



Archives of Ecotoxicology

Journal homepage: <https://office.scicell.org/index.php/AE>

Bisphenol A Analogues: A Brief Review of their Occurrence in Food, Biological Samples and Endocrine Effects

Nikola Knížatová^a*, Katarína Tokárová^a, Hana Greifová^a, Tomáš Jambor^b, Peter Massányi^a, Norbert Lukáč^a^a Slovak University of Agriculture in Nitra, Faculty of Biotechnology and Food Sciences, Department of Animal Physiology, Tr. A. Hlinku 2, 949 76 Nitra, Slovak Republic^b Slovak University of Agriculture in Nitra, Faculty of Biotechnology and Food Sciences, Centrum BioFood, Tr. A. Hlinku 2, 949 76 Nitra, Slovak Republic

Article info

Received 30 October 2020

Revised 11 November 2020

Accepted 28 December 2020

Published online 30 December 2020

Review paper

Keywords:

Bisphenol A;

BPA Analogues;

Endocrine disruptors

Abstract

Bisphenol A (BPA) is the most well-known compound from the bisphenol family. There is increasing evidence that bisphenol BPA used in plastics, receipts, food packaging, and other products might be harmful to human health due to its actions as an endocrine-disrupting chemical, therefore BPA is being replaced by compounds very similar in structure, but data on the occurrence and effects of these BPA analogs are limited. Therefore, there is increasing concern regarding human exposure to bisphenol analogs (BPs) due to their widespread use and potential adverse effects. The main objective of this work was to investigate human exposure to BPs and the associated endocrine activities. We performed a literature review of the available research made in humans, in *in vivo* and *in vitro* tests. The findings support the idea that exposure to BPs may have an impact on human health, especially in terms of endocrine disruption.

1. Introduction

Endocrine disruptors are compounds that alter normal functioning of the endocrine system, and their bioaccumulation in humans may cause adverse health effects (Andujar et al., 2019). Bisphenol A was first synthesized in 1905, with the condensation of phenol and acetone in the presence of acid as the catalyst (Rykowska and Wasiak, 2006), afterward, its production levels increased, and nowadays BPA is one of the most extensively used bisphenols, mostly as a monomer in the production of polycarbonate plastics and epoxy resins (Michałowicz, 2014). In recent years, there is increasing evidence of possible negative effects of bisphenol A (BPA) used in plastics, receipts, food packaging, and other products to human health due to its actions as an endocrine-disrupting chemical (EDC) (Rochester, 2013; Rochester et. Bolden, 2015). Scientists, regulators, and the general public have raised concerns about the use of BPA, which has prompted the industry to seek alternative chemicals such as bisphenol AF (BPAF), bisphenol B (BPB), bisphenol F (BPF), and bisphenol S (BPS) (Vandenberg et al. 2010; Rochester et. Bolden, 2015). Ideally, substitutes used to replace a chemical of concern should be inert, or at least far less toxic than the original chemical, but as seen in Figure 1, BPAF, BPB, BPF, and BPS are structural analogues to BPA, thus its effects in physiological systems may be similar (Rochester et. Bolden, 2015). Although BPA alternatives have been largely used, so far, their toxicological

information is limited (Eladak et al., 2015). Given (anti-)estrogenic and (anti-)androgenic activities of BPA, several studies have demonstrated similar activities of BPA alternatives (Rochester et Bolden, 2015).

2. Material and methods

A review of the available literature was conducted in October 2020. PubMed/Medline and Scopus databases were searched using the keywords "Bisphenol A analogues", "Bisphenol A substitutes", "hormone effect", "endocrine disruption", and "endocrine activity". Data published between 2000 and 2020 were considered. We conducted a systematic review to identify the occurrence in food and biological samples, as well as adverse effects of bisphenols and their endocrine activities by focusing on animal models and *in vitro* mechanistic studies. After critical analysis of results, lines of evidence were built using a weight-of-evidence approach to establish a biologically plausible link.

3. Results and Discussion

Occurrence of Bisphenols

Bisphenol A (BPA) is one of the highest-volume chemicals used widely in the production of diverse consumer products, and its use has resulted in ubiquitous existence in the environment and organisms (Zhang et al., 2018).

*Corresponding author: nikola.knizatova@gmail.com<https://doi.org/10.36547/ae.2020.2.4.89-94>

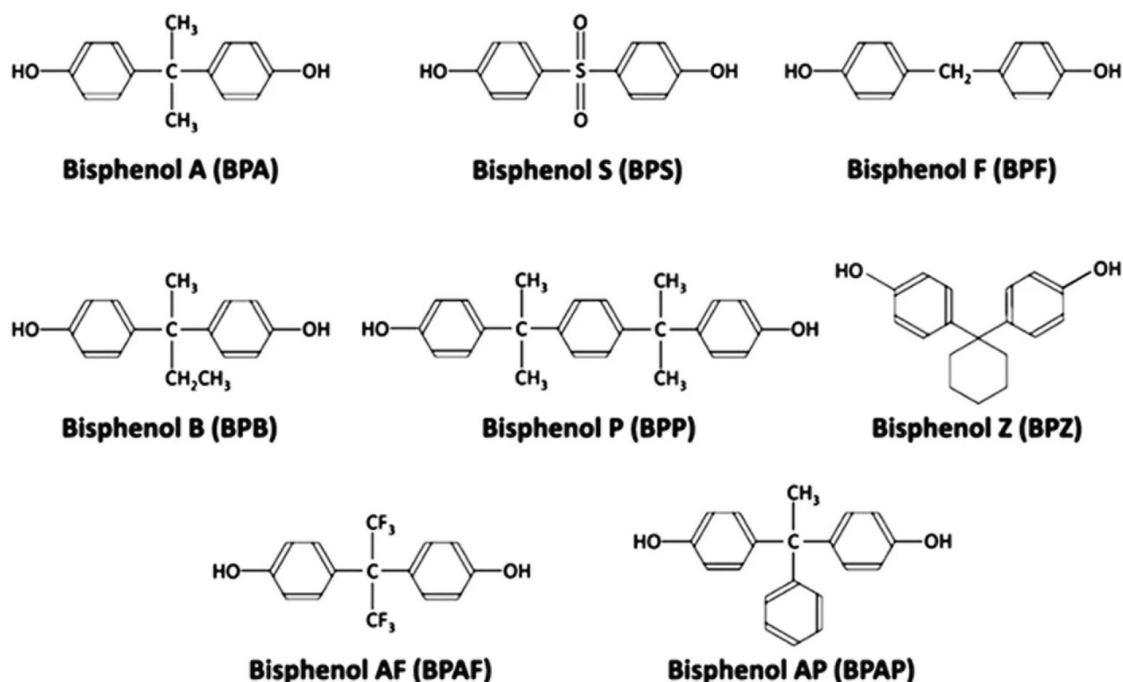


Figure 1. Chemical structure of bisphenol analogues. (Yamazaki et al., 2015)

The occurrence of BPA in more than 90% of 2,517 urine samples tested, with a geometric mean of 2.6 $\mu\text{g/L}$ (Calafat et al., 2008), in several studies of human biomonitoring, BPA has regularly been detected in urine, blood, milk, and other biological samples (Azzouz et al., 2015; Covaci et al., 2015; Gramec-Skledar et al., 2016; Ye et al., 2015; Zimmers et al., 2014), which indicates the high human exposure. BPS and BPF have been detected in many everyday products, such as personal care products (e.g., body wash, hair care products, makeup, lotions, toothpaste) (Liao and Kannan 2014), paper products (e.g., currency, flyers, tickets, mailing envelopes, airplane boarding passes) (Liao et al. 2012c), and food (e.g., dairy products, meat and meat products, vegetables, canned foods, cereals) (Liao and Kannan 2013). BPS, BPF, and BPA have been detected in indoor dust at the following concentrations: BPS, 0.34 $\mu\text{g/g}$; BPF, 0.054 $\mu\text{g/g}$; BPA, 1.33 $\mu\text{g/g}$ (Liao et al. 2012b). BPS and BPF have also been detected in surface water, sediment, and sewage effluent, generally at lower concentrations than BPA, but in the same order of magnitude (Fromme et al. 2002; Song et al. 2014; Yang et al. 2014). In humans, BPS and BPF have been detected in urine at concentrations and frequencies comparable to BPA (Liao et al. 2012a; Zhou et al. 2014). In urine samples from 100 American, nonoccupationally exposed adults, Liao et al. (2012a) found BPF in 55% of samples at concentrations up to 212 ng/mL , and BPS in 78% of samples at concentrations up to 12.3 ng/mL . BPA was found in 95% of the samples, with concentrations up to 37.7 ng/mL (Rochester et al. 2015). Little information is available on the occurrence of bisphenol analogues (BPs) in foods. In a study conducted in the United States, Liao and Kannan (2013) determined the prevalence of BPA, BPF, and BPS ($N = 267$) in nine food categories and found that 75% of the samples contained BPs, with total concentrations ranging from below the quantification limit to 1130 ng/g fresh weight (4.38 ng/g overall mean value). In preserved and ready-to-eat foods, the highest concentrations of BPF and bisphenol P (BPP) were 1130 ng/g and 237 ng/g respectively. BPs in drinks and vegetables, by comparison, were detected at concentrations of 0.341 ng/g and 0.698 ng/g , respectively. In canned food, higher levels of individual and total BPs were found than in foods that came in containers of plastic, glass, or paper. In a study conducted in China, Liao and Kannan

(2014) determined the presence of eight BPs ($N = 289$) in 13 food categories using high-performance liquid chromatography-tandem mass spectrometry. BPA and BPF were the most commonly observed BPs, detected at mean value concentrations of 4.94 ng/g and 2.50 ng/g fresh weight, respectively. In canned goods (27.0 ng/g), the highest overall concentration (sum of eight BPs) was observed, followed by fish and meat (16.5 ng/g), and drinks (15.6 ng/g). By comparison, milk and dairy products, cooking oils, and eggs (2-3 ng/g) had the lowest overall concentration. In canned foods (56.9 ng/g), higher total concentrations were found than in foods containing glass (0.43 ng/g), paper (11.9 ng/g), or plastic (6.40 ng/g). The presence of BPA analogs in canned vegetables, fruits, and soft drinks (Gallart-Ayala et al., 2011a; Gallart-Ayala et al., 2011b) and honey (Cesen et al., 2016; Sadeghi et al., 2016), fish (Sadeghi et al., 2016) and mustard (Zoller et al., 2016) has been documented in many studies. Mustard is one of the most commonly used condiments in the world and is the main source of BPF in humans, in Europe and possibly worldwide, according to some authors (Zoller et al., 2016). Although BPA is the most studied BP, BPs are widely used in epoxy coatings applied in drinking water delivery systems and have also been found in drinking water. BPs from coatings may be exposed to chemical oxidants (disinfectants), which, in comparison to the parent compounds, have the potential to form by-products with increased or decreased estrogenic activity (Lane et al., 2015). In babies under six months of age, breast milk is the primary source of nutrition and can also be used as a surrogate for internal exposure levels in mothers and fetuses. In breast milk samples, BPA, BPF, BPS, and BPAF were found by Niu et al. (2017), with BPA being the most abundant BP, followed by BPF. Li et al., (2020) detected BPs in 181 serum samples from pregnant Chinese women. Ten BPs, including bisphenol S (BPS), bisphenol F (BPF), bisphenol AF (BPAF), bisphenol B (BPB), bisphenol P (BPP), bisphenol Z (BPZ), bisphenol AP (BPAP), tetrabromobisphenol A (TBBPA), tetrabromobisphenol S (TBBPS), and tetrachlorobisphenol A (TCBPA), were positively identified and quantified in serum samples with total BP concentrations (sum of bisphenols: $\sum\text{BPs}$) of 0-144 ng/mL .

Adverse Effects of Bisphenols

The presence of BPA analogues in food, environmental, and human biological samples indicates that it could affect the body. The most widely studied effect of BPA is estrogen activity, and its effects on other hormonal receptors have also been reported (Gramac-Skledar et al., 2016). However, limited studies have confirmed that BPs have related BPA-like endocrine-disrupting activities (Liao et al., 2012). The estrogenicity of BPs was first reported in 1998 in cultures of the human breast cancer cell line MCF7 using an E-SCREEN assay (Perez et al., 1998). Later, in 2002, by evaluating the induction of pS2 (mRNA and protein) and progesterone receptors as well as the expression of the luciferase reporter gene transfected into MVLN cells, the effects of these chemicals on the expression of estrogen-controlled genes were demonstrated (Rivas et al., 2002). The estrogenic effect of certain BPs has also been reported to be higher than that of BPA (Cao et al., 2017). BPS, for example, has a higher hormonal activity, which can probably be due to its heavy polarity and the presence of the sulfonyl group (Caballero-Casero et al., 2016; Gallart-Ayala et al., 2011b), as well as to its thermal stability and light resistance (Deceuninck et al., 2015; García-Córcoles et al., 2018). In addition, by inducing the proliferation and migration of MCF-7 clonal cells, BPS and BPF have been shown to be involved in the development of breast cancer (Kim et al., 2017). Van Leeuwen et al. (2019) recently stated that most *in vitro* studies of BPA analogs have comparable or higher estrogenic activity than BPA, as well as greater antiandrogenic properties. Other BPA analogues have shown both antiestrogenic and antiandrogenic activity. The most studied bisphenol analogues are BPS and BPF. In a systematic review of 32 studies (25 *in vitro* and 7 *in vivo*), the potency of BPF and BPS was found to be in the same order of magnitude as that of BPA and to have comparable hormonal effects (Rochester et al., 2015). In addition, the study found that BPS and BPF had hormonal effects, such as changes in organ weights and levels of enzyme expression, beyond those of BPA. The authors concluded that BPS and BPF tended to have similar potency and mechanisms of action to BPA, which had similar effects on health. In terms of their toxicological profiles, including metabolic, carcinogenic, and reproductive effects, as well as oxidative stress and DNA damage, other authors have also reported on the similarity between BPS and BPF and BPA (Rosenmai et al., 2014; Rochester et al., 2015; Roelofs et al., 2015; Gallo et al., 2017). Adverse reproductive consequences secondary to exposure to BPA analogs, such as decreased sperm and oocyte production and steroidogenesis, have also been indicated in some studies in animal models (Siracusa et al., 2018). BPS was shown to reduce the weight of gonads and alter plasma estrogen and testosterone in zebrafish, as well as to decrease egg development and hatchability, with longer hatching times, and to increase embryo malformations (Qui et al., 2019). Shi et al. (2018) have shown that prenatal exposure to physiologically relevant doses of BPA analogues is likely to affect male reproductive functions due to a spermatogenic defect in the developing testis. The effect of low dose chronic exposure to BPB, BPF, and BPS on hypothalamo-pituitary-testicular behaviors in adult rats was shown by Ullah et al. (2019). Shi et al. (2019) concluded that the initiation of puberty was accelerated by prenatal exposure to bisphenols, and the female mice had fertility problems, irregular estrous cyclicity, and dysregulated expression of steroidogenic enzymes, especially at lower doses. Kolla et al. (2018) compared the exposure effect of BPA and BPS on female mouse mammary gland development during the perinatal phase. Age-specific and dose-specific effects of BPS that were different from the effects of BPA were observed in the study. Furthermore, using L1 larvae of the *Caenorhabditis elegans* model animal, Zhou (2018)

measured low-concentration BPS toxicity. Multiple indicators have been examined at physiological, biochemical, and molecular levels, the overall results showed that BPS was less noxious compared with the effects of BPA, indicating that individual bisphenols could have specific effects. Eladak et al. (2015) conducted research, which showed that 10 nmol/L BPS and BPF can minimize the secretion of basal testosterone by fetal human and mouse testicles. Desdoits-Lethimonier et al. (2017) showed that BPE, BPF, BPB, and BADGE exhibited antiandrogenic properties in adult human testes using an *ex vivo* culture system. In addition, BPA, BPAF, BPB, BPF, BPS, and bisphenol Z (BPZ) have been found to alter thyroid endocrine system function in a study conducted on the GH3 rat cell line, which appears to be increased by 17 β -estradiol (Lee et al., 2018). Serra et al. (2019) reported that existing information on BPB's estrogenic activity and inhibition of testosterone production is similar to BPA's endocrine activity.

3. Conclusion

There is increasing concern regarding human exposure to bisphenol analogues (BPs) due to their widespread use and potential adverse effects. It is not surprising that these replacements also pose a danger to wildlife and human health, considering the similarities between BPA and BPA analogues in terms of their metabolism and behavior, including hormonal effects beyond those of BPA. Regulations for the safety evaluation of consumer goods should be expanded to include all substances in the same category of chemicals. Furthermore, more work is required to find chemical alternatives without harmful health effects, as recommended by various researchers. The trend towards replacement of BPA analogs in consumer goods, especially food contact materials, should be exercised with caution and should include effective and frequent monitoring to assess their effects on human health.

Acknowledgments

The present work was developed with the support of the Res. Centre AgoBioTech built under the project Building Research Centre, AgroBioTech ITMS 26220220180 and the APVV-15-0543, APVV-19-0243, APVV-18-0312, VEGA 1/0038/19.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

- Andújar, N., Gálvez-Ontiveros, Y., Zafra-Gómez, A., Rodrigo, L., Álvarez-Cubero, M., Aguilera, M., Monteaguo, C., Rivas, A., 2019. Bisphenol A Analogues in Food and Their Hormonal and Obesogenic Effects: A Review. *Nutrients*, 11(9), 2136. <http://dx.doi.org/10.3390/nu11092136>
- Azzouz, A., Rascón, A.J., Ballesteros, E., 2015. Simultaneous determination of parabens, alkylphenols, phenylphenols, bisphenol A and triclosan in human urine, blood and breast milk by continuous solid-phase extraction and gas chromatography-mass spectrometry. *J. Pharm. Biomed. Anal.* 119, 16-26. <http://dx.doi.org/10.1016/j.jpba.2015.11.024>
- Caballero-Casero, N., Lunar, L., Rubio, S., 2016. Analytical methods for the determination of mixtures of bisphenols and derivatives in human and environmental exposure sources and biological fluids. A review. *Anal. Chim. Acta*, 908, 22-53. <http://dx.doi.org/10.1016/j.aca.2015.12.034>

4. Calafat, A.M., Ye, X., Wong, L.Y., Reidy, J.A., Needham, L.L., 2008. Exposure of the U.S. population to bisphenol A and 4-tertiary-octylphenol: 2003-2004. *Environ. Health Perspect.* 116, 39-44. <http://dx.doi.org/10.1289/ehp.10753>
5. Cao, H., Wang, F., Liang, Y., Wang, H., Zhang, A., Song, M., 2017. Experimental and computational insights on the recognition mechanism between the estrogen receptor α with bisphenol compounds. *Arch. Toxicol.* 91, 3897-3912. <https://doi.org/10.1007/s00204-017-2011-0>
6. Cesen, M., Lambropoulou, D., Laimou-Geraniou, M., Kosjek, T., Blanznik, U., Heath, D., Heath, E., 2016. Determination of Bisphenols and Related Compounds in Honey and Their Migration from Selected Food Contact Materials. *J. Agric. Food. Chem.* 64, 8866-8875. <https://doi.org/10.1021/acs.jafc.6b03924>
7. Covaci, A., Den Hond, E., Geens, T., Govarts, E., Koppen, G., Frederiksen, H., Knudsen, L.E., Mørck, T.A., Gutleb, A.C., Guignard, C., Cocco, E., Horvat, M., Heath, E., Kosjek, T., Mazej, D., Tratnik, J.S., Castaño, A., Esteban, M., Cutanda, F., Ramos, J.J., Berglund, M., Larsson, K., Jönsson, B.A., Biot, P., Casteleyn, L., Joas, R., Joas, A., Bloemen, L., Sepai, O., Exley, K., Schoeters, G., Angerer, J., Kolossa-Gehring, M., Fiddicke, U., Aerts, D., Koch, H.M., 2015. Urinary BPA measurements in children and mothers from six European member states: Overall results and determinants of exposure. *Environ. Res.* 141, 77-85. <https://doi.org/10.1016/j.envres.2014.08.008>
8. Deceuninck, Y., Bichon, E., Marchand, P., Boquien, C.Y., Legrand, A., Boscher, C., Antignac, J.P., Le Bizet, B., 2015. Determination of bisphenol A and related substitutes/analogues in human breast milk using gas chromatography-tandem mass spectrometry. *Anal. Bioanal. Chem.* 407, 2485-2497. <https://doi.org/10.1007/s00216-015-8469-9>
9. Desdoits-Lethimonier, C., Lesné, L., Gaudriault, P., Zalko, D., Antignac, J.P., Deceuninck, Y., Platel, C., Dejuq-Rainsford, N., Mazaud-Guittot, S., Jégou, B., 2017. Parallel assessment of the effects of bisphenol A and several of its analogs on the adult human testis. *Hum. Reprod.* 32, 1465-1473. <https://doi.org/10.1093/humrep/dex093>
10. Eladak, S., Grisin, T., Moison, D., Guerquin, M.-J., N'Tumba-Byn, T., Pozzi-Gaudin, S., Benachi, A., Livera, G., Rouiller-Fabre, V., Habert, R., 2015. A new chapter in the bisphenol A story: bisphenol S and bisphenol F are not safe alternatives to this compound. *Fertility and Sterility*, 103(1), 11-21. <https://doi.org/10.1016/j.fertnstert.2014.11.005>
11. Fromme, H., Küchler, T., Otto, T., Pilz, K., Müller, J., Wenzel, A., 2002. Occurrence of phthalates and bisphenol A and F in the environment. *Water Res.* 36:1429-1438. [https://doi.org/10.1016/S0043-1354\(01\)00367-0](https://doi.org/10.1016/S0043-1354(01)00367-0)
12. Gallart-Ayala, H., Moyano, E., Galceran, M.T., 2011b. Analysis of bisphenols in soft drinks by on-line solid phase extraction fast liquid chromatography-tandem mass spectrometry. *Anal. Chim. Acta.* 683, 227-233. <https://doi.org/10.1016/j.jaca.2010.10.034>
13. Gallart-Ayala, H., Moyano, E., Galceran, M.T., 2011a. Fast liquid chromatography-tandem mass spectrometry for the analysis of bisphenol A-diglycidyl ether, bisphenol F-diglycidyl ether and their derivatives in canned food and beverages. *J. Chromatogr. A* 1218, 1603-1610. <https://doi.org/10.1016/j.chroma.2011.01.026>
14. Gallo, P., Pisciotano, I.D.M., Esposito, F., Fasano, E., Scognamiglio, G., Mita, G.D., Cirillo, T., 2017. Determination of BPA, BPB, BPF, BADGE and BFDGE in Canned Energy Drinks by Molecularly Imprinted Polymer Cleaning up and UPLC with Fluorescence Detection. *Food Chem.* 220, 406-412. <https://doi.org/10.1016/j.foodchem.2016.10.005>
15. García-Córcoles, M.T., Cipa, M., Rivas, A., Olea-Serrano, F., Vílchez, A.J., Zafra-Gómez, A., 2018. Determination of Bisphenols with Estrogenic Activity in Plastic Packaged Baby Food Samples Using Solid-Liquid Extraction and Clean-up with Dispersive Sorbents Followed by Gas Chromatography Tandem Mass Spectrometry. *Talanta*. 178, 441-448. <https://doi.org/10.1016/j.talanta.2017.09.067>
16. Gramac-Skledar, D., Peterlin-Mašič, L., 2016. Bisphenol A and its analogs: Do their metabolites have endocrine activity? *Environ. Toxicol. Pharmacol.* 47, 182-199. <https://doi.org/10.1016/j.etap.2016.09.014>
17. Kim, J., Choi, H., Lee, H., Lee, G., Hwang, K., Choi, K., 2017. Effects of bisphenol compounds on the growth and epithelial mesenchymal transition of MCF-7 CV human breast cancer cells. *J. Biomed. Res.* 31, 358-369. <https://doi.org/10.7555/IBR.31.20160162>
18. Kolla, S., Morcos, M., Martin, B., Vandenberg, L.N., 2018. Low dose bisphenol S or ethinyl estradiol exposures during the perinatal period alter female mouse mammary gland development. *Reprod. Toxicol.* 78, 50-59. <https://doi.org/10.1016/j.reprotox.2018.03.003>
19. Lane, R.F., Adams, C.D., Randtke, S.J., Carter, R.E., 2015. Chlorination and chloramination of bisphenol A, bisphenol F, and bisphenol A diglycidyl ether in drinking water. *Water Res.* 79, 68-78. <https://doi.org/10.1016/j.watres.2015.04.014>
20. Lee, J., Kim, S., Choi, K., Ji, K., 2018. Effects of bisphenol analogs on thyroid endocrine system and possible interaction with 17 β -estradiol using GH3 cells. *Toxicol. Vitro*. 53, 107-113. <https://doi.org/10.1016/j.tiv.2018.08.005>
21. Li, A., Zhuang, T., Shi, W., Liang, Y., Liao, C., Song, M., Jiang, G., 2020. Serum concentration of bisphenol analogues in pregnant women in China. *Science of The Total Environment*, 707, 136100. <https://doi.org/10.1016/j.scitotenv.2019.136100>
22. Liao, C., Kannan, K., 2013. Concentrations and profiles of bisphenol A and other bisphenol analogues in foodstuffs from the United States and their implications for human exposure. *J. Agric. Food. Chem.* 61, 4655-4662. <https://doi.org/10.1021/jf400445n>
23. Liao, C., Kannan, K., 2014. A survey of alkylphenols, bisphenols, and triclosan in personal care products from China and the United States. *Arch. Environ. Contam. Toxicol.* 67, 50-59. <https://doi.org/10.1007/s00244-014-0016-8>
24. Liao, C., Liu, F., Alomirah, H., Loi, V.D., Mohd, M.A., Moon, H.B., Nakata, H., Kannak, K., 2012a. Bisphenol S in urine from the United States and seven Asian countries: occurrence and human exposures. *Environ. Sci. Technol.* 46, 6860-6866. <https://doi.org/10.1021/es301334j>
25. Liao, C., Liu, F., Guo, Y., Moon, H.B., Nakata, H., Wu, Q., Kannan, K., 2012b. Occurrence of eight bisphenol analogues in indoor dust from the United States and several Asian countries: implications for human exposure. *Environ Sci Technol* 46:9138-9145. <https://doi.org/10.1021/es302004w>
26. Liao, C., Liu, F., Kannan, K., 2012c. Bisphenol S, a new bisphenol analogue, in paper products and currency bills and its association with bisphenol A residues. *Environ Sci Technol* 46:6515-6522. <https://doi.org/10.1021/es300876n>
27. Liao, A., Kannan, K., 2014. A survey of bisphenol A and other bisphenol analogues in foodstuffs from nine cities in China. *Food Addit. Contam. Part A Chem. Anal. Control Expo. Risk Assess.* 31, 319-329. <https://doi.org/10.1080/19440049.2013.868611>
28. Liao, C., Kannan, K., 2013. Concentrations and profiles of bisphenol A and other bisphenol analogues in foodstuffs from the united states and their implications for human exposure. *J. Agric. Food Chem.* 61, 4655-4662. <https://doi.org/10.1021/jf400445n>

29. Liao, C., Liu, F., Kannan, K., 2012. Bisphenol, S. A new bisphenol analogue, in paper products and currency bills and its association with bisphenol A residues. *Environ. Sci. Technol.* 46, 6515–6522. <https://doi.org/10.1021/es300876n>
30. Michałowicz, J., 2014. Bisphenol A - sources, toxicity and biotransformation. *Environ. Toxicol. Pharmacol.* 37, 738–758. <https://doi.org/10.1016/j.etap.2014.02.003>
31. Niu, Y., Wang, B., Zhao, Y., Zhang, J., Shao, B., 2017. Highly sensitive and high-throughput method for the analysis of bisphenol analogues and their halogenated derivatives in breast milk. *J. Agric. Food Chem.* 65, 10452–10463. <https://doi.org/10.1021/acs.jafc.7b04394>
32. Perez, P., Pulgar, R., Olea-Serrano, F., Villalobos, M., Rivas, A., Metzler, M., Pedraza, V., Olea, N., 1998. The estrogenicity of bisphenol A-related diphenylalkanes with various substituents at the central carbon and the hydroxy groups. *Environ. Health Perspect.* 106, 167–174. <https://doi.org/10.1289/ehp.98106167>
33. Qui, W., Fang, M., Liu, C., Zheng, C., Chen, B., Wang, K.J., 2019. In vivo actions of bisphenol F on the reproductive neuroendocrine system after long-term exposure in zebrafish. *Sci. Total Environ.* 2019, 15, 995–1002. <https://doi.org/10.1016/j.scitotenv.2019.02.154>
34. Rivas, A., Lacroix, M., Olea-Serrano, F., Laos, I., Leclercq, G., Olea, N., 2002. Estrogenic effect of a series of bisphenol analogues on gene and protein expression in MCF-7 breast cancer cells. *J. Steroid Biochem. Mol. Biol.* 82, 45–53. [https://doi.org/10.1016/s0960-0760\(02\)00146-2](https://doi.org/10.1016/s0960-0760(02)00146-2)
35. Roelofs, M.J.E., van den Berg, M., Bovee, T.F.H., Piersma, A.H., Van Duursen, M.B.M., 2015. Structural bisphenol analogues differentially target steroidogenesis in murine MA-10 Leydig cells as well as the glucocorticoid receptor. *Toxicol.* 329, 10–20. <https://doi.org/10.1016/j.tox.2015.01.003>
36. Rochester J. R., 2013. Bisphenol A and human health: a review of the literature. *Reprod. Toxicol.* 42, 132–155. <https://doi.org/10.1016/j.reprotox.2013.08.008>
37. Rochester, J. R., Bolden, A. L., 2015. Bisphenol S and F: A Systematic Review and Comparison of the Hormonal Activity of Bisphenol A Substitutes. *Environ. Health Perspect.* 123, 643–650. <https://doi.org/10.1289/ehp.1408989>
38. Rosenmai, A.K., Dybdahl, M., Pedersen, M., Van Vugt-Lussenburg, B.M.A., Wedebye, E.B., Taxvig, C., Vinggaard, A.M., 2014. Are structural analogues to bisphenol a safe alternatives? *Toxicol. Sci.* 139, 35–47. <https://doi.org/10.1093/toxsci/kfu030>
39. Rykowska, I., Wasiak, W., 2006. Properties, threats, and methods of analysis of bisphenol A and its derivatives. *Acta Chromatographica* 16, 7–27.
40. Sadeghi, M., Nematifar, Z., Fattahi, N., Pirsahab, M., Shamsipur, M., 2016. Determination of Bisphenol A in Food and Environmental Samples Using Combined Solid-Phase Extraction-Dispersive Liquid-Liquid Microextraction with Solidification of Floating Organic Drop Followed by HPLC. *Food Anal. Meth.* 9, 1814–1824. <https://doi.org/10.1007/s12161-015-0357-6>
41. Serra, H., Beausoleil, C., Habert, R., Minier, C., Picard-Hagen, N., & Michel, C., 2019. Evidence for Bisphenol B Endocrine Properties: Scientific and Regulatory Perspectives. *Environmental Health Perspectives*, 127(10), 106001. <https://doi.org/10.1289/ehp5200>
42. Shi, M., Sekulovski, N., MacLean, J.A., 2nd, Hayashi, K., 2018. Prenatal Exposure to Bisphenol A Analogues on Male Reproductive Functions in Mice. *Toxicol. Sci.* 163, 620–631. <https://doi.org/10.1093/toxsci/kfy061>
43. Shi, M., Sekulovski, N., MacLean, J.A., Whorton, A., Hayashi, K., 2019. Prenatal Exposure to Bisphenol A Analogues on Female Reproductive Functions in Mice. *Toxicol. Sci.* 168, 561–571. <https://doi.org/10.1093/toxsci/kfz014>
44. Song, S., Song, M., Zeng, L., Wang, T., Liu, R., Ruan, T., Jiang, G., 2014. Occurrence and profiles of bisphenol analogues in municipal sewage sludge in China. *Environ. Pollut.* 186:14–19. <https://doi.org/10.1016/j.envpol.2013.11.023>
45. Ullah, A., Pirzada, M., Jahan, S., Ullah, H., Turi, N., Ullah, W., Siddiqui, M.F., Zakria, M., Lodhi, K.Z., Khan, M.M., 2018. Impact of low-dose chronic exposure to bisphenol A and its analogue bisphenol B, bisphenol F and bisphenol S on hypothalamo-pituitary-testicular activities in adult rats: A focus on the possible hormonal mode of action. *Food Chem. Toxicol.* 121, 24–36. <https://doi.org/10.1016/j.fct.2018.08.024>
46. Van Leeuwen, S.P., Bovee, T.F., Awchi, M., Klijnstra, M.D., Hamers, A.R., Hoogenboom, R.L., Portier, L., Gerssen, A., 2019. BPA, BADGE and analogues: A new multi-analyte LC-ESI-MS/MS method for their determination and their in vitro (anti)estrogenic and (anti)androgenic properties. *Chemosphere*, 221, 246–253. <https://doi.org/10.1016/j.chemosphere.2018.12.189>
47. Vandenberg, L. N., Chahoud, I., Heindel, J. J., Padmanabhan, V., Paumgarten, F. J. & Schoenfelder, G., 2010. Urinary, circulating, and tissue biomonitoring studies indicate widespread exposure to bisphenol A. *Environ. Health Perspect.* 118, 1055–1070. <https://doi.org/10.1289/ehp.0901716>
48. Yamazaki, E., Yamashita, N., Taniyasu, S., Lam, J., Lam, P.K., Moon, H.B., Jeong, Y., Kannan, P., Achyuthan, H., Munuswamy, N., Kannan, K., 2015. Bisphenol A and other bisphenol analogues including BPS and BPF in surface water samples from Japan, China, Korea and India. *Ecotoxicol. Environ. Saf.* 122, 565–572. <https://doi.org/10.1016/j.ecoenv.2015.09.029>
49. Yang, Y., Lu, L., Zhang, J., Yang, Y., Wu, Y., Shao, B., 2014. Simultaneous determination of seven bisphenols in environmental water and solid samples by liquid chromatography-electrospray tandem mass spectrometry. *J. Chromatogr. A* 1328, 26–34. <https://doi.org/10.1016/j.chroma.2013.12.074>
50. Ye, X., Wong, L.Y., Kramer, J., Zhou, X., Jia, T., Calafat, A.M., 2015. Urinary concentrations of bisphenol A and three other bisphenols in convenience samples of U.S. adults during 2000–2014. *Environ. Sci. Technol.* 49, 11834–11839. <https://doi.org/10.1021/acs.est.5b02135>
51. Zhang, Y.F., Ren, X.M., Li, Y.Y., Yao, X.F., Li, C.H., Qin, Z.F., Guo, L.H., 2018. Bisphenol A alternatives bisphenol S and bisphenol F interfere with thyroid hormone signaling pathway in vitro and in vivo. *Environmental Pollution*, 237, 1072–1079. <https://doi.org/10.1016/j.envpol.2017.11.027>
52. Zhou, X., Kramer, J.P., Calafat, A.M., Ye, X., 2014. Automated on-line column-switching high performance liquid chromatography isotope dilution tandem mass spectrometry method for the quantification of bisphenol A, bisphenol F, bisphenol S, and 11 other phenols in urine. *J. Chromatogr. B. Analyt. Technol. Biomed. Life. Sci.* 944, 152–156. <https://doi.org/10.1016/j.jchromb.2013.11.009>
53. Zhou, D., 2018. Ecotoxicity of bisphenol S to *Caenorhabditis elegans* by prolonged exposure in comparison with bisphenol A. *Environ. Toxicol. Chem.* 37, 2560–2565. <https://doi.org/10.1002/etc.4214>
54. Zimmers, S.M., Browne, E.P., O'Keefe, P.W., Anderton, D.L., Kramer, L., Reckhow, D.A., Arcaro, K.F., 2014. Determination of free bisphenol A (BPA) concentrations in breast milk of U.S. women using a sensitive LC/MS/MS method. *Chemosphere* 104, 237–243. <https://doi.org/10.1016/j.chemosphere.2013.12.085>

55. Zoller, O., Brüscheiler, B.J., Magnin, R., Reinhard, H., Rhyn, P., Rupp, H., Zeltner, S., Felleisen, R., 2016. Natural occurrence of bisphenol F in mustard. Food Addit. Contam. Part A Chem. Anal. Control Expo. Risk Assess. 33, 137–146. <https://doi.org/10.1080/19440049.2015.1110623>