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PROPERTIES, THREATS, AND METHODS OF ANALYSIS OF BISPHENOL A AND ITS DERIVATIVES

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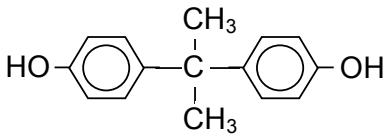
SUMMARY

Excess female sex hormones, estrogenic compounds, can have deleterious effects on living organisms. Estrogen and its derivatives can disrupt natural hormone balance in both men and women. This disruption is of particular importance in the young, because the changes triggered are irreversible. Many compounds, for example organochlorine pesticides, alkylphenols, polychlorobiphenyls, organotin compounds, and bisphenol A and its derivatives, have recently been shown to have effects on humans similar to those of estrogen. This paper is devoted to the last of these compounds, its usage, methods of analysis, and its migration from packaging into food.

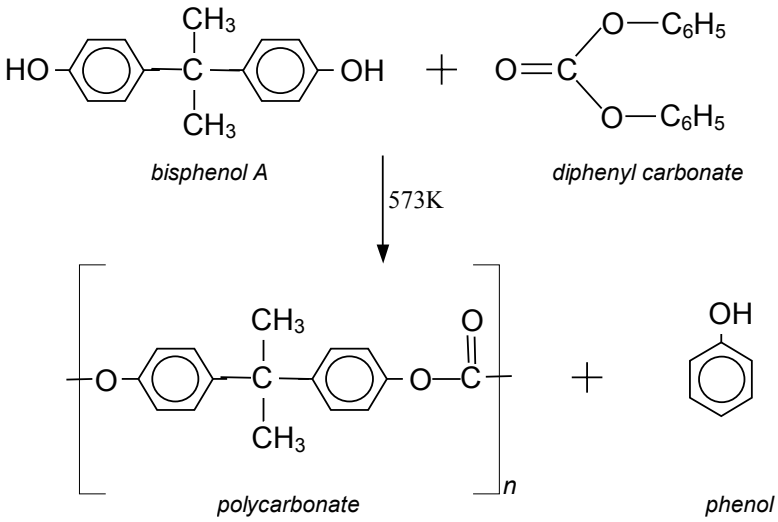
CHARACTERISTICS OF BISPHENOL A

Although the estrogenic properties of bisphenol A (2,2-bis-(4-hydroxyphenyl)propane, BPA) were reported as early as 1936 by Dodds and Lawson [1], only recently have these properties attracted much attention [2–4]. Bisphenol A was first synthesized in 1905. It is obtained by condensation of phenol with acetone in the presence of a strongly acidic ion-exchange resin, in the gel form, as a catalyst. Bisphenol A is a moderately water-soluble compound (300 mg L^{-1} at room temperature) and it dissociates in an alkaline environment (pK_a 9.9–11.3).



BPA, 2,2-bis-(4-hydroxyphenyl)propane

Bisphenol A is the main ingredient used for production of polycarbonate, epoxy, unsaturated polyester, and polysulfone resins [5–11]. The scheme below illustrates the process of synthesis of polycarbonate resins.



Bisphenol A is also used as a component of synthetic plastic materials, e.g. poly(vinyl chloride) [12,13], and as an antioxidant in glues, plastics, and ink [14–18]. In 2001 global production of BPA (started in 1957 in the USA) was estimated to be approximately 2.5 million tons [19].

Materials containing BPA have been used for many applications, for example as a varnish on the inside of cans and as other packaging used for storage of food products, beverages, and pharmaceuticals [20–23]. Polycarbonates have been commonly used for production of components of medical equipment (for dialysis and blood oxygenation), bottles for feeding infants, and kitchen dishes. The wide use of polycarbonates follows mainly from their particular properties – light weight, durability, high tensile strength, high modulus of elasticity, high melting point, and high vitrification temperature [24–30]. Products made of polycarbonates should be marked with the symbol 

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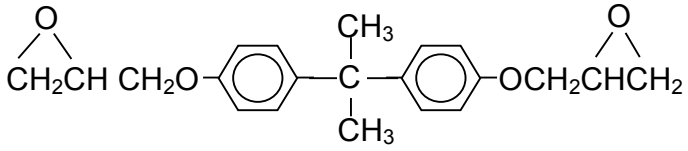
For many years BPA was treated as neutral to human health. Detection of BPA in the natural environment, in drinking water, and in food products (since 1990) has, however, aroused the interest of many researchers. At almost the same time a negative effect of this compound on human health was established. Consequently, in 1996 BPA was classified by the European Commission as a substance of external origin with a harm-

ful effect on human health. Numerous toxicological and biochemical studies have confirmed that bisphenol A has estrogenic properties and an agonistic effect toward the estrogenic receptor. In recent studies [31,32] bisphenol A was classified as a xenobiotic disturbing hormonal balance in humans and other animals, a so-called endocrine disruptor. Bisphenol A has been proved to have estrogenic activity even at concentrations below 1 ng L^{-1} [33–40].

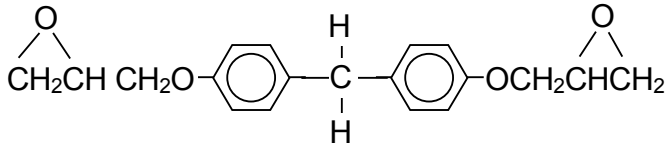
Because of the complexity of the hormone system, the mechanisms of xenobiotic activity leading to endocrine disruption are difficult to identify and are not yet known. The effects of exposure to bisphenol A can be particularly harmful to the fetus, infants, and young children, because of lack of feedback regulating the activity, synthesis, and elimination of hormones. Contact with BPA at that time may lead to irreversible changes appearing even after much delay. A study on mice revealed that a concentration of BPA as low as 20 ppm in drinking water is sufficient to bring about genetic changes in mice fetuses. The changes are mainly a result of disturbance of the distribution of chromosomes in the daughter cells. As a consequence of such changes in mice ovum cells, and hence in fetuses, there may be too many or too few chromosomes. In humans, disturbances of this type are the main reason for miscarriages and genetic defects, e.g. Down's syndrome. Although dangerous effects of BPA on human ovum cells have not yet been established, the processes involved in the creation of ovum cells in humans and mice are similar, so one might foresee that BPA is very dangerous for humans also.

DERIVATIVES OF BISPHENOL A

Two derivatives of BPA, bisphenol A diglycide ether (BADGE) and bisphenol F diglycide ether (BFDGE), are also of industrial importance. The structural formulae of these derivatives are given below.



BADGE, 2,2-bis-(4-hydroxyphenyl)propane-bis-(2,3-epoxypropyl) ether



BFDGE, bis-(4-glycidyloxyphenyl)methane

Bisphenol A diglycide ether (BADGE) is synthesized by reaction of bisphenol A with epichlorohydrin. BADGE is the main compound used in the production of epoxy resins used for internal coating of food-product packaging. It has been estimated that approximately 75% of the epoxy resins currently in use have been produced using BADGE. This compound is also used as a varnish to cover the inside walls of cans and other vessels used to store food products. BADGE has been classified as a mutagenic compound, i.e. as a compound triggering DNA changes (mutations). Although mutagenic substances can also promote neoplasmic diseases, their most threatening effect is initiation of genetic diseases in children of humans exposed to their activity. Although all cancerogenic substances cause mutations, not all mutations are genetically inherited, because mutagenic substances cause changes in DNA in the sex cells. If the amount of damage exceeds the efficiency of the repair apparatus in the sex cells, formation of sex cells with altered genetic information may occur, leading to diseases or defects which become apparent in subsequent generations.

The other derivative, BFDGE, is also used for production of epoxy resins and as a varnish for coating the inside walls of cans used to store food products.

ANALYSIS OF BISPHENOL A AND ITS DERIVATIVES

It is apparent from the recent increase in the number of publications devoted to bisphenol A and its derivatives that interest in these compounds is growing. Many authors have studied migration of bisphenol A and its derivatives into food from the polymer packaging in which it is stored, especially at elevated temperatures (e.g. microwave heating or other thermal process) and as a consequence of incorrect use of packaging [41–45].

The Scientific Committee on Food (SCF), an advisory body of the European Commission on the safety of food, after comprehensive analysis of all aspects of bisphenol A toxicity, has specified the tolerable daily intake (TDI) of bisphenol A as 0.01 mg kg^{-1} body mass per day. On the

basis of the established migration of bisphenol A from packaging into food products, total exposure to BPA from all sources related to food products (including migration from synthetic polycarbonates and epoxy resins) has been estimated to be from 0.48 to 1.6 μm kg^{-1} body mass per day, for adults and children, respectively.

The limits of migration established by the European Commission are 3 mg kg^{-1} body mass for BPA and 1 mg kg^{-1} body mass for BADGE and BFDGE [46]. Table I lists concentrations of BPA occurring in a variety of food products, human blood serum, and umbilical blood [31].

Table I

Concentration of BPA in selected products, human blood serum, and umbilical blood

Food products	0.07–0.42 ppb
Food products for infants	0.1–13.2 ppb
Powdered milk	~45 ng g^{-1}
Water	0.016–0.5 μg L^{-1}
Blood serum	0.46–0.56 ppb
Umbilical blood	0.46–0.62 ppb

Although BPA concentrations in the food products are low, they are used daily or a few times a day, so the dose accumulated could be much higher than is apparent from the table. The problem of exposure to BPA is particularly important for infants and it should also be emphasized that bisphenol A is not the only compound with estrogenic properties; others include pesticides, alkylphenols, and polychlorinated biphenyls.

The polarity of these compounds and their low concentrations cause significant problems in devising appropriate analytical methods. The literature on the analysis of bisphenol A and its derivatives reveals that three techniques, liquid–liquid extraction (LLE) [64,67,68,72,102,111], solid-phase extraction (SPE) [47–55], and solid-phase micro-extraction (SPME) [56, 57] have usually been used for isolation and concentration of these compounds. Liquid–liquid extraction is the most popular technique, because of its ease of application. Solid-phase extraction (SPE), based on use of solid-phase adsorbents, has recently aroused much interest. Sample preparation by solid-phase extraction is not difficult or time consuming. It can be performed with commercially available extraction columns, e.g. those made by J.T. Baker. For determination of bisphenol A the adsorbent C_{18} is usually used. Solid-phase micro-extraction (SPME) is another popular technique recently used for analysis of bisphenol A. In this method no solvents are

needed and the amounts of matrix required for determinations are very small compared with those needed in other methods, e.g. SPE.

Extracts are usually analyzed by high-performance liquid chromatography (HPLC) with different methods of detection (e.g. UV, MS, fluorescence), gas chromatography (GC) in combination with MS, electrochemical methods [58–61], and micellar electrokinetic chromatography (MEKC) [62,63]. A review of the literature on the determination of bisphenol A and its derivatives by gas chromatography is presented in Table II; a similar review for HPLC is presented in Table III. The papers mentioned report determination of bisphenol A in environmental samples, for example surface water, waste water, and underground water, and in food products stored in packaging made from polycarbonates, etc. Bisphenol A has also been detected in tap water stored in infant feeding bottles made of PC, and in human blood.

CONCLUSION

It has been well established and well documented that bisphenol A can be released from polycarbonates. Comprehensive analysis commissioned by many organizations with the objective of protection of the natural environment and control of world industry has shown that the amount of bisphenol A migrating into food products from PC packaging is, in general, below 5 ppm, assuming correct use of the packaging and other products made of PC. Although our research shows [93] that the amount of BPA migrating into food products is low, its concentration in food products must be monitored, because of the high potential risk this compound poses to consumer health. It should be emphasized that release of bisphenol A is favored by elevated temperature (e.g. heating in a microwave oven or when the packaging is subjected to other forms of thermal treatment), improper use of packaging and containers, mechanical cleaning, and use of detergents for cleaning [85,93,127].

It must be emphasized that the amounts of BPA migrating from packaging to food products do not mean PC packaging is a health hazard and should be avoided. The level of BPA migration should, however, be monitored to reassure users continually that this packaging really is safe (assuming correct use). It must also be kept in mind that humans are exposed not only to this one compound but to many potentially risky materials in the environment. Therefore, even if the concentration of each hazardous compound is below a safe limit, their sum can exceed the level tolerated by an organism and trigger negative effects.

Table II

Determination of bisphenol A by gas chromatography

No	Detector	Sample	Detection limit	Sample preparation	Chromatographic data	Ref. no.
1	GC–MS	Rain water, sea water	0.6 ng mL^{-1}	LLE: dichloromethane	CC[a]: HP-1 (30 m × 0.25 mm i.d. × 0.25 μm)	[64]
2	GC–MS	Drinking water	0.005 μg mL^{-1}	SPE: C_{18}	CC: HP-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[65]
3	GC–MS	Drinking water	0.04 μg L^{-1}	SPME: different SPME fiber coatings SPE: LiChrolut EN 100 mg + RP-18 250 mg	CC: HP-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[66]
4	GC–MS	Drinking water	0.2 μg L^{-1}	SPME: fiber coatings-polyacrylate and Carbowax-divinylbenzene SPE: C_{18}	CC: HP-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[57]
5	GC–MS	Drinking water	0.006 μg L^{-1}	LLE: trichloromethane	CC: HP1-MS (30 m × 0.25 mm i.d. × 0.25 μm)	[67]
6	GC–MS	Drinking water	4 ng L^{-1}	LLE: ethyl acetate SPE: C_{18}, PS-DVB	CC: HP-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[68]
7	GC–MS	Blood	5 pg mL^{-1}	SPE: C_{18}	CC: DB-5 (30 m × 0.25 μm i.d. × 0.25 μm)	[69]
8	GC–MS	Drinking water	0.1 ng g^{-1}	SPME: fibers coated with PDMS 100 and 7 μm thickness; PA 85 μm; CW-DVB 65 μm	CC: HP-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[70]
9	GC–MS	Sewage water/sludge	0.125 μg g^{-1}; 0.9 μg mL^{-1}	Soxhlet extraction, supercritical-fluid extraction, accelerated solvent extraction	CC: DB-17MS (60 m × 0.25 mm i.d. × 0.25 μm)	[71]

No	Detector	Sample	Detection limit	Sample preparation	Chromatographic data	Ref. no.
10	GC–MS	Drinking water	0.4 ng L^{-1}	LLE: dichloromethane	CC: HP-1 (30 m × 0.32 mm i.d. × 0.25 μm)	[72]
11	GC–MS	Drinking water	1 ng mL^{-1}	LLE: dichloromethane	CC: DB-35MS (30 m × 0.258 mm i.d. × 0.25 μm)	[73]
12	GC–MS	Blood	0.1 ng mL^{-1}	SPE: IST Isolute C_{18}	CC: DB-1 (30 m × 0.32 mm i.d. × 0.25 μm)	[74]
13	GC–MS	Urine	0.1 ng mL^{-1}	SPE: PS–DVB	CC: DB-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[75]
14	GC–MS	Drinking water	0.6 ng mL^{-1}	LLE: dichloromethane	CC: DB-1 (30 m × 0.32 mm i.d. × 0.25 μm)	[76]
15	GC–MS	Migration from cans into food	No available data	Extraction 3% acetic acid	CC: DB-5 (30 m × 0.25 mm i.d. × 0.25 μm)	[77]
16	GC–MS	Human milk	0.09 ng g^{-1}	SPE: aminopropyl	CC: DB-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[78]
17	GC–MS	River water, sea water	5.3 ng L^{-1}	SPE: Loss CN, Loss X, Loss SI-1, DSC-18, DSC-Si, DPA-6S, Isolute C_{18}, Isolute C_{18}/ENV^{+}	CC: ZB-5 (30 m × 0.25 mm i.d. × 0.25 μm)	[79]
18	GC–MS	Food	0.1 ng g^{-1}	SPME: PDMS, PA, CW-DVB	CC: HP-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[80]
19	GC–MS	River water	0.1 μg L^{-1}	SPE: graphitized carbon black (GCB)	CC: DB-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[81]
20	GC–MS	Drinking water	0.3 μg L^{-1}	Semi-automated hollow-fiber membrane extraction	CC: HP-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[82]
21	GC–MS, GC–MS–MS	Drinking water	0.5 ng L^{-1}	SPE: C_{18}	CC for GC–MS: CP-SIL8 CB (30 m × 0.25 mm i.d. × 0.25 μm) connected to a 5 m × 0.53 mm i.d. deactivated Siltek guard column CC for GC–MS–MS: BPX-5 (30 m × 0.25 mm i.d. × 0.25 μm)	[83]
22	GC–MS	Powdered milk	1.0 ng g^{-1}	SPE: C_{18} Envi-18	CC: DB-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[84]
23	GC–MS	Water from baby bottles	0.1 μg L^{-1}	SPE: ENV+IST	CC: Zebron ZB-5 (30 m × 0.25 mm i.d. × 0.25 μm)	[85]

No	Detector	Sample	Detection limit	Sample preparation	Chromatographic data	Ref. no.
24	GC–MS–MS	Sediments	2.5 ng L^{-1}	SPE: C_{18}-HF	CC: DB-5MS (30 m × 0.3 mm i.d. × 0.25 μm)	[86]
25	GC–MS	Drinking water	0.3 μg L^{-1}	SPE	CC: HP-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[87]
26	GC–MS	Drinking water	0.3 μg L^{-1}	Extraction: with graphitized carbon black (GCB)	CC: DB-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[88]
27	GC–MS	Water	0.04 μg L^{-1}	SPE	CC: HP-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[89]
28	GC–MS	Drinking water	0.6 ng L^{-1}	Extraction: acetone, ethyl acetate, dichloromethane, hexane	CC: DB-1 (30 m × 0.32 mm i.d. × 0.25 μm)	[90]
29	GC–MS	Food stimulant from can	0.2 μg L^{-1}	Extraction: acetic acid	CC: DB-5 (30 m × 0.25 mm i.d. × 0.25 μm)	[91]
30	GC–MS	Drinking water	0.1 μg L^{-1}	SPE: C_{18} SPME: DVB-CAR-PDMS	CC: DB-5MS (30 m × 0.25 mm i.d. × 0.25 μm)	[92]
31	GC–FID	Drinking water	0.5 μg L^{-1}	SPE: C_{18}	CC: CP-SIL 5CB (10 m × 0.53 mm i.d. × 0.25 μm)	[93]

[a]Capillary column

Table III

Determination of bisphenol A by HPLC

No	Detector	Sample	Detection limit	Sample preparation	Chromatographic data	Ref. no.
1	HPLC–FL[a]	Drinking water	3 μg L^{-1}	SPE: C_{18}	MPh[b]: acetonitrile–water 30:70 (%, *v*/*v*) MoS[c]: isocratic elution C[d]: Capcell Pac C_{18} (150 mm × 4.6 mm i.d. × 5 μm)	[94]
2	HPLC–FL	Drinking water	0.03 μg L^{-1}	Extraction: dichloromethane	MPh: methanol–water–acetonitrile 25:26.2:48.8 (%, *v*/*v*) MoS: isocratic elution C: Shandon Hypercarb S (150 mm × 4.6 mm i.d. × 7 μm)	[95]
3	HPLC–UV	Urine	0.1 ng mL^{-1}	LLE: ethyl acetate	MPh: acetonitrile–tetrahydrofuran–water 35:35:30 (%, *v*/*v*) MoS: gradient elution C: ODS-80 (150 mm × 6 mm i.d.)	[96]
4	HPLC–UV	Drinking water	0.36 ng L^{-1}	Extraction	MPh: 20 mM phosphate buffer–acetonitrile 65:35 (%, *v*/*v*) MoS: gradient elution C: Shim-pack VP-ODS (150 mm × 4.6 mm i.d. × 5 μm)	[97]
5	HPLC–ECD	Drinking water	0.36 ng L^{-1}	SPE: C_{18}	MPh: 20 mM phosphate buffer–acetonitrile 65:35 (%, *v*/*v*) MoS: gradient elution C: Shim-pack VP-ODS (150 mm × 4.6 mm i.d. × 5 μm)	[98]
6	HPLC–UV	Milk, butter	1 μg L^{-1}, 3 μg L^{-1}	LLE: acetonitrile SPE: C_{18}	MPh: acetonitrile–water 40:60 (%, *v*/*v*) MoS: isocratic elution C: RP_{18} (150 mm × 4.6 mm i.d. × 5 μm)	[99]
7	HPLC–FL	Honey	20 ng mL^{-1}	SPE: GL-Pak PLS-2 (polystyrene divinylbenzene polymer)	MPh: acetonitrile–water 30:70 (%, *v*/*v*) MoS: isocratic elution C: Capcell PAC C_{18} (150 mm × 4.6 mm i.d. × 5 μm)	[100]

No	Detector	Sample	Detection limit	Sample preparation	Chromatographic data	Ref. no.
8	HPLC–FL	Plastics	0.08 ng mL^{-1}	SPE: C_{18}	MPh: acetonitrile–0.1 M Tris buffer–methanol–tetrahydrofuran 60:10:28.5:1.5 (%, *v*/*v*) MoS: isocratic elution C: Develosil ODS-5 (250 mm × 1.5 mm i.d. × 5 μm)	[101]
9	LC–MS	Sterilized medical devices	N/A		MPh: ethanol-water 10:90 (%, *v*/*v*) MoS: gradient elution C: Symmetry C_{18} (150 mm × 2.1 mm i.d. × 3.5 μm)	[102]
10	HPLC–FL	Solid matrices	0.25 μg L^{-1}	SPE: C_{18}	MPh: methanol–water 60:40 (%, *v*/*v*) MoS: gradient elution C: Synergi Polar-RP 80A (150 mm × 4.6 mm i.d. × 4 μm)	[103]
11	HPLC–UV	Drinking water	0.03 μg L^{-1}	LLE: dichloromethane – acetonitrile	MPh: acetonitrile–water 1:1 (*v*/*v*) MoS: gradient elution C: ODS-80Ts (250 mm × 4.6 mm i.d. × 5 μm)	[104]
12	HPLC–UV	Drinking water	0.2 μg mL^{-1}		MPh: acetonitrile–water 1:1 (*v*/*v*) MoS: gradient elution C: C_{18} (150 mm × 4.6 mm i.d. × 5 μm)	[105]
13	LC–MS	Serum	20 ng mL^{-1}	Direct injection analysis	MPh: acetonitrile–water 40:60 (%, *v*/*v*) MoS: isocratic elution C: Mightysil RP-18 (150 mm × 2 mm i.d. × 5 μm)	[106]
14	HPLC–MS	Drinking water	2 ng L^{-1}	SPE: LiChrolut RP-18	MPh: acetonitrile–water 10:90 (%, *v*/*v*) MoS: gradient elution C: LiChrospher 100 RP-18 (250 mm × 4 mm i.d. × 5 μm)	[107]
15	LC–Coulometric	Mineral water	0.25 pmol	LLE: ethyl acetate	MPh: acetonitrile–water 40:60 (%, *v*/*v*) containing 0.2% H_3PO_4 MoS: isocratic elution C: Intersil ODS-2 (150 mm × 4.6 mm i.d. × 5 μm)	[108]

No	Detector	Sample	Detection limit	Sample preparation	Chromatographic data	Ref. no.
16	LC–MS	Water, fish tissue	0.1 μg L^{-1} 50 ng g^{-1}	SPE: Sep-Pak C_{18}, Sep-Pak NH_2	MPh: acetonitrile–water 30:70 (%, *v*/*v*) MoS: gradient elution C: Zorbax Eclipse XDB-C_{18} (150 mm × 2.1 mm i.d. × 5 μm)	[109]
17	LC–MS	Water	0.2 μg L^{-1}	MASE (microwave-assisted Soxwave extraction) SPE	MPh: solvent A: methanol–water 20:80 (%, *v*/*v*) solvent B: methanol 100% MoS: gradient elution C: Zorbax Eclipse XDB (150 mm × 2.1 mm i.d. × 5 μm)	[110]
18	HPLC–FL	Mineral water, wine	0.25 μg L^{-1} 2.5 μg L^{-1}	SPE: C_{18}	MPh: acetonitrile–water 20:80 (%, *v*/*v*) MoS: gradient elution C: LiChrospher 100 RP-18 (250 mm × 4 mm i.d. × 5 μm)	[111]
19	HPLC–FL	Food	0.02 mg L^{-1}	Extraction: (3% (*w*/*v*) acetic acid and 10% (*v*/*v*) ethanol)	MPh: acetonitrile–water 30:70 (%, *v*/*v*) MoS: gradient elution C: Kromasil 100 C_{18} (150 mm × 40 mm i.d. × 5 μm)	[112]
20	HPLC–UV	Drinking water, river water	0.03 μg L^{-1}	CFLME (an on-line coupled continuous flow liquid membrane extraction and C_{18})	MPh: acetonitrile–water 45:55 (%, *v*/*v*) MoS: gradient elution C: C_{18} Diamonsil (150 mm × 4.6 mm i.d. × 5 μm)	[113]
21	LC–MS–MS	Water	1 ng L^{-1}	SPE: C_{18}	MPh: acetonitrile–water 40:55 (%, *v*/*v*) MoS: gradient elution C: LC-18 Alltima (25 cm × 4.6 mm i.d. × 5 μm)	[114]
22	LC–MS	Drinking water	0.5 ng L^{-1}	SPE: C_{18}	MPh: A (methanol–acetonitrile), B (water), both acidified with 0.5%(*v*/*v*) acetic acid and 0.1% (*v*/*v*) triethylamine MoS: gradient elution C: Hypersil Green Env (150 mm × 4.6 mm i.d. × 5 μm)	[83]

No	Detector	Sample	Detection limit	Sample preparation	Chromatographic data	Ref. no.
23	HPLC–FL	River water	1 ng L^{-1}	SPE: C_{18}	MPh: acetonitrile–water 70:30 (%, *v*/*v*) containing 0.05% trifluoroacetic acid MoS: isocratic elution C: YMC-Pak TMS (150 mm × 4.6 mm i.d. × 5 μm)	[115]
24	HPLC–ECD	Drinking water	0.36 ng L^{-1}	SPE: C_{18}	MPh: 20 mM (sodium) phosphate buffer–acetonitrile 60:40 (%, *v*/*v*) MoS: isocratic elution C: Shim-pac VP-ODS (150 mm × 4.6 mm i.d. × 5 μm)	[116]
25	HPLC–ECD, UV	Drinking water	0.36 ng L^{-1}	Empore disk (47 mm o.d. of SDB-XD – styrene–divinylbenzene)	MPh: 20 mM (sodium) phosphate buffer–acetonitrile 60:40 (%, *v*/*v*) MoS: isocratic elution C: Shim-pac VP-ODS (150 mm × 4.6 mm i.d. × 5 μm)	[117]
26	RP-HPLC–FL	Simulants	29 ng mL^{-1}	Standard mixture BPA in methanol	MPh: acetonitrile–water 35:65 (%, *v*/*v*) MoS: gradient elution C: Pecosphere CRT C_{18} RC (150 mm × 5 mm i.d. × 5 μm)	[118]
27	RP-HPLC–UV	Simulants	0.1 μg mL^{-1}		MPh: acetonitrile–water 30:70 (%, *v*/*v*) MoS: isocratic elution C: Waters Nova Pak (150 mm × 3.9 mm i.d. × 4 μm)	[119]
28	HPLC–UV	Drinking water	0.01 μg L^{-1}	SPE: PRP-1 poly(styrene–divinylbenzene)	MPh: A. water–acetic acid 99:1 (*v*/*v*) B. methanol MoS: gradient elution C: Zorbax Eclipse XDB-C8 (150 mm × 4.6 mm i.d. × 5 μm)	[120]
29	HPLC–MS	Foodstuffs or food simulants	1 mg kg^{-1}	Extraction acetonitrile	MPh: acetonitrile–water 30:70 (%, *v*/*v*) MoS: isocratic elution C: Kromasil 100 C_{18} (150 mm × 0.4 cm i.d. × 5 μm)	[121]

No	Detector	Sample	Detection limit	Sample preparation	Chromatographic data	Ref. no.
30	HPLC–UV–FL	Food	3 μg L^{-1} for FL 30.00 μg L^{-1} for UV	Extraction (*n*-heptane–acetonitrile–water)	MPh: acetonitrile–water 30:70 (%, *v*/*v*) MoS: gradient elution C: Kromasil 100 C_{18} (250 mm × 0.4 cm i.d. × 5 μm)	[122]
31	RP–LC–FL	Drinking water	0.3 pmol mL^{-1}	SPE: C_{18}	MPh: acetonitrile–water 75:25% (%, *v*/*v*) MoS: isocratic elution C: TSKgel SuperOctyl (100 mm × 3.9 mm i.d. × 2 μm)	[123]
32	HPLC–FL	Drinking water	1 pmol mL^{-1}	SPE: C_{18}	MPh: acetonitrile MoS: isocratic elution C: TSKgel ODS-120T (250 mm × 4.6 mm i.d. × 5 μm)	[124]
33	RP-HPLC–UV	Solid samples	0.03 μg g^{-1}	SPE: C_{18}	MPh: methanol–water 60:40 (%, *v*/*v*) MoS: gradient elution C: Synergi Polar-RP 80A (150 mm × 4.6 mm i.d. × 4 μm)	[125]
34	HPLC–UV, FL	Drinking water	0.09 μg g^{-1} for UV 0.04 μg L^{-1} for FL	Extraction: dichloromethane	MPh: water–acetonitrile 75:25 (%, *v*/*v*) M of S: gradient elution C: XTerra C-18 (100 mm × 4.6 mm i.d. × 5 μm)	[126]
35	HPLC–UV	Drinking water	0.2 μg L^{-1}	SPE: C_{18}	MPh: water–acetonitrile 75:25 (%, *v*/*v*) MoS: gradient elution C: LiChrospher 100 RP18 (250 mm × 4 mm i.d. × 5 μm)	[93]

[a]Fluorescence
[b]Mobile phase
[c]Mode of separation
[d]Column

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