Revista de Chimie
https://revistadechimie.ro
https://doi.org/10.37358/Rev. Chim.1949

Occurrence of Phenolic Endocrine Disruptors in Danube Delta, Romania

FLORENTINA LAURA CHIRIAC*, IULIANA PAUN, VASILE IANCU, PIRVU FLORINELA, MARCELA NICULESCU, TOMA GALAON
National Research and Development Institute for Industrial Ecology - ECOIND, Drumul Podu Dambovitei 71-73, 060652, Bucharest, Romania

Abstract: *In the last decade, the use of chemical compounds with a molecular structure similar to that of BPA has been reported more and more as alternatives to BPA in various industrial products. This comes as a result of banning partial or total use of BPA because of its endocrine disrupting properties. However, bisphenol analogues have been shown to have similar or even greater negative properties than BPA. Thus, particular attention has been given to the risks they have for aquatic systems and human health. In this context, the present study aimed to determine the concentration level at which some of the bisphenol analogues (BPS, BPB, BPE, BPC and BPE), BPA and its major metabolite, 4-HAP, are found in surface waters. For this purpose, 11 sampling points were established in the geographical area of the Danube Delta. Among the seven targeted pollutants, only four were detected in the analyzed samples. 4-HAP metabolite was the most abundant compound in the analyzed samples, with concentrations ranging from 3.56 to 30.9 ng/L. BPA concentrations were, in most cases approximately three times lower than those determined for 4-HAP. The next bisphenol analog after 4-HAP, in the decreasing order of concentrations, was BPE, for which the concentration level ranged between LOQ and 12.4 ng/L. Lowest concentrations were detected for BPS, with a maximum level of 1.96 ng/L.*

Keywords*: endocrine disruptors, bisphenol analogues, surface water, Danube Delta*

1. Introduction

Due to the increase in anthropogenic pollution, Bisphenol A (BPA) is currently one of the most common and dangerous industrial pollutants. This organic compound is known for its ability to interfere with the normal functioning of the endocrine system, thus representing a high concern for the health of aquatic and terrestrial organisms [1]. Its use in a wide range of industries like in manufacturing of polycarbonate plastics, food packing materials and medical devices, makes human exposure to BPA become very facile. Due to the adverse effects in rodents and humans (metabolic, reproductive, cardiovascular, developmental and immune effects), since 2017, it reached the list of substances of high concern by European Chemical Agency [1,2]. For this reason, several bisphenol analogues have begun to be applied as alternatives for BPA in various industrial products: personal care products, thermal paper, flame retardants and foodstuffs. This includes: Bisphenol C (BPC), Bisphenol F (BPF), Bisphenol B (BPB), Bisphenol S (BPS) and, Bisphenol E (BPE). Although the reason for replacing BPA with other analogues was due to its negative effects on the environment and human health with less dangerous compounds, recent studies show that their use is not safer. Many papers reported that these compounds are less biodegradable and display also neurotoxicity, toxicity, cytotoxicity and endocrine disruptor properties even higher than BPA [3-5]. Thus, Helies-Toussaint and colleagues demonstrated, in a recent study, the involvement of BPS and BPA in steatosis and obesity [6]. Moreover, based on studies of fetal human tissue, it has been shown that a number of bisphenol analogues (BPB, BPF, BPS and BPE) have an anti-androgenic effect similar to that of BPA [7].

**email:florentina.chiriac88@gmail.com*

Concern over the use of these analogues comes from their detection both in environmental samples, such as wastewater, surface water, sediment, sewage sludge and indoor dust, and in biological samples like human urine or plasma [8-11]. Thus, bisphenol analogues such as BPS and BPF showed the highest concentrations in the aquatic environment, while BPS, BPF and BPA were reported at the highest concentrations in indoor air and sediment [12]. Due to the easiness with which these organic pollutants can migrate along water sources, starting from wastewater treatment plants to rivers and finally reaching the seas or oceans, it is important to consider the aquatic environment as the starting ecosystem tested to detect occurrence of these compounds. In addition, considering the physical-chemical properties of these organic pollutants (water solubility, log Kow, low volatility), it is anticipated that they are highly persistent in the environment and also that they show bioaccumulation potential [13]. Advancing along the food chain, these organic pollutants can easily reach from aquatic environment to aquatic organisms and then to humans, both of them being vulnerable to their endocrine disruptive and toxic properties.

This study targeted the determination of concentration levels at which endocrine disruptors such as bisphenol analogues as well as the major metabolite of BPA, 4-hydroxiacetophenone (4-HAP), are found in the Danube Delta region. This geographical area was chosen due to its positioning before the Danube River flow into the Black Sea. In recent years, similar studies were reported which aimed to establish the occurrence of endocrine disruptive organic pollutants in the Danube River, both on the territory of Romania and on the territory of other countries that the Danube River goes through. Many of them were focused on determining hormone-like contaminants (Equilin, Estrone, 17α-Estradiol, 17β-Estradiol, 17α-Ethinylestradiol, Estriole, ethinyl-estradiol and nonylphenol), but quite a few on determining the level of Bishenol A or its analogues [14-17].

2. Materials and methods

2.1. Sampling

To assess the degree of contamination of the Danube Delta area with endocrine disruptors in the BPs class, eleven sampling points were selected from which surface water was collected: Bazin Caraorman, Crisan, Chilia, Bratul Sf. Gheorghe-Canalul Paladin, Lacul Razim-Gura Dunavat, Pardina, Ceatal Ismail, Canal Taranova, Murighiol, Periprava, Ceatal-Sf. Gheorghe, in November 2019. The samples are designated S1-S11. The sampling was made in dark bottles and kept at 4^{o}C until analysis.

2.2. Chemicals

Analytical standards: Bisphenol A, Bisphenol B, Bisphenol C, Bisphenol E, Bisphenol F, Bisphenol S, 4-hydroxiacetophenone and $^{13}C_{12}$-BPA were acquired from Sigma-Aldrich (Germania). HPLC grade Methanol (MeOH) used for mobile phase was purchased from Merck (Darmstadt, Germania), while glacial acetic acid (AA) of analytical purity was purchased from Sigma-Aldrich (Germania).

2.3. Solid Phase extraction

Target analytes were isolated and concentrated from the water samples using solid phase extraction procedure, with an automatic SPE extractor (AutoTrace SPE 280, Thermo Scientific) using StrataX polymeric SPE cartridges (500 mg, 6 mL). First, the cartridges were preconditioned with water and methanol (10 mL each). Afterwards, 200 mL aliquot of surface water samples, spiked with internal standard, was loaded through the cartridges at 5 mL/min flow rate. The adsorbent phase was rinsed with water (10 mL) and dried with nitrogen gas for 30 min. The analytes were desorbed using methanol (2 x 4 mL) and the organic extracts were reduced to dryness. The residue was finely recollected in 1 mL Aq 0.1% AA/Methanol, in equal percentage and stored at 4^{o}C until LC-MS/MS analysis.

2.4. Instrumental Analysis

A HPLC system (Agilent 1260) coupled to a MS triple-quadrupole detector (Agilent 6410B) were used for BPs quantification. Five microliters of the samples, after extraction, were injected into a hydrophobic Luna C18(2) chromatographic column (150 mm long, 2.0 mm inner diameter and 3.0 µm stationary phase particle diameter) for analytes separation, previously heated at constant temperature of 35ºC. A mixture of acetic acid (0.01%) and methanol was used as mobile phase at a flow rate of 0.15 mL/min. The analytes elution was done in isocratic regime in less than thirteen minutes (Figure 1).

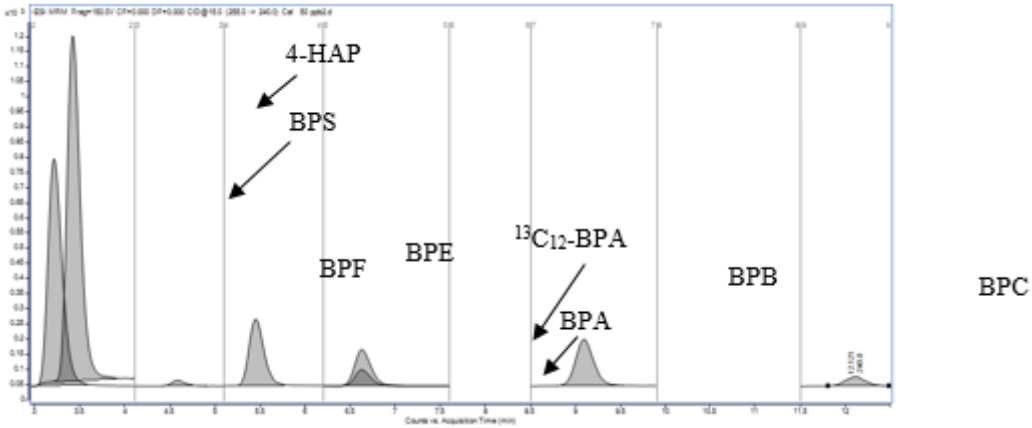

Figure 1. MRM chromatograms of a standard solution of 50 µg/L in methanol of the seven compounds and the internal standard

For analyte quantification, the mass spectrometer detector was used in Multiple Reaction Monitoring mode, with electrospray source set to negative polarity. The MS parameters used for simultaneous detection of the seven compounds, fragmentor voltage, collision energy (CE), cell accelerator voltage (CAV), capillary voltage (CV) and Dwell-time, are given in Table 1. The ESI source parameters were: 300ºC as drying gas temperature, 6 mL/min for drying gas flow-rate and 40 psi as nebulizer gas pressure.

Table 1. The MS parameters for analytes detection.

Analyte	tR (min)	MRM transition	Fragmentor (V)	CE (V)	CAV (V)	CV	Dwell-time (msec)
BPS	3.2	249-108	150	25	6	6000	200
4-HAP	3.4	135-92.0	130	25	8		200
BPF	4.6	199-92.9	150	22	2		250
BPE	5.4	213-198	145	15	1		250
BPA	6.6	227-212	150	15	1		250
$^{13}C_{12}$-BPA	6.6	239-224	150	15	1		250
BPB	9.1	241-212	150	15	1		250
BPC	12.1	255-240	150	15	1		250

2.5. Quality Assurance/Quality Control

For the correct identification and attribution of the seven bisphenols, several quality control measures were provided. In order to test for interferences as well as to verify the background contamination, the analysis of the samples was accompanied by the analysis of a blank solvent, a procedural blank and a standard solution of known concentration. Each sample was analyzed in duplicate. The identification and quantification of the analytes was performed by the internal standard method. Calibration curves were plotted in the concentration range 0.25-100 µg/L, obtaining correlation coefficients greater than 0.999 for all seven compounds. The procedural blank sample proved to be free of the targeted BPs. The recoveries were situated between 85% and 97%, with the relative standard deviations ranged (RSD%) from 9.2% to 13.1%. Considering the concentration factor of the SPE

extraction (200 times) as well as the recovery values, the method quantitation limits were situated between 1.2 and 4.5 ng/L.

3. Results and discussions

3.1. Occurrence of BPs in Surface Water Samples from Danube Delta

LC-MS/MS analysis of Danube Delta samples revealed the presence of only four of the seven targeted pollutants in the tested samples (Sample S6 MRM chromatograms given in Figure 2). In the analyzed samples, only four of the seven BPs compounds were detected: BPA, 4-HAP, BPS and BPE. The other three bisphenol compound (BPC, BPF and BPB) were not found in any of the surface water samples.

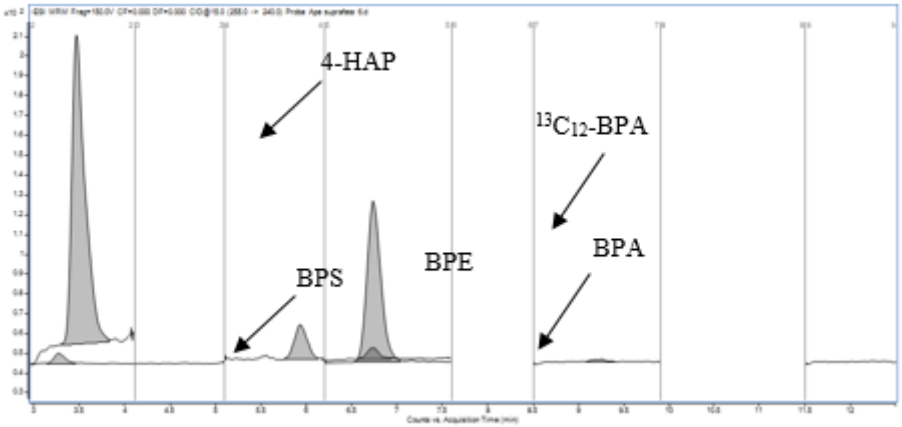

Figure 2. MRM chromatogram for sample S6

The most abundant compound proved to be the BPA metabolite 4-HAP, followed by BPE and BPA. At the opposite side, the lowest concentrations were determined for BPS. This organic pollutant was detected in only three of the analyzed samples, in concentration lower than 2 ng/L. The measured concentrations are graphically represented in Figure 3.

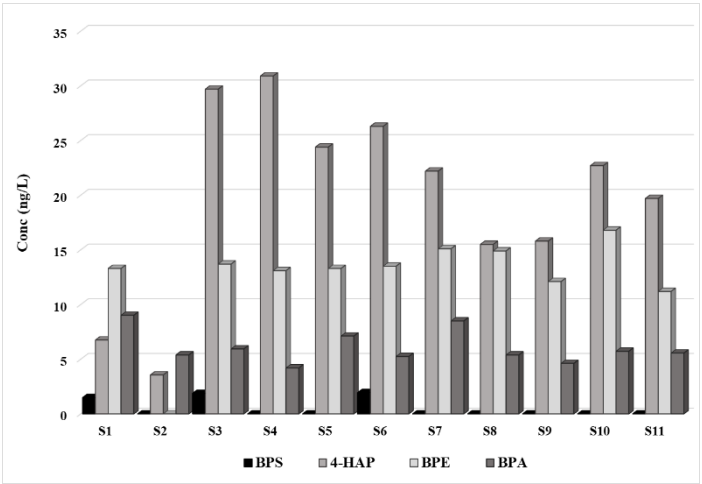

Figure 3. Concentration levels of the investigated BPs in the analyzed samples

3.2. Bisphenol Concentration and Composition Profiles

As it can be seen in Table 2, the highest level of 4-HAP was determined in S4 sampling site, where a value of 30 ng/L was measured, while the lowest concentration was determined for S2 sampling site, with a measured value of only 3.56 ng/L. This organic pollutant was determined in all of the analyzed samples, with an average of 19.77 ng/L. In more than half of the analyzed samples, the concentration

of 4-HAP exceeded the mean value determined for this compound, which was 19.77 ng/L. BPE was detected in 91% of all the samples. Levels of BPE, except for the sample taken from sampling point S1, for which this compound has not been determined, did not vary much among the sampling point ranging from not detected 11.2 to 16.8 ng/L, with a mean value of 12.45 ng/L. BPA was shown to be present in all surface water samples at a lower concentration level compared to its previously discussed analogues. Concentration range in which the BPA determined values were situated was quite narrow, between 4.2 and 9.06 ng/L, with a mean value of 6.07 ng/L. The fourth analyte, BPS, was determined with a rather low frequency, of only 27% and in an extremely low concentration level, the minimum value registered being <LOQ while the maximum value was 1.94 ng/L.

Table 2. Statistical data calculated for BPs determined concentration

Analytes	Min[a]	Max[a]	Average[a]	Median[a]	Sum[a]	Frequency[b]	RSD[b]
BPS	LOQ	1.94	0.48	ND	5.31	27	50.6
4-HAP	3.56	30.9	19.77	22.2	218	100	44.3
BPE	ND	16.8	12.45	13.3	137	91	12.7
BPA	4.2	9.02	6.07	5.56	66.7	100	25.2

[a]values expressed in ng/L; [b]values expressed in %

Figure 4 reports percentage distribution of BPs concentration in the analyzed samples. The percentage composition of the four identified analytes proved to be quite similar for most of the analyzed samples: 43-64% 4-HAP, 27-42% BPE and 9-19% BPA. Due to the low concentration level and the low frequency with which BPS was determined in samples compared to the other three analytes, it was not included in this discussion. Exception from this percentage distribution is done by the samples taken from the sampling points S1 and S2. For sample S1, the percentage of BPE was higher than that corresponding to the other two analogues. Regarding sample S2, the absence of the BPE compound from the sample component, as well as the low concentration of 4-HAP compared to the other samples, made the percentage distribution of these analytes different from that of samples S3-S11.

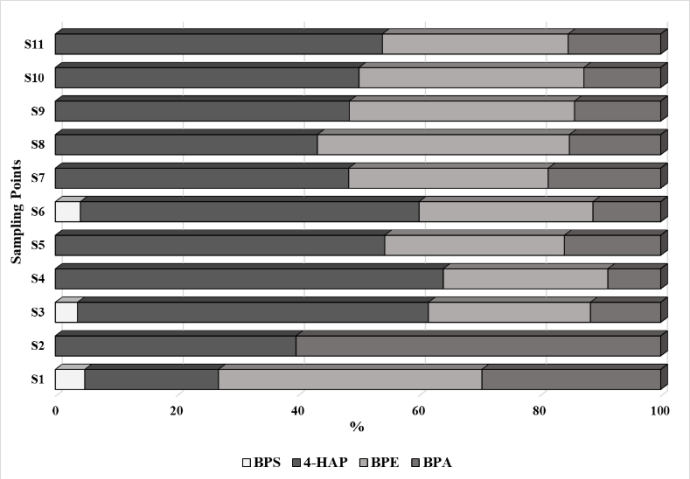

Figure 4. Percentage profiles of individual BPs in each surface water samples

3.3. Comparison with Similar Studies

Similar studies that have tracked the detection of these pollutants in surface waters have been reported in different regions of the world (Table 3). Considering the organic pollutants observed in this study, only for BPA, BPB, BPF and BPS were reported concentration values in the aquatic environment. Compared with the concentration level detected in rivers and lakes from countries with large populations, such as China, Japan or India, the values determined in the surface waters taken from the Danube Delta were much lower [12,18-20]. Comparing the data obtained with those reported

in Germany, it can be observed an extremely closed concentration range for BPA values [21]. Studies on the BPA levels in the Danube River, reported in 2010 an average concentration of 68 ng/L for samples taken along the Danube River from the source to the Black Sea, while in 2015 a much higher BPA concentration range was highlighted with values between LOQ and 693 ng/L [16,17].

Table 3. Comparison of BPs in different rivers and lakes (ng/L)

Country	BPA	BPB	BPF	BPS	References
China	1-47	ND-28	ND-1600	ND-7200	[16, 18-20]
Korea	4.6-270	ND	ND-6130	ND-41	[18,20]
India	ND-2000	ND	ND-290	ND-7200	[18,20]
Japan	ND-900	ND	ND-28000	ND-15	[18,20]
Germany	0.5-14	NA	0.1-180	NA	[21]

3.4. Toxicity and Bioaccumulation Potential

The major concern regarding the presence of bisphenol analogues in surface waters is mainly due to their ability to interfere with the functions of the endocrine system of living organisms. Another possible major threat for human health is the fact that surface waters are also used as main source for obtaining drinking water and the consumption of aquatic fauna by humans can generate the transfer of these pollutants from the environment into the human body. Acute toxicity studies, reported in the literature for bisphenol analogues, performed for three species of aquatic organisms: algae, daphnia and fish revealed that they are toxic in concentrations higher than 1 mg/L (Table 4). Following these studies, it has been proven that fish are the most sensitive species under the action of these organic contaminants, while algae were the most resistant species. It was reported that the substances in question have low to moderate acute toxicity and a low estrogen activity. Among the tested compounds, BPS showed no estrogen activity. Regarding the metabolite 4-HAP, no studies have been performed regarding its toxicity to aquatic organisms.

Table 4. Literature data regarding toxicity studies for Bisphenol analogues

Analyte	Aquatic species	Test endpoint	EC50[a] (mg/L)	References
BPA	Algae	72h	2.2	[22]
	Daphnia	48h	3.9	[23]
	Fish	48h	3.6	[23]
BPE	Algae	-	-	-
	Daphnia	48h	18	[24]
	Fish	48h	0.058	[25]
BPS	Algae	96h	6.9	
	Daphnia	48h	55	[24]
	Fish	72h	155	[26]

[a] Half maximal effective concentration

It is known that the bioaccumulation capacity of a chemical compound is closely related to the octanol-water partition coefficient of the respective substance [27,28]. Bioaccumulation potential increases with the increase of hydrophobicity index (octanol-water partition coefficient). It was previously shown by author X [29,30] that bioaccumulation potential appears at log Kow values higher than 4. The estimated log Kow, using EPI Suite model, are 1.35 for 4-HAP, 1.65 for BPS, 3.19 for BPE and 3.64 for BPA. Given the log Kow values less than 4, the compounds detected in the analyzed samples have a low bioaccumulation potential. Although it has a log Kow value closer to the limit that makes it capable of bioaccumulation, BPA is not a significant bio accumulative compound [31]. Considering the low concentration level at which bisphenol analogues and 4-HAP were determined and also their lower than 4 octanol-water partition coefficients, these compounds do not present, up until now, a major risk for the Delta Danube ecosystem.

4. Conclusions

Banning or limiting the use of BPA in various industrial areas by different countries has led to the need to use similar compounds in order to replace BPA, such as BPS, BPE, BPC, BPE and BPB. Many of these compounds were proved to have endocrine disruptive or toxic properties which are comparable to BPA or even higher than this molecule. In order to monitor the concentrations of these organic pollutants, and in addition to the main metabolite of BPA (4-HAP), in aquatic systems, the geographical area of the Danube Delta was chosen for the study. In all 11 sampling sites, only four of the seven analytes were detected: BPA, 4-HAP, BPE and BPS. The most abundant compound was found to be 4-HAP metabolite, with concentration values in the range 3.56-30.9 ng/L. The lowest concentrations were determined for BPS, the highest detected concentration being 1.92 ng/L. The calculated average concentrations varied in the order: BPS < BPA < BPE < 4-HAP. By studying the spatial distribution of the bisphenol analogues, a relatively homogeneous distribution was observed comparing the eleven sampling sites, with two exceptions registered for S1 and S2. Comparing the results obtained in this study with those reported in the specialized literature, we can conclude that, for the moment, none of the labeled organic pollutants represents, individually, any danger to the Danube Delta ecosystem.

Acknowledgments: The authors acknowledge the financial support provided by the Ministry of Research and Innovation through the national research programme "Nucleu", contract number 38N/2018, Project code PN 18 05 01 01.

References

1.ROCHESTER, J.R., Bisphenol A and Human Health: A Review of the Literature, *Reprod. Toxicol.*, **42**, 2013, 132–155.
2.CRAIN, D.A., ERIKSEN, M., IGUCHI, T., JOBLING, S., LAUFER, H., LEBLANC, G.A., GUILLETTE JR., L.J., An Ecological Assessment of Bisphenol-A: Evidence from Comparative Biology, *Reprod. Toxicol.*, **24**, 2007, 225–239.
3.CHOI, K., Endocrine Disruption Potentials of Bisphenol A Alternatives - are Bisphenol A Alternatives Safe from Endocrine Disruption?, *Korean J. Environ. Health Sci.*, **39**, 2013, 1–18.
4.YAMAGUCHI, A., ISHIBASHI, H., ARIZONO, K., TOMINAGA, N., In Vivo and In Silico Analyses of Estrogenic Potential of Bisphenol Analogs Inmedaka (Oryzias latipes) and Common Carp (Cyprinus Carpio), *Ecotoxicol. Environ. Saf.*, **120**, 2015, 198–205.
5.ZHANG, T., XUE, J.C., GAO, C.Z., QIU, R.L., LI, Y.X., HUANG, M.Z., KANNAN, K., Urinary Concentrations of Bisphenols and Their Association with Biomarkers of Oxidative Stress in People Living Near E-Waste Recycling Facilities in China, *Environ. Sci. Technol.*, **50**, 2016, 4045–4053.
6.HELIES-TOUSSAINT, C., PEYRE, L., COSTANZO, C., CHAGNON, M.C., RAHMANI, R., Is Bisphenol S a Safe Substitute for Bisphenol A in Terms of Metabolic Function? An In Vitro Study, *Toxicol. Appl. Pharmacol*., **280**(2), 2014, 224–235.
7.ROCHESTER, J.R., BOLDEN, A.L., Bisphenol S and F: A Systematic Review and Comparison of the Hormonal Activity of Bisphenol A Substitutes, *Environ. Health Perspect.*, **123**, 2015, 643–650.
8.YANG, Y., LU, L., ZHANG, J., YANG, Y., WU, Y., SHAO, B., Simultaneous Determination of Seven Bisphenols in Environmental Water and Solid Samples by Liquid Chromatography-Electrospray Tandem Mass Spectrometry, *J. Chromatogr. A*, **1328**, 2014, 26–34.
9.THAYER, K.A., TAYLOR, K.W., GARANTZIOTIS, S., SCHURMAN, S.H., KISSLING, G.E., HUNT, D., HERBERT, B., CHURCH, R., JANKOWICH, R., CHURCHWELL, M.I., SCHERI, R.C., BIRNBAUM, L.S., BUCHER, J.R., Bisphenol A, Bisphenol S, and 4-Hydroxyphenyl 4-Isoprooxyphenylsulfone (BBSIP) in Urine and Blood of cashiers, *Environ. Health. Perspect.*, **124**, 2016, 437–444.

10.CHIRIAC, F.L., PAUN, I., PIRVU, F., IANCU, V., GALAON, T., Fast and Sensitive LC-MS Detection of Bisphenol A and Butylhydroxyanisole in WWTP Sewage Sludge, *Rev. Chim.*, **70**(6), 2019, 2123-2127
11.PETRE, J., GALAON, T., IANCU, V.I., VASILE, G.G., STANESCU, E., PASCU, L.F., SIMION, M., CRUCERU, L., Simultaneous Analysis of Selected Dissolved Pharmaceuticals in the Water of the Danube River and its Three Major Tributaries in Romania, *Rev. Chim*., **67**(8), 2016, 1436-1440.
12.YAMAZAKI, E., YAMASHITA, N., TANIYASU, S., LAM, J., LAM, P.K.S., Ecotoxicology and Environmental Safety Bisphenol A and Other Bisphenol Analogues Including BPS and BPF in Surface Water Samples from Japan, China, Korea and India, *Ecotoxicol. Environ. Saf.*, **122**, 2015, 565–572.
13.SONG, M., LIANG, D., LIANG, Y., CHEN, M., WANG, F., WANG, H., JIANG, G., Assessing Developmental Toxicity and Estrogenic Activity of Halogenated Bisphenol A on Zebrafish (Danio rerio), *Chemosphere*, **112**, 2014, 275-281.
14.AVAR, P., ZRINYI, Z., MAASZ, G., TAKATSY, A., LOVAS, S., G.-TOTH, L., PIRGER, Z., β-Estradiol and Ethinyl-Estradiol Contamination in the Rivers of the Carpathian Basin, *Environ. Sci. & Pollut. Res.*, **23**(12), 2016, 11630-11638.
15.GALAON, T., PETRE, J., IANCU, V.I., CRUCERU, L., VASILE, G.G., PASCU, L.F., LEHR, C.B., Detection of Estrogen Hormones in Danube River and Tributaries Using Liquid Chromatography-Mass Spectrometry, *Rev. Chim.*, **67**(8), 2016, 1474-1478.
16.LOOS, R., LOCORO, G., CONTINI, S., Occurrence of Polar Organic Contaminants in the Dissolved Water Phase of the Danube River and Its Major Tributaries Using SPE-LC-MS^2 Analysis, *Water Res.*, **44**, 2010, 2325-2335.
17.MILANOVIC, M., SUDJI, J., LETIC, N.G., RADONIC, J., SEKULIC, M.T., MILORADOV, M.V., MILIC, N., Seasonal Variations of Bisphenol A in the Danube River by the Municipality of Novi Sad, Serbia, *J. Serb. Chem. Soc.*, **80**(0), 2015, 1–13.
18.JIN, H., ZHU, L., Occurrence and Partitioning of Bisphenol Analogues in Water and Sediment from Liaohe River Basin and Taihu Lake, China, *Water Res.*, **103**, 2016, 343–351.
19.YAN, Z., LIU, Y., YAN, K., WU, S., HAN, Z., GUO, R., CHEN, M., YANG, Q., ZHANG, S., CHEN, J., Bisphenol Analogues in Surface Water and Sediment from the Shallow Chinese FreshWater Lakes: Occurrence, Distribution, Source Apportionment, and Ecological and Human Health Risk, *Chemosphere*, **184**, 2017, 318-328.
20.KANG, J.H., KONDO, F., Bisphenol A in the Surface Water and Freshwater Snail Collected from Rivers Around a Secure Landfill, *Bull. Environ. Contam. Toxicol.*, **76**, 2006, 113-118.
21.FROMME, H., KUCHLER, T., OTTO, T., PILZ, K., MULLER, J., WENZEL, A., Occurrence of Phthalates and Bisphenol A and F in the Environment, *Water Res.*, **36**, 2002, 1429-1438.
22.DEBENEST, T., GAGNE, F., PETIT, A.N., ANDRE, C., KOHLI, M., BLAISE, C., Ecotoxicity of a Brominated Flame Retardant (tetrabromobisphenol A) and Its Derivatives to Aquatic Organisms, *Comp. Biochem. Physiol., C: Comp. Pharmacol. Toxicol.*, **152**, 2010, 407-412.
23.TISLER, T., KREL, A., GERZELJ, U., ERJAVEC, B., DOLENC, M.S., PINTAR, A., Hazard Identification and Risk Characterization of Bisphenols A, F and AF to Aquatic Organisms, *Environ. Pollut.*, **212**, 2016, 472-479.
24.CHEN, M.Y., IKE, M., FUJITA, M., Acute Toxicity, Mutagenicity, and Estrogenicity of Bisphenol A and Other Bisphenols, *Environ. Toxicol.*, **17**, 2002, 80-86.
25.OWCZAREK, K., KUDLAK, B., SIMEONOV, V., MAZERSKA, Z., NAMIESNIK, J., Binary Mixtures of Selected Bisphenols in the Environment: Their Toxicity in Relationship to Individual Constituents, *Molecules*, **23**, 2018, 3226.
26.MOREMAN, J., LEE, O., TRZNADEL, M., DAVID, A., KUDOH, T., TYLER, C.R., Acute Toxicity, Teratogenic, and Estrogenic Effects of Bisphenol A and Its Alternative Replacements Bisphenol S, Bisphenol F, and Bisphenol AF in Zebrafish Embryo-Larvae, *Environ. Sci. Technol.*, **51**(21) 2017, 12796-12805.

27.MACKAY, D., ARNOT, J.A., GOBAS, F.A.P.C., POWELL, D.E., Mathematical Relationships Between Metrics of Chemical Bioaccumulation in Fish, *Environ. Toxicol. Chem.*, **32**, 2013, 1459–1466.
28.WEN, Y., HE, J., LIU, X., LI, J.J., ZHAO, Y.H., Linear and Non-Linear Relationships Between Bioconcentration and Hydrophobicity: Theoretical Consideration, *Environ. Toxicol. Pharmacol.*, **34**, 2012, 200–208.
29.COSTANZA, J., LYNCH, D.G., BOETHLING, R.S., ARNOT, J.A., Use of the Bioaccumulation Factor to Screen Chemicals for Bioaccumulation Potential, *Environ. Toxicol. Chem.*, **31**(10), 2012, 2261–2268.
30.GALAON, T., MEDVEDOVICI, A., DAVID, V., Hydrophobicity Parameter (log Kow) Estimation for Some Phenolic Compounds of Pharmaceutical Interest from Retention Studies with Mobile Phase Composition in Reversed-Phase Liquid Chromatography, *Sep. Sci. Technol.*, **43**(1), 2008, 147-163.
31.CORRALES, J., KRISTOFCO, L.A., STEELE, W.B., YATES, B.S., BREED, C.S., WILLIAMS, E.S., BROOKS, B.W., Global Assessment of Bisphenol A in the Environment: Review and Analysis of Its Occurrence and Bioaccumulation, *Dose-Response*, **13**(3), 2015, 1–29.

Manuscript received: 14.04.2020