well in the cosmetics, leather, textile and paper industry. It is also used as a disinfectant in households and hospitals. Multitude of products contain this compound, but the producers uses the trade names of *o*-PP, for example Chemcide, Cotane, Dowicide, Nipacide, among others [30]. *o*-PP is a by-product of the synthesis of phenols and in the microbial desulfurization of dibenzothiophene in fossil fuels [31]. *Meta*- and *para*-phenylphenol are components of the most popular disinfectants used in households [32].



orto-fenylofenol *meta*-fenylofenol *para*-fenylofenol

Fig. 1. The molecular structures of phenylphenols

Wide range of application phenylphenols caused their presence in many parts of the environment. These chemicals were detected in surface water, riverine sediments, sewage sludge [12, 33] and in marine sediments [34]. Studies have shown that phenylphenols are also present in indoor air and dust [35]. Besides, *o*-PP was detected in canned beer and canned soft drinks in United States and Germany. The performed studies indicated on the *o*-PP presence in 49 samples of soft drinks among 55 analyzed samples, at the concentration level of μg/dm^3. The highest concentration *o*-PP was found in a lemon flavored cola, equaled 16.9 μg/dm^3 [30]. Phenylphenols can bioaccumulate in aquatic organisms, *eg o*-PP was detected in bile of deep-sea fish at the concentration ranged from 8.4 to 192.7 ng/cm^3 [36].

It was reported that phenylphenols affects the endocrine system, showing estrogenic and antiandrogenic activity. Estrogenicity of phenylphenols strongly depends on the position of the hydroxyl function and increased in the following order: *ortho*- < *meta*- < *para*-phenylphenol [32]. Paris et al observed also that androgen receptors antagonist activity of *ortho*-phenylphenol is 3-4-fold smaller than *meta*- and *para*-phenylphenol [32]. Phenylphenols have got carcinogenic and genotoxic properties [37, 38].

Bisphenol A

Bisphenol A (BPA), 4,4'-dihydroxy-2,2-diphenylpropane (Fig. 2), is a chemical used as stabilizing material for the production of polycarbonate, epoxy resins, unsaturated polyesters resins and polyacrylate and polysulphone resins. Epoxy resins are used in food contact surface lacquer coatings for cans, and in protective coatings and finishes. BPA is

also used in resin-based dental sealants and bonding agents [39]. The *specific migration limit* (SML) for BPA from plastic materials to food of 600 ng/g was established by European Commission [40].

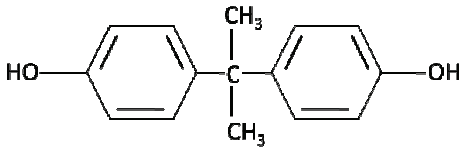


Fig. 2. The molecular structure of BPA

BPA was found in river water at the concentrations ranged from 0.06 to 0.33 μg/dm^3 [39]. Significant levels of this compound was detected in fish and shellfish. Averaging concentrations of BPA in crabs and squid were equalled to 213 and 118 μg/kg, respectively [41]. It was also detected in human blood [20].

BPA is an endocrine disruptor, showing estrogenic and antiandrogenic activity leading to the interference of reproductive system. BPA is able to activate estrogen receptors at concentration lower than 1 μM [32]. This compound has been also classified as carcinogenic and mutagenic, producing adverse effects on animal, aquatic life and human health [40]. Broad applications of BPA caused this compound can enter into human body by ingestion or adsorption. Exposure to BPA during the early stage of pregnancy can seriously affect the embryonic development and maintenance of pregnancy. Exposure fetuses, infants and children to BPA may effect on development of the prostate gland and brain and behavioral effects [42].

Conclusions

Widespread application of phenolic compounds has caused the spread of these chemicals in the environment. They have been detected in wastewater influents and effluents, surface waters, and in riverine and marine sediments. Wastewater treatment plants using conventional treatment methods are not effective in removing most of these compounds, therefore, they are considered as the main sources of phenolic compounds in surface water.

Many of phenolic derivatives (parabens, alkylphenols, bisphenol A, phenylphenols etc.) interferes with endocrine system of living organisms, causing disturbance in male and female reproduction system *eg* formation of breast and prostate tumours and the endometriosis. Due to the ability of EDCs to bioaccumulation and bioconcentration in the food chain also people are exposed to their adverse effects. Therefore, in order to limit human exposure to phenolic compounds, releasing these chemicals into environment should be definitely reduced.

References

[1] United States Environmental Protection Agency, Special report on environmental endocrine disruption: an effects assessment and analysis EPA/630/R-96/012 1997.

[2] Petrović M, Eljarrat E, López de Alda MJ, Barceló D. Trends Anal Chem. 2001;20:637-648. DOI: 10.1016/S0165-9936(01)00118-2.

[3] Taylor MR, Harrison PTC. Chemosphere. 1999;39:1237-1248. DOI: 10.1016/S0045-6535(99)00191-5.
[4] Esplugas S, Bila DM, Gustavo L, Krause T, Dezotti M. J Hazard Mater. 2007;149:631-642. DOI: 10.1016/j.jhazmat.2007.07.073.
[5] Korotkova EI, Avramchik OA, Angelov TM, Karbainov YA. Electrochim Acta. 2005;51:324-332. DOI: 10.1016/j.electacta.2005.04.031.
[6] Giordano F, Bettini R, Donini C, Gazzaniga A, Caira MR, Zhang GGZ, Grant DJW. J Pharm Sci. 1999;88:1210-1216. DOI: 10.1021/js9900452.
[7] Rastogi SC, Schouten A, Dekruijf N, Weijland JW. Contact Dermatitis. 1995;32:28-30. DOI: 10.1111/j.1600-0536.1995.tb00836.x.
[8] Janjua NR, Mortensten GK, Andersson AM, Kongshoj B, Skakkebaek NE, Wulf HC. Environ Sci Technol. 2007;41:5564-5570. DOI: 10.1021/es0628755.
[9] Regueiro J, Becerril E, Garcia-Jares C, Lompart M. J Chromatogr A. 2009;1216:4693-4702. DOI: 10.1016/j.chroma.2009.04.025.
[10] Paxeus N. Water Res. 1996;30:1115-22. DOI: 10.1016/0043-1354(95)00278-2.
[11] Jonkers N, Kohler HP, Dammshauser A, Giger W. Environ Pollut. 2009;157:714-723. DOI: 10.1016/j.envpol.2008.11.029.
[12] Peng X, Yu Y, Tang C, Tan J, Huang Q, Wang Z. Sci Total Environ. 2008;397:158-166. DOI: 10.1016/j.scitotenv.2008.02.059.
[13] Lemini C, Hernández A, Jaimez R, Franco Y, Avila ME, Castell A. Toxicol Ind Health. 2004;20:123-132. DOI: 10.1191/0748233704th202oa.
[14] Okubo T, Yokoyama Y, Kano K, Kano I. Food Chem Toxicol. 2001;39:1225-1232. DOI: 10.1016/S0278-6915(01)00073-4.
[15] Darbre PD, Byford JR, Shaw LE, Horton RA, Pope GS, Sauer MJ. J Appl Toxicol. 2002;22:219-226. DOI: 10.1002/jat.860.
[16] Darbre PD, Byford JR, Shaw LE, Hall S, Coldham NG, Pope GS. J Appl Toxicol. 2003;23:43-51. DOI: 10.1002/jat.886.
[17] Oishi S. Arch Toxicol. 2002;76:423-429. DOI: 10.1007/s00204-002-0360-8.
[18] Oishi S. Food Chem Toxcol. 2002;40:1807-1813. DOI: 10.1016/S0278-6915(02)00204-1.
[19] Ye X, Bishop AM, Needham LL, Calafat AM. Anal Chim Acta. 2008;622:150-156. DOI: 10.1016/j.aca.2008.05.068.
[20] Ye X, Wong LY, Jia LT, Needham LL, Calafat AM. Environ Int. 2009;35:1160-1163. DOI: 10.1016/j.envint.2009.07.011.
[21] Jiménez-Díaz I, Vela-Soria F, Zafra-Gómez A, Navalón A, Ballesteros O, Navea N, Fernández MF, Olea N, Vílchez JL. Talanta. 2011;84:702-709. DOI: 10.1016/j.talanta.2011.01.075.
[22] Darbre PD, Aljarrah A, Miller WR, Coldham NG, Sauer MJ, Pope GS. J Appl Toxicol. 2004;24:5-13. DOI: 10.1002/jat.958.
[23] Zhang Z, Wu Z, He L. Chemosphere. 2008;73:859-863. DOI: 10.1016/j.chemosphere.2008.05.016.
[24] Guenther K, Heinke V, Thiele B, Kleist E, Prast H, Raecker T. Environ Sci Technol. 2002;36:1676-1680. DOI: 10.1021/es010199v.
[25] Amiridou D, Voutsa D. J Hazard Mater. 2011;185:281-286. DOI: 10.1016/j.jhazmat.2010.09.031.
[26] Ferrara F, Ademollo N, Orru MA, Silvestroni L, Funari E. Chemosphere. 2011;82:1044-1049. DOI: 10.1016/j.chemosphere.2010.10.064.
[27] Chen GW, Ding WH, Ku HY, Chao HR, Chen HY, Huang MCh, Wang SL. Food Chem Toxicol. 2010;48:1939-1944. DOI: 10.1016/j.fct.2010.04.038.
[28] Directive 2000/60/EC of the European Parliament and of the Council of the 23 October 2000 Establishing a Framework for Community Action in the Field of Water Policy. Official Journal of the European Communities L 2000, 1-72.
[29] Tollefsen KE, Nilsen AJ. Ecotoxicol Environ Saf. 2008;69:163-172. DOI: 10.1016/j.ecoenv.2007.04.010.
[30] Coelhan M, Yu JT, Roberts AL. Food Chem. 2009;112:515-519. DOI: 10.1016/j.foodchem.2008.05.107.
[31] Alcon A, Martin AB, Santos VE, Gomez E, Garcia-Ochoa F. Biochem Eng J. 2008;39:486-495. DOI: 10.1016/j.bej.2007.11.005.
[32] Paris F, Balaguer P, Térouanne B, Servant N, Lacoste C, Cravedi JP, Nicolas JC, Sultan Ch. Mol Cell Endocrinol. 2002;193:43-49. DOI: 10.1016/S0303-7207(02)00094-1.
[33] Bolz U, Hagenmaier H, Körner W. Environ Pollut. 2001;115:291-301. DOI: 10.1016/S0269-7491(01)00100-2.

[34] Aguera A, Fernandez-Alba AR, Piedra L, Mezcua M, Gomez MJ. Anal Chim Acta. 2003;480:93-205. DOI: 10.1016/S0003-2670(03)00040-0.
[35] Rudel RA, Camann DE, Spengler JD, Korn LR, Brody JG. Environ Sci Technol. 2003;37(20):4543-4553. DOI: 10.1021/es0264596.
[36] Escartin E, Porte C. Environ Sci Technol. 1999;33:2710-2714. DOI: 10.1021/es9902322.
[37] Nunoshiba T, Watanabe E, Takahashi T, Daigaku Y, Ishikawa S, Mochizuki M, Ui A, Enomoto T, Yamamoto K. Mutat Res. 2007;617:90-97. DOI: 10.1016/j.mrfmmm.2007.01.002.
[38] Sasaki YF, Saga A, Akasaka M, Yoshida K, Nishidate E, Quan Su Y, Mztzsusaka N, Tsuda S. Mutat Res. 1997;395:198-198. DOI:10.1016/S1383-5718(97)00168-X.
[39] Funakoshi G, Kasuya S. Chemosphere. 2009;75:491-497. DOI: 10.1016/j.chemosphere.2008.12.050.
[40] Viñas P, Campillo N, Martínez-Castillo N, Hernández-Córdoba M. Anal Bioanal Chem. 2010;397:115-125. DOI: 10.1007/s00216-010-3464-7.
[41] Basheer C, Kee Lee H, Siang Tan K. Baseline. 2004;48:1145-1167. DOI: 10.1016/j.marpolbul.2004.04.009.
[42] Wang YQ, Chen TT, Zhang HM. Spectrochim Acta Part A. 2010;75:1130-1137. DOI: 10.1016/j.saa.2009.12.071.

ZWIĄZKI FENOLOWE W ŚRODOWISKU - WYSTĘPOWANIE I WPŁYW NA ORGANIZMY ŻYWE

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Abstrakt: Wiele związków organicznych stosowanych jako środki konserwujące w kosmetykach, lekach i żywności niekorzystnie wpływa na zdrowie ludzi i zwierząt. W ostatnich latach szczególną uwagę naukowców na całym świecie zwracają związki chemiczne, powodujące różnego rodzaju zakłócenia w układzie hormonalnym organizmów żywych. Do związków tych, określanych mianem syntetycznych związków endokrynnych (*endocrine disrupting compounds* - EDCs), zalicza się m.in. szeroką gamę pochodnych fenolowych (np. parabeny, fenylofenole, alkilofenole, bisfenol A) i wiele innych. Związki endokrynne mogą naśladować lub blokować działanie naturalnych hormonów, powodując zmiany w układzie rozrodczym, immunologicznym oraz powstawanie nowotworów, co w konsekwencji prowadzi do poważnego zachwiania równowagi ekologicznej. EDCs, podobnie jak ich naturalne odpowiedniki, wykazują aktywność hormonalną już przy bardzo niskich stężeniach, rzędu pg g^{-1} i ng g^{-1}. Większość oczyszczalni ścieków nie jest przystosowana do wydajnego usuwania EDCs ze strumienia ścieków, dlatego też związki te są obecne w wielu elementach środowiska, m.in. w osadach rzecznych i morskich, jak również wodzie powierzchniowej, będącej często rezerwuarem wody pitnej.

Słowa kluczowe: związki fenolowe, ksenoestrogeny, EDCs, parabeny, alkilofenole, bisfenol A, fenylofenole