Bisphenols

Subjects: Anatomy & Morphology
Contributor: Francesca Gorini

Bisphenols (BPs), and especially bisphenol A (BPA), are known endocrine disruptors (EDCs), capable of interfering with estrogen and androgen activities, as well as being suspected of other health outcomes.

Keywords: Bisphenol A ; bisphenols ; endocrine disruptors ; thyroid hormones ; thyroid cancer

1. Introduction

Bisphenol A(BPA) is a monomer in the manufacture of polycarbonate plastics and epoxy resins widely used in diverse consumer products such as food and liquid containers, protective coatings inside metallic food and beverage cans and medical devices, as well as in flame retardants and thermal papers[1] [24]. It is one of the 2000 endocrine disruptors known as “highest volume” chemicals, with an annual production of at least 8 million tons throughout the world[2].

2. Bisphenols in the Environment and Humans

BPA can be released from both effluent discharge of manufacturing plants and from transport, processing, and disposal of waste of BPA-containing products in landfills and incinerators[3] . Less than 1% of environmental BPA has been estimated to occur in the atmosphere, where it undergoes photo-oxidation and breakdown[4]. Nonetheless, the presence of BPA in the environment, though at low levels and despite the short half-life, is ubiquitous[5].

Due to its lipophilicity, detectable levels of the unconjugated form of BPA were measured in adipose tissue, brain, liver, and breast milk in humans (Table 1a). Moreover, BPA can pass through the placenta and amniotic fluid thereby exposing the fetus, as well as the developing infant, to exposure and accumulation[6] (Table 1a).

The first safety standard for humans set by the US-Environmental Protection Agency in 1988, adopted by the Food and Drug Administration as the reference dose and based on the LOAEL for BPA, was 50 micrograms per kilogram of body weight per day[7]. In 2013, the re-evaluation of BPA exposure and toxicity led the European Food Safety Authority to considerably reduce the safe level of BPA from 50 to 4 µg/kg/day (31). Human exposure to BPA is continuous and widespread, and diet is likely the major source of exposure in all population groups because of the ability of BPA to migrate from polycarbonate containers and metallic cans to food and beverages[8]. In 2011, the European Union banned the manufacture of baby bottles containing BPA[9], followed in 2012 by the Food and Drug Administration[10]. Infants and toddlers exhibit the highest estimated external average exposure because of their elevated consumption of food and beverages per kg of body weight[8] (Table 1a). Other routes of exposure are represented by inhalation of outdoor and indoor air, ingestion of domestic dust, dermal contact with thermal paper and cosmetics, and, for children, mouthing of toys[8]. The estimates for exposure to dietary and non-dietary sources are at least one order lower than the tolerable daily intake set by the European Food Safety Authority, except daily intake of infants fed with canned liquid formula in polycarbonate bottles (Table 1a).

BPA has a half-life in humans of about 6 h[11]. Following the oral exposure, in humans BPA is absorbed from the gastrointestinal tract and then metabolized in the liver, where is primarily conjugated with glucuronic acid to the non-active BPA-glucuronide, which is the main metabolite in urine and blood[11]. Urinary total BPA (conjugated + free), considered the most appropriate biomarker to assess human exposure[12], was detected among the different age classes in 88% to 98% of volunteers who participated in the National Health and Nutrition Examination Survey[12]. Significantly higher concentrations have been detected in children than in adolescents and adults whereas BPA levels measured in the blood of adults are approximately one order of magnitude lower than those found in the corresponding urine[13] (Table 1a).

Several structural analogues were introduced in the market to replace BPA[14]. Bisphenol F (BPF; 4,4′-dihydroxydiphenylmethane), bisphenol S (BPS; 4,4′-sulfonyldiphenol), and bisphenol Z (BPZ; 1,1-bis(4-hydroxyphenyl)-cyclohexane) are used in epoxy resin products[15], in cleaning products and thermal paper[16], and in highly heat resistant plastic materials and electrical insulation[17], respectively. BPAF (1,1,1,3,3,3-hexafluoro-2,2-bis(4-hydroxyphenyl)propane) is a fluorinated derivative widely used in the manufacturing of polycarbonate copolymers with 10,000 to 500,000 pounds annually produced in the United States[18]. BPA substitutes have been detected in various environmental matrices, and, with a few exceptions, their concentration values in urine are lower than those of BPA[19] (Table 1b).

Tetrabromobisphenol A (TBBPA), a persistent compound synthesized by bromination of BPA initially replaced polybrominated diphenylthers, at present is the most widely employed brominated flame retardant, with a reported 2011 volume of 120 million pounds in the United States[20]. In the last years, tetrabromobisphenol S (TBBPS) and tetrachlorobisphenol A (TCBPA) have been extensively used as alternatives to TBBPA[21]. TBBPA is measured in the environment and in human body[22], and TBBPA exposure represents a significant health risk especially for children residing in an e-waste processing region[23] (Table 1c).

Table 1. Concentration of bisphenols in the environment and human body, and estimated exposure by age groups to bisphenol A (a), principal bisphenol A substitutes (b), and halogenated derivatives of bisphenol A (c).

(a) Bisphenol A		
Environmental Matrix	**Concentration**	**Reference**
Surface water	**nd-1.95 μg/L**	[24]
Sediments (industrialized areas)	**nd-13,370 μg/kg dry weight**	[18]
Soil	**<0.01–1000 μg/kg**	[6]
Indoor dust	**nd-39.1 μg/g**	[25]
Atmosphere	**10^{-3}–1.74 ng/m^3**	[26]
Landfill leachate (hazardous waste site)	**Up to 17,200 μg/L**	[27]
Human Body	**Concentration**	**Reference**
Brain	**Mean: 0.91 ng/g**	[28]
Liver	**Mean: 1.30 ng/g**	[29]
Adipose tissue	**Mean: 3.78 ng/g**	[28]
Breast milk	**Mean: 0.61 μg/L**	[29]
Blood (adults)	**Mean: 0.20 μg/L**	[13]
Cord blood	**Mean: 0.13 μg/L**	[13]
Urine (European adult population)	**Geometric mean: 2.5–3.6 μg/L**	[8]
Urine (North America children)	**Geometric mean: 1.3–3.7 μg/L**	[8]
Urine (North America adults)	**Geometric mean: 1.0–2.6 μg/L**	[8]
Age Group/Source of Exposure	**Average External Exposure**	**Reference**
Infants (0–3 month)/Formula fed from polycarbonate bottles	**2.4 μg/kg/day**	[30]
Infants (0–6 month)/Formula fed from non- polycarbonate bottles	**0.03 μg/kg/day**	[8]
Infants (6–12 month) and toddlers (12–36 month)/Diet	**0.375 μg/kg/day**	[8]
Infants (6–12 month) and toddlers (12–36 month)/Oral dust and toys	**0.007–0.009 μg/kg/day**	[8]
Infants (0–12 month) and toddlers (12–36 month)/Inhalation	**0.7 μg/kg/day**	[8]
General population (>3 years)/Diet	**0.116–0.290 μg/kg/day**	[8]
General population (>3 years)/Thermal paper	**0.059–0.094 μg/kg/day**	[8]
General population (>3 years)/Cosmetics	**0.002 μg/kg/day**	[8]
General population (>3 years)/Inhalation	**0.2–0.4 μg/kg/day**	[8]
(b) Principal Bisphenol A Substitutes		
Environmental Matrix	**Concentration**	**Reference**

Surface water (BPF)	**nd-2.850 μg/L**	[24]
Sediments in industrialized areas (BPF)	**nd-9650 μg/kg dry weight**	[18]
Indoor dust (sum of several bisphenols including BPF, BPS, BPZ)	**0.00083–26.6 μg/g**	[26]
Human Body	**Concentration**	**Reference**
Urine (BPS: general population—USA/Asian countries)	**Geometric mean: 0.030–1.18 μg/L**	[31]
Age Group	**Estimated Exposure**	**Reference**
Children and adolescents (<20 years)—USA/Asian countries (BPS)	**Median: 0.009 μg/kg/day**	[31]
Adults (≥20 years) – USA/Asian countries (BPS)	**Median: 0.004 μg/kg/day**	[31]
(c) Tetrabromobisphenol A		
Environmental Matrix	**Concentration**	**Reference**
Atmosphere (e-waste dismantling site)	**66.01–95.04 ng/m^3**	[32]
Indoor dust	**42.21–46,191 ng/g dry weight**	[23]
Sediments	**Up to 518 ng/g**	[33]
Soil (industrialized areas)	**1.64–7758 ng/g dry weight**	[34]
Surface water	**0.85–4.87 μg/L**	[33]
Human Body	**Concentration**	**Reference**
Breast milk	**4.110 ng/g lipid weight**	[35]
Cord serum	**Mean: 0.199 ng/g fresh weight**	[35]
Age group/Source of Exposure	**Average External Exposure**	**Reference**
Infants/Breast-feeding	**<0.00018–0.171 μg/kg/day**	[36]
Infants/Dust ingestion (e-waste recycling site)	**0.00031–0.054 μg/kg/day**	[23]
Adults/Dust ingestion (e-waste recycling site)	**0.00004–0.0075 μg/kg/day**	[23]
Adults/High fish consumers	**0.00026 μg/kg/day**	[36]

References

1. Antonia M. Calafat; Xiaoyun Ye; Lee-Yang Wong; John A. Reidy; Larry L. Needham; Exposure of the U.S. Population to Bisphenol A and 4- tertiary -Octylphenol: 2003–2004. *Environmental Health Perspectives* **2008**, *116*, 39-44, 10.1289/ehp.10753.
2. Jaromir Michałowicz; Bisphenol A – Sources, toxicity and biotransformation. *Environmental Toxicology and Pharmacology* **2014**, *37*, 738-758, 10.1016/j.etap.2014.02.003.
3. Shelby Flint; Tricia Markle; Sarah Thompson; Elizabeth Wallace; Bisphenol A exposure, effects, and policy: A wildlife perspective. *Journal of Environmental Management* **2012**, *104*, 19-34, 10.1016/j.jenvman.2012.03.021.
4. Adeline Colin; Cristina Bach; Christophe Rosin; Jean-François Munoz; Xavier Dauchy; Is Drinking Water a Major Route of Human Exposure to Alkylphenol and Bisphenol Contaminants in France?. *Archives of Environmental Contamination and Toxicology* **2013**, *66*, 86-99, 10.1007/s00244-013-9942-0.
5. Laura Canesi; Elena Fabbri; Environmental Effects of BPA. *Dose-Response* **2015**, *13*, 1559325815598304, 10.1177/1559325815598304.
6. Jone Corrales; Lauren A. Kristofco; W. Baylor Steele; Brian S. Yates; Christopher S. Breed; E. Spencer Williams; Bryan W. Brooks; Global Assessment of Bisphenol A in the Environment. *Dose-Response* **2015**, *13*, 155932581559830, 10.1177/1559325815598308.
7. Sarah A. Vogel; The Politics of Plastics: The Making and Unmaking of Bisphenol A “Safety”. *American Journal of Public Health* **2009**, *99*, S559-S566, 10.2105/ajph.2008.159228.

8. EFSA, European Food Safety Authority. Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs. EFSA Panel on Food Contact Materials E Flavourings and Processing Aids (CEF). EFSA J. 2015, 13, 3978.
9. Commission Directive 2011/8/EU of 28 January 2011 amending Directive 2002/72/EC as regards the restriction of use of Bisphenol A in plastic infant feeding bottles (Text with EEA relevance 4). Available online: https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:026:0011:0014:EN:PDF (accessed on 14 February 2020).
10. Food and Drug Administration (FDA). Food Additive Regulations Amended to No Longer Provide for the Use of BPA-Based Materials in Baby Bottles, Sippy Cups, and Infant Formula Packaging. In 2012, 77 Fed. Reg. 41,899. Available online: https://www.federalregister.gov/documents/2012/07/17/2012-17366/indirect-food-additives-polymers (accessed on 14 February 2020).
11. Laura N. Vandenberg; Russ Hauser; Michele Marcus; Nicolas Olea; Wade V. Welshons; Human exposure to bisphenol A (BPA). *Reproductive Toxicology* **2007**, *24*, 139-177, 10.1016/j.reprotox.2007.07.010.
12. CDC (Centers for Disease Control and Prevention). Fourth National Report on Human Exposure to Environmental Chemicals; CDC: Atlanta, GA, USA, 2013; pp. 1–770
13. Tao Zhang; Hongwen Sun; Kurunthachalam Kannan; Blood and Urinary Bisphenol A Concentrations in Children, Adults, and Pregnant Women from China: Partitioning between Blood and Urine and Maternal and Fetal Cord Blood. *Environmental Science & Technology* **2013**, *47*, 4686-4694, 10.1021/es303808b.
14. SangWoo Lee; Cheolmin Kim; Hyesoo Shin; Young Lim Kho; Kyungho Choi; Comparison of thyroid hormone disruption potentials by bisphenols A, S, F, and Z in embryo-larval zebrafish. *Chemosphere* **2019**, *221*, 115-123, 10.1016/j.chemosphere.2019.01.019.
15. Guo-Min Huang; Xiao-Feng Tian; Xue-Dong Fang; Fu-Jian Ji; Waterborne exposure to bisphenol F causes thyroid endocrine disruption in zebrafish larvae. *Chemosphere* **2016**, *147*, 188-194, 10.1016/j.chemosphere.2015.12.080.
16. Johanna R. Rochester; Ashley L. Bolden; Bisphenol S and F: A Systematic Review and Comparison of the Hormonal Activity of Bisphenol A Substitutes. *Environmental Health Perspectives* **2015**, *123*, 643-650, 10.1289/ehp.1408989.
17. J.I. Cacho; N. Campillo; P. Viñas; M. Hernández-Córdoba; Stir bar sorptive extraction coupled to gas chromatography–mass spectrometry for the determination of bisphenols in canned beverages and filling liquids of canned vegetables. *Journal of Chromatography A* **2012**, *1247*, 146-153, 10.1016/j.chroma.2012.05.064.
18. Chunyang Liao; Fang Liu; Hyo-Bang Moon; Nobuyoshi Yamashita; Sehun Yun; Kurunthachalam Kannan; Bisphenol Analogues in Sediments from Industrialized Areas in the United States, Japan, and Korea: Spatial and Temporal Distributions. *Environmental Science & Technology* **2012**, *46*, 11558-11565, 10.1021/es303191g.
19. Xiaoliu Zhou; Joshua P. Kramer; Antonia M. Calafat; Xiaoyun Ye; 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. *Journal of Chromatography B* **2014**, *944*, 152-156, 10.1016/j.jchromb.2013.11.009.
20. Office of Chemical Safety & Pollution Prevention, EPA. Doc. No.740-R1-4004, TSCA Work Plan Chemical Problem Formulation and Initial Assessment: Tetrabromobisphenol A and Related Chemicals Cluster Flame Retardants 10, 2015. Available online: https://www.epa.gov/sites/production/files/2015-09/documents/tbbpa_problem_formulation_august_2015.pdf (accessed on 14 February 2020).
21. Nuoya Yin; Shaojun Liang; Shengxian Liang; Renjun Yang; Bowen Hu; Zhanfen Qin; Aifeng Liu; Francesco Faiola; TBBPA and Its Alternatives Disturb the Early Stages of Neural Development by Interfering with the NOTCH and WNT Pathways. *Environmental Science & Technology* **2018**, *52*, 5459-5468, 10.1021/acs.est.8b00414.
22. Tyler Malkoske; Yulin Tang; Wenying Xu; Shuili Yu; Hongtao Wang; A review of the environmental distribution, fate, and control of tetrabromobisphenol A released from sources. *Science of The Total Environment* **2016**, *null*, 1608-1617, 10.1016/j.scitotenv.2016.06.062.
23. Yuanyuan Wu; Yanyan Li; Duan Kang; Jingjing Wang; Yanfang Zhang; Dongli Du; Bishu Pan; Zhenkun Lin; Changjiang Huang; Qiaoxiang Dong; et al. Tetrabromobisphenol A and heavy metal exposure via dust ingestion in an e-waste recycling region in Southeast China. *Science of The Total Environment* **2016**, *541*, 356-364, 10.1016/j.scitotenv.2015.09.038.
24. Eriko Yamazaki; Nobuyoshi Yamashita; Sachi Taniyasu; James Lam; Paul K.S. Lam; Hyo-Bang Moon; Yunsun Jeong; Pranav Kannan; Hema Achyuthan; Natesan Munuswamy; et al. Bisphenol A and other bisphenol analogues including BPS and BPF in surface water samples from Japan, China, Korea and India. *Ecotoxicology and Environmental Safety* **2015**, *122*, 565-572, 10.1016/j.ecoenv.2015.09.029.
25. Chunyang Liao; Fang Liu; Ying Guo; Hyo-Bang Moon; Haruhiko Nakata; Qian Wu; Kurunthachalam Kannan; Occurrence of Eight Bisphenol Analogues in Indoor Dust from the United States and Several Asian Countries:

Implications for Human Exposure. *Environmental Science & Technology* **2012**, *46*, 9138-9145, 10.1021/es302004w.

26. Pingqing Fu; Kimitaka Kawamura; Ubiquity of bisphenol A in the atmosphere. *Environmental Pollution* **2010**, *158*, 3138-3143, 10.1016/j.envpol.2010.06.040.
27. Takashi Yamamoto; Akio Yasuhara; Hiroaki Shiraishi; Osami Nakasugi; Bisphenol A in hazardous waste landfill leachates. *Chemosphere* **2001**, *42*, 415-418, 10.1016/s0045-6535(00)00079-5.
28. Tinne Geens; Hugo Neels; Adrian Covaci; Distribution of bisphenol-A, triclosan and n-nonylphenol in human adipose tissue, liver and brain. *Chemosphere* **2012**, *87*, 796-802, 10.1016/j.chemosphere.2012.01.002.
29. Yen Sun; Miki Irie; Naoya Kishikawa; Mitsuhiro Wada; Naotaka Kuroda; Kenichiro Nakashima; Determination of bisphenol A in human breast milk by HPLC with column-switching andfluorescence detection. *Biomedical Chromatography* **2004**, *18*, 501-507, 10.1002/bmc.345.
30. World Health Organization & Food and Agriculture Organization of the United Nations (2011). In Proceedings of the Joint FAO/WHO Expert Meeting to Review Toxicological and Health Aspects of Bisphenol A: Final Report, Including Report of Stakeholder Meeting on Bisphenol A, Ottawa, ON, Canada, 1–5 November 2010. Available online: https://apps.who.int/iris/bitstream/handle/10665/44624/97892141564274_eng.pdf?sequence=1&isAllowed=y (accessed on 14 February 2020)
31. Chunyang Liao; Fang Liu; Husam Alomirah; Vu Duc Loi; Mustafa Ali Mohd; Hyo-Bang Moon; Haruhiko Nakata; Kurunthachalam Kannan; Bisphenol S in Urine from the United States and Seven Asian Countries: Occurrence and Human Exposures. *Environmental Science & Technology* **2012**, *46*, 6860-6866, 10.1021/es301334j.
32. Kou Liu; Jun Li; Shengjun Yan; Wei Zhang; Yaojian Li; Dan Han; A review of status of tetrabromobisphenol A (TBBPA) in China. *Chemosphere* **2016**, *148*, 8-20, 10.1016/j.chemosphere.2016.01.023.
33. Suwen Yang; Shengrui Wang; Hongliang Liu; Zhenguang Yan; Tetrabromobisphenol A: tissue distribution in fish, and seasonal variation in water and sediment of Lake Chaohu, China. *Environmental Science and Pollution Research* **2012**, *19*, 4090-4096, 10.1007/s11356-012-1023-9.
34. Zhi-Cheng Zhu; She-Jun Chen; Jing Zheng; Mi Tian; An-Hong Feng; Xiao-Jun Luo; Bi-Xian Mai; Occurrence of brominated flame retardants (BFRs), organochlorine pesticides (OCPs), and polychlorinated biphenyls (PCBs) in agricultural soils in a BFR-manufacturing region of North China. *Science of The Total Environment* **2014**, *481*, 47-54, 10.1016/j.scitotenv.2014.02.023.
35. Gaud Dervilly-Pinel; Jean-Philippe Antignac; Daniel Zalko; Alain Berrebi; Jean-Pierre Cravedi; Daniel Maume; Philippe Marchand; Fabrice Monteau; Anne Riu; François Andre; et al. Exposure assessment of French women and their newborns to tetrabromobisphenol-A: Occurrence measurements in maternal adipose tissue, serum, breast milk and cord serum. *Chemosphere* **2008**, *73*, 1036-1041, 10.1016/j.chemosphere.2008.07.084.
36. EFSA Panel on Contaminants in the Food Chain (CONTAM). Scientific Opinion on Tetrabromobisphenol A (TBBPA) and its derivatives in food: TBBPA and its derivatives in food. EFSA J. 2011, 9, 2477. Available online: https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2011.2477 (accessed on 14 February 2020)

Retrieved from https://encyclopedia.pub/entry/history/show/7565