

Bisphenol A in food as a result of its migration from food packaging

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1. Introduction

Materials and articles or devices intended to contact with food (Food Contact Materials; FCMs) play a key role in the food industry due to their diverse functions. The packaging is very important in the preservation of food, maintaining both quality and safety, acting as a barrier against factors responsible for chemical, physical and microbiological deterioration. As packaged foods have increasing importance in the diet of populations, mainly in developed countries, toxicological concerns arising from food-packaging interactions have increased (Bernardo, Navas, Murata, & Alcântara, 2015). Migration of plastics components to food such as monomers, additives, dyes, inks, varnishes, among others (Bernardo et al., 2015), may affect the organoleptic properties of food and produce harmful effects on health if not properly controlled and if the levels exceed the toxicological values or legislation (Fasano, Bono-Blay, Cirillo, Montuori, & Lacorte, 2012). Within the last decade, it has become accepted that FCMs are contributors to human xenobiotics' exposure (Joint Fao/WHO Expert Meeting, 2010) due to the worldwide debate on substances like bisphenol A (BPA) and their impact on the endocrine system. The estrogenic activity of BPA was reported for the first time in 1993 (Krishnan, Stathis, Permuth, Tokes, & Feldman, 1993). Although BPA is considered a very weak environmental estrogen, since its affinity for estrogen receptors is 10,000 to 100,000 times weaker than that of estradiol (Vom Saal & Hughes, 2005), a large number of *in vitro* studies have shown that the effects of BPA are mediated by genomic and non-genomic estrogen response mechanisms, with disruption of cellular function occurring at doses as low as 1 pM (0.23 ng/L). Based on the works of Zoeller and co-workers (Zoeller, Bansal, & Parris, 2005), Wetherill *et al.* (Wetherill, Petre, Monk, Puga, & Knudsen, 2002) and Akingbemi *et al.* (Akingbemi, Sottas, Koulova, Klinefelter, & Hardy, 2004) it is also possible to conclude that BPA has the

ability to disrupt the action of thyroid hormone, cause the proliferation of human prostate cancer cells and at very low doses per trillion may block the synthesis of testosterone. Thus, it has become inevitable to place limits on human exposure to these compounds, such as risk management particularly targeted at vulnerable groups as infants and young children. Unfortunately, other biphenols that belong to the BPA family, such as bisphenol S (BPS), bisphenol F (BPF), bisphenol AP (BPAP) and bisphenol AF (BPAF) which have also been used in various industrial applications, also exhibit estrogenic activity with potential toxicity. In addition, most of them when are likened to BPA, exhibit ~~a~~-higher resistance to biodegradability; (European Food Safety Agency, 2013) Feng et al., 2016).

This review covers various aspects of the problematic of BPA in FCMs. The properties and sources of the exposure of BPA are addressed and the most common analytical techniques used for determining the BPA concentration as well as the levels of BPA detected in food as a result of its migration are discussed. Finally, the legal evolution of BPA in FCM over the last two decades will also be focused as well as ~~the~~-future perspectives.

2. Properties of BPA

Bisphenol A [2,2-bis(4-hydroxyphenyl)propane], CAS No. 80-05-7, EEC packaging material Ref. No. 13480, commonly known as BPA, is one of the highest-volume chemicals produced worldwide (Lorber et al., 2015a). It results from the condensation of 2 mol of phenol with 1 mol of acetone in the presence of an acid catalyst (Figure 1). BPA has the chemical formula $C_{15}H_{16}O_2$, with a molecular weight (MW) of 228.29 g/mol, belonging to the group of diphenylmethane derivatives and bisphenols and is a reasonably water-soluble compound (300 mg/L at room temperature). BPA is separate

in an alkaline environment (pKa 9.9–11.3). It was first synthesized in 1891 by the Russian chemist Aleksandr Dianin, but until the early 1930s, its properties and estrogenic activity were not met (Dodds & Lawson, 1936).

In 1938, Dodds and his colleagues studied the biologic properties of various bisphenols and detected the estrogenic properties of bisphenol A. In this study, they concluded that the estrogenic capacity of bisphenols is related to the presence of OH groups in the para position (Bernardo et al., 2015).

In 1953, Dr. Daniel Fox of General Electric and Dr. Hermann Schnell of Bayer AG discovered the ability of bisphenol A to form crosslinks (polymerize) with phosgene to polycarbonate. In its turn, in 1957 (in the USA) and in 1958 (in Europe), the industrial production of bisphenol A was started to be used in the manufacture of polycarbonate (Bernardo et al., 2015).

The presence of hydroxyl groups in BPA determines their reactivity. Similar to other phenols, BPA can be converted into ethers, esters and salts. In addition, BPA undergoes electrophilic substitution such as nitration, sulfonation, or alkylation (Bernardo et al., 2015).

The global BPA production in 2011 reached approximately 4.4 million tonnes. It grew by just over 372,000 tonnes in 2012 surpassing the 4.7 million tonnes mark. Asia is the dominant BPA manufacturer with nearly 53% share of the overall production volume, followed by Europe and North America, holding 25% and 18% market shares, respectively (Merchant Research, 2017). According to the report “Global Bisphenol A Market 2015-2019” (“Global Bisphenol A Market Trends, Forecast 2015–2019,” 2015), the analysts forecast the global bisphenol A market to grow at a CAGR (Compound Annual Growth Rate) of 5.1 percent over the period 2014-2019.

The BPA is part of the group of endocrine disrupting compounds (ECDs) exogenous to the organism substances found in the environment, in food and in products intended for consumers, that interfere with the biosynthesis of hormones, metabolism and the actions resulting from these, causing an alteration in the normal homeostasis of the exposed individual or their descendants (Diamanti-Kandarakis et al., 2009). It has been shown that BPA has an affinity for estrogen receptors and therefore has the ability to produce estrogenic effects. Importantly, the most serious of the ECDs and therefore of BPA effects, have been seen in children of mothers exposed to this agent during pregnancy and breastfeeding. Therefore many studies focus on the evaluation of prenatal exposure and adverse effects on children (Braun & Hauser, 2011). BPA and endocrine disruptors follow a particular behavior in their dose-effect, i.e. the maximum effect occurs at low doses; so it is of interest, to evaluate and analyze the effects occurring at very low concentrations (Vandenberg et al., 2012).

3. Sources of diet exposure to BPA

The general population can be exposed to BPA from dietary (food, drinking water) and non-dietary (dust, air, thermal paper, cosmetics, toys, etc.) sources (Cwiek-Ludwicka, 2015). The studies on the exposure to BPA showed that diet or nutrition is the main source in all population groups. This is due to the migration of BPA into the food from the FCMs, such as polycarbonate (PC) plastics and epoxy resins (Cwiek-Ludwicka, 2015).

In the scientific opinion published by the European Food Safety Agency (EFSA) in 2015, an assessment of dietary exposure to BPA was performed. The highest concentrations of BPA were found in food and packaged products (18.68 µg/kg) when compared with unpackaged foods (1.5 µg/kg) (EFSA, 2015a).

The packaged food categories in which the most relevant concentrations of BPA were observed include cereals, meat, fish, spices, ready to eat food, snacks and ice cream. These categories reach values above 30 µg/kg of BPA (EFSA, 2015a). Among unpackaged foods, the highest concentrations of BPA were found in meat and fish, with values of 9.4 µg/kg and 7.4 µg/kg of BPA, respectively (EFSA, 2015a). According to Repossi et al. (Repossi, Farabegoli, Gazzotti, Zironi, & Pagliuca, 2016) the direct contamination of fish with BPA can be caused by the leach of plastics in oceans. The major source of BPA in seafood is plastic debris. As regards contamination of meat, according to (Deceuninck et al., 2019) the source of BPA is a post-mortem, i.e. after the life of the animals. They suggest the BPA contamination comes from the contact with material containing BPA, for example during the processing. Although, there is another possibility to consider, which is laboratory contamination. Measurement of BPA at very low levels, in particular in biological samples, is challenging due to the potential laboratory contamination. In studies that measure the BPA in human blood samples, this has been a problem (Deceuninck et al., 2019).

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3.1. BPA and Polycarbonates (PC)

BPA is used in the production of Polycarbonates (PC). PCs are thermoplastic polymers produced by two different ways: i) condensation/polymerization reaction of BPA and carbonyl chloride (Figure 2) or ii) melt-transesterification reaction between BPA and diphenylcarbonate. There are a large variety of ordinary products (e.g. baby bottles, water bottles, medical devices) that use PCs (Oliveira, 2015).

BPA migrates from PC to liquid foods through the diffusion of residual BPA present in PC, after the manufacturing process and hydrolysis of the polymer. The release of BPA

from PC containers into food also depends on factors such as the food simulant (e.g. ethanol 10%, v/v, acetic acid 3%, w/v) and its pH, contact time and contact temperature (Mercea, 2009; Hoekstra & Simoneau, 2013; Kitahara, Takahashi, Tsukagoshi, & Fujii, 2010). Authors (Maragou, Makri, Lampi, Thomaidis, & Koupparis, 2008) and (Kubwabo et al., 2009) have observed that BPA migration from PC bottles significantly increased with temperature. Temperature is the critical factor favoring BPA migration from PC bottles to water. (Nam, Seo, & Kim, 2010) showed that the level of migration of BPA greatly increased at temperatures over 80 °C. This is caused by hydrolysis of carbonate linkage and can be avoided by sterilization under 80 °C (Maia et al., 2009). Acidic and alkali solutions cause polymer degradation via hydrolysis, resulting in increased BPA migration as shown by (Oliveira, 2015). Moreover, Biedermann-Brem & Grob (2009) found that an increased pH resulting from the use of hard water strongly increases the liberation of BPA from the PC. They also show that with milk type beverages, the release of BPA from PC is likely to be far lower, since the proteins buffer a neutral pH. After incubation for 8 h, 72 h and 240 h in food-simulating solvents (10% ethanol at 70 °C and corn oil at 100 °C) the BPA migration increased, as obtained by Wong, Leo, & Seah (2005), so they concluded that BPA migration increased with incubation time

3.2. BPA and Epoxy Resins

Epoxy resins are manufactured from a reaction between epichlorohydrin (ECH) and bisphenol A (BPA) (Figure 3). The epoxy resins have good mechanical properties and are used as thermosetting polymers with an extensive range of applications (Oliveira, 2015). This polymer is present in nearly all soda and beer cans and in the most diverse

canned foods such as fish, vegetables and fruits. (Groshart, Okkerman, & Pijnenburg, 2001). Cunha, Almeida, Mendes, & Fernandes (2011) reported the presence of BPA and bisphenol B (BPB) in canned beverages and powdered infant formula in the Portuguese market. They analyzed thirty canned beverages and seven reconstituted powdered infant formula samples, the BPA was detected in twenty-one of the beverages (ranging from 0.03 to 4.70 $\mu\text{g/L}$) and in two infant formula samples (0.23 and 0.40 $\mu\text{g/L}$). Munguía-López, Gerardo-Lugo, Peralta, Bolumen, & Soto-Valdez (2005), carried out overall migration tests of BPA from organosol and epoxy can coatings to a fatty-food simulant and tuna, to verify the effect of heat processing, the effect of storage time and the effect of temperature. They concluded there is no relationship between the coating type and the level of migration detected. Some authors reported that the canned samples subjected to the heating process and/or cans damage by denting presented a significant increase in the migration levels of BPA; however, no sample contained BPA exceeding the European Union limit for migration was found at the time of the study (set at 600 $\mu\text{g/g}$). Nouredine El Moussawi et al. (2018) investigated the migration of BPA from two types of tinplate cans, before and after sterilization, respectively. They observed that BPA levels, after sterilization, increased from an average of 0.15 to 109 $\mu\text{g/kg}$, therefore the BPA migration was around 10.5 $\mu\text{g/dm}^2$ for both types of cans. They found that the temperature and contact time did not have a significant influence on BPA levels in the sterilized cans. In turn, in non-sterilized cans, these two factors have a significant influence on the levels of BPA.

3.3. BPA and Paper Products

Thermal paper is another application of BPA, here BPA is used as a developer because it is efficacious, available, and affordable (United States Environmental Protection

Agency, 2014). Thermal paper is a standard paper grade that has been covered with a thermal reactive layer or thermal sensitive layer. (United States Environmental Protection Agency, 2014). This covering is made from a leuco dye (colorformer), a developer (coreactant), and in some systems, a sensitizer (modifier). Properties like image color, scanning characteristics, and durability are determined by the combination of these components (United States Environmental Protection Agency, 2014).

In the retail sector, the exposure to BPA by a human is through handling once the thermal paper is used primarily in conventional receipts (Kostyantyn Pivnenko, Laner, & Astrup, 2018). Although the paper is recycled, and knowing that some BPA contained in the paper is removed during this process, a fraction of it can remain in the recycled materials and thus contaminate new paper products (Kostyantyn Pivnenko, Laner, & Astrup, 2016). K. Pivnenko, Pedersen, Eriksson, & Astrup (2015) in their experiments have shown that migration of BPA was found in all analyzed waste paper samples. As BPA is only used for a limited range of paper products (i.e. thermal paper, paper, cupboard), this suggests potential spreading of BPA through recycling of secondary waste paper. BPS is an important substitute for BPA, as it was identified in more than 70% of the waste paper samples. No significant differences in BPA and BPS concentrations were observed between source segregated and residual waste paper. Biedermann, Tschudin, & Grob (2010) discovered that the total mass of BPA on a receipt is 250–1000 times higher than the amount of BPA typically found in a food or baby formula can, as well as the amount that migrates from a BPA based plastic baby bottle.

Hormann et al. (2014) found that when combined, absorption of oral and dermal BPA resulted in a rapid and dramatic mean maximum increase in BPA-unconjugated (bioactive) of 7 ng/mL in serum and 20 mg BPA/g of total creatinine in urine within of

90 min. This observation resulted from the experiment when men and women held a thermal paper document immediately after using a hand sanitizer and then eat hand-fried potatoes.

4. Analytical Methods for Determination of Bisphenol A

Several methods for determining BPA in foodstuffs have been developed in the last 10-15 years. These methods require highly sensitive and selective techniques because of the residual levels at which BPA is found and because of the complexity of the food matrices (Chapin et al., 2008). Szczepańska, Kudlak, & Namieśnik (2018) schematically show the most common analytical approaches for the determination of analytes in samples with different matrix compositions.

Extraction and cleanup, prior to instrumental analysis, are the most challenging parts of BPA analysis and are often the critical steps in establishing the detection limits for the methods (Cao, 2012). The development of the techniques of preparation of samples for analysis has, in the last years, unquestionable progress, in which, there was a growing introduction of the concept of green chemistry in the laboratory practice (Szczepańska et al., 2018). According to Table 1 the most ~~used~~ extraction techniques used to determine BPA are: Solid Phase Extraction (SPE), Liquid-Liquid Extraction (LLE), Solid Phase Microextraction (SPME), Stir Bar Sorptive Extraction (SBSE), Ultrasound-Assisted Dispersive Liquid-Liquid Microextraction (UA-DLLME), Pressurised Liquid Extraction (PLE) and Quick Easy Cheap Effective Rugged Safe (QUECHERS). Ferrer et al. (2011) in their work, made optimization of the extraction process of BPA in powdered infant formulas samples and powdered skimmed milk samples, by pressurized liquid extraction (PLE). They varied the PLE apparatus conditions (preheat time, purge time and the statistic time), varied the solvent or

250 mixtures used (because the nature of the solvent is the most significant parameter of the
251 extraction) and varied the PLE temperatures, PLE number cycles and PLE matrix
252 dispersant agents. The optimized conditions established were: ethyl acetate as a solvent,
253 70 °C of temperature, reversed-phase silica C18 as a dispersing agent and three cycles
254 of extraction. Cunha et al. (2011) quantified BPA in canned beverages (soft drinks and
255 beers) and powdered infant formula, using dispersive liquid-liquid micro-extraction
256 (DDLME) as extraction technique as an alternative to the classical liquid-liquid
257 extraction procedures. Therefore, to develop and optimize the DLLME procedure they
258 studied some parameters such as the volume and nature of extractive and dispersive
259 solvents and the quantity of derivatizing reagent. According to both extraction recovery
260 obtained and the volume of the sedimented phase, the extractive/dispersive solvent
261 pairs, were chosen. The appraisal of the extractive solvent volume must take into
262 account that lower volumes enhance the enrichment factor, although reducing the
263 volume of the sediment phase. Taking all these factors into consideration, they
264 concluded that the ~~optimised~~optimized procedure consisted in the injection of a mixture
265 containing tetrachloroethylene (extractant), acetonitrile (dispersant) and acetic
266 anhydride (~~derivatising~~derivatizing reagent) directly into an aliquot of beverage
267 samples or into an aqueous extract of powdered milk samples. On the other hand, Yin et
268 al. (2018) quantified BPA in three kinds of milk, including plastic-wrapped milk, paper-
269 wrapped milk, and bottled milk, using a novel porous aromatic framework (PAFs), as
270 solid-phase extraction (SPE) sorbent, once PAFs possess high surface areas,
271 homogeneous porous distribution and a π - π conjugated array systems. This group
272 synthesized PAF-6 because of the strong hydrogen bonding and inclusion complexation
273 between BPA and PAFs. They showed, that the SPE conditions optimized to achieve
274 high extraction efficiency of the new material towards BPA are: 20 mg of PAF-6, 5 ml

of methanol as eluent, 3 ml/min flow rate, samples with pH 6 and 10 ml of sample volume.

The determination of BPA in food is performed mainly by liquid chromatography (LC) with different detectors (LC/UV, LC/FL, LC/ECD, LC/MS, and LC/MS-MS) or by gas chromatography (GC) coupled with mass detectors (GC/MS and GC/MS-MS) (Tables 2 and 3). For example, if we compare the results, reported by (Jurek & Leitner, (2017,

2018) –where the same samples were analysed by LC-MS/MS and GC-MS/MS, respectively, we verified that equivalent results can be obtained with both methods.

However other techniques have also been developed. For example, for *in situ* determination of BPA in several beverages, Shi, Liang, Zhao, Liu, & Tian (2017) produced a glassy carbon electrode (GCE) modified with molybdenum selenide/reduced graphene oxide (MoSe₂/rGO).

The data in the tables conclusively indicates that the MS detector is the most commonly used for both LC and GC. The major advantages of this detector are its high selectivity, high sensitivity, and universality. Sanchis, Yusà, & Coscollà (2017) and Guerreiro, Oliveira, Melo, Lima, & Catharino (2018) concluded that LC offers the advantage of simplicity over GC since the latter requires a derivatization step. Other techniques such as electrochemical LC detection (LC-ECD) and immunoassays have been used to a lesser extent (Chapin et al., 2008).

Table 2 compiles the conditions of GC-MS and GC/MS-MS methods to determine BPA. These methods present limits of quantification (LOQ) lower than 0.05 mg/Kg, which correspond to the actual SML of BPA according to the EU legislation. Table 3 compiles LC methods (including ~~High-High~~-Performance LC (HPLC) and Ultra High-Performance LC (UHPLC)) that determine BPA with different detectors (e.g.: Fluorescence detector (FL), Ultraviolet detector (UV) or Detector Diode Array (DAD),

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Electrochemical detector (ECD), Mass spectrometry (MS), and tandem mass spectrometry (MS/MS). Quantification limit of these methods is lower than 0.05 mg/kg (Specific Migration Limit (SML) legislated value in EU). However, it can be verified that the choice of the detector, influences the values of detection limit (LOD) and the values of the quantification limit (LOQ) obtained. Grumetto, Montesano, Seccia, Albrizio, & Barbato (2008) verified that the determination of BPA by HPLC-FL when compared to the determination of BPA by HPLC-UV presented lower LOD values (1.1 µg/kg and 20.2 µg/kg, respectively), meaning that FL detector is more sensitive than UV detector. -Comparing the results of BPA 's LODs, determined by LC-FL/MS (Inoue, Murayama, Takeba, Yoshimura, & Nakazawa, 2003) and LC-FL (Kang & Kondo, 2002), are also different, i.e. 20 ng/ml and 2 ng/ml, respectively.-López-Cervantes & Paseiro-Losada (2003) in turn, verified that in the determination of BPA by LC-MS the values of LOD were lower than those using HPLC-FL and HPLC-UV (LOD (LC-MS): 500 µg/L; LOD (HPLC-UV): 30 µg/L and LOD (HPLC-FL): 3 µg/L). Guerreiro et al. (2018) report High-Resolution Mass Spectrometry (HRMS) as a reliable tool, due to its speed and sensitivity -to accurately, characterize several contaminants in food by migration. (Regueiro & Wenzl, (2015) developed and validated a method based on stable-isotope dilution liquid chromatography-tandem mass spectrometry for the analysis of BPA in solid foodstuffs. They proved that to obtain an inexpensive and efficient procedure for the extraction of BPA from complex foodstuffs, the ultrasound-assisted extraction with acetonitrile/methanol (80:20 v/v) proceeded by sample disruption with sand, is the appropriate method. They evidenced that by using SPE with PSA sorbent, a selective clean-up of sample extracts is achieved. They also demonstrated that by applying a derivatization step with pyridine-3-sulfonyl chloride

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(PS chloride) the ESI ionization efficiency of BPA is highly improved, allowing the decrease of the limits of detection (LODs).

In the last years, remarkable progress has been made in the methods used to determine BPA. These new methods allow, for example, developing new, simpler and more effective methodologies to determine BPA in real and complex food samples.

Within the food sector, nanotechnology allows developing packaging materials with new and improved properties. Substances may be added in FCMs, in the form of nanoparticles, to increase the functionality of these materials, which includes an improved barrier, optical and thermal properties. (Q. Chaudhry, Castle, & Watkins, 2017) (Yang et al., 2018), used halides modified Au nanoparticles (NPs) substrates for rapid and sensitive determination of BPA in milk by SERS (Surface-Enhanced Raman Scattering) method with the assistance of sulfates. The halides can be served as cleaning agents to modify gold nanoparticles (Au NPs) substrate for selective SERS detection of BPA. Therefore, the proposed SERS strategy is expected to provide a potential practical application in the field of food safety for the residue detection of the contaminants in foodstuffs. Reguera, Sanllorente, Herrero, Sarabia, & Ortiz (2018) studied the impact that the presence of nanoparticles in food could have on the migration behavior (from FCMs) of substances such as BPA. They evaluated if the release of BPA from PC tableware into food simulants is different in the presence or in the absence of Ag NPs. They concluded that the amount of BPA migrated into simulant B (acetic acid 3%) in the presence of Ag NPs was 13.34 $\mu\text{g/L}$, at least twice the quantity that migrates in the absence of them.

5. Exposure Assessment

Human exposure to BPA occurs through the occupational pathway, environmental and food contact (Pielichowski & Michalowski, 2014).

Occupational exposure occurs mainly through industry workers (Bernardo *et al.*, 2015).

The environmental exposure results from air pollution, water, and soils with BPA (Pielichowski & Michalowski, 2014). There are several non-food applications where

BPA is used, including epoxy resin-based paints, medical devices, dental materials, surface coatings, printing inks, thermal paper (e.g. for cash receipts), flame retardants and common plastic products (e.g. CDs, DVDs) (European Food Safety Authority,

2006; Geens *et al.*, 2012; EFSA, 2015a). The dietary exposure results from the use of polycarbonates plastics for contact with food, or even from the use of epoxy resins in the lining of canned food (Geens *et al.*, 2012). Among the various routes of human

exposure to bisphenol A mentioned above, dietary exposure is the most distressing, since it can reach a greater number of people (Geens *et al.*, 2012). Potential dietary

exposure to BPA should be assessed according to different consumption patterns. For babies aged 0-6 months, according to the Report of Joint FAO / WHO Expert Meeting

2010 (Joint Fao/WHO Expert Meeting, 2010) in this age group, 81% of the exposure to the migration of BPA was from the PC bottles and 19% for liquid infant formulas

packaged in PC containers or metal cans coated with epoxy. Approximately 1% of exposure, results from the contribution of the migration of BPA from an epoxy resin

that is in contact with the powder milk formula. Therefore, in the last few years, restrictive regulations have been implemented in order to protect lactents and children

(see section 6 on Legal status related to BPA in FCM).

Migration tests of chemical substances from FCMs into foodstuffs or food simulants, which simulate the properties of food, could be used for evaluating consumer exposure

to these substances (Cwiek-Ludwicka & Ludwicki, 2014). Since the exposure assessments combine data on concentrations of a chemical substance present in food with the quantity of those foods consumed (EFSA, 2011), it may be evaluated indirectly by quantifying a given migrant into the food or food simulants (Cwiek-Ludwicka & Ludwicki, 2014). There are several factors₂ that directly affect the substance migration rate: the type of packaging material, the concentration of the substance in the packaging material, the chemical nature of food products which are in contact with food package, the temperature, time and also the ratio surface area of the packaging material/amount or volume of the food product (Cwiek-Ludwicka & Ludwicki, 2014). From migration testing into food simulants or from the monitoring of chemical substances in food, migration data for food contact plastics can be obtained (Cwiek-Ludwicka & Ludwicki, 2014). The Regulation (EU) No. 10/2011 (Regulation (EU) No 10/2011, 2011) and amendments, establish the tests that can be performed using food simulants, to evaluate migration. These migration tests are essential due to the analytical difficulties resulting in the analysis of compounds at trace levels in complex food matrixes. In recent years BPA has been discussed, in the years 2006, 2008, 2010 and 2015, EFSA has carried out various studies and has issued a total of 4 scientific opinions about the health risk of consumers with respect to BPA.

In 2006, EFSA conducted a risk characterization of BPA, which included an assessment of exposure to BPA through diet. EFSA established a value of 0.05 mg BPA/kg bw/day as Tolerable Daily Intake (TDI) (European Food Safety Authority, 2006).

In 2008, EFSA made an assessment of toxicokinetics of BPA, which stated that the dependent age differences in toxicokinetics observed in animals and humans after exposure to BPA do not affect the value established as TDI in 2006, reaffirming the proposed value (EFSA, 2008).

399 In 2010, all results of those studies were collected, and the risk of BPA was reassessed.
400 In the EFSA's opinion of 2010, it was concluded that the new studies do not provide
401 scientific evidence that may change the set TDI value. However, in some animal
402 studies, the effects of BPA had some uncertainty previously unobserved and may have
403 toxicological relevance. In these studies, some errors were found in their methodology,
404 so that EFSA concluded, that the results should reconsider a new assessment with newly
405 available data (Leinen, Dalli, Bánáti, & Geslain-Lanéelle, 2010). In 2011, the French
406 Agency for Sanitary Food Safety (ANSES) published a scientific opinion on the risks of
407 BPA, which showed significant differences in the opinion of the EFSA from 2010. This
408 French report emphasized the potential dangers presented by the BPA and the need to
409 reduce their exposure (ANSES, 2011). After this, EFSA considered necessary a deeper
410 reassessment of BPA and its potential risks (EFSA, 2011).
411 Throughout the year 2015, the EFSA publication (EFSA, 2015b) contains a
412 comprehensive assessment of BPA, taking into account the exposure to BPA non-
413 dietary sources (EFSA, 2015b). Another novelty compared to previous reports, has been
414 the approach of a new TDI value, 4µg/kg bw/day. This report concludes that BPA does
415 not poses risks to the health of exposed, however, emphasizes the need to assess in more
416 detail the exposure of non-dietary sources (Cwiek-Ludwicka, 2015).
417 In 2017, in order to ensure a transparent, efficient and rigorous reassessment of
418 consumer safety related to BPA, EFSA published a technical report (EFSA, 2017a). The
419 European Food Safety Authority (EFSA) has taken on the task of developing a protocol
420 detailing the approach and methodology for the hazard of BPA, identification, and
421 characterization (EFSA, 2017a). The overall objective of this risk assessment will be to
422 assess whether new scientific evidence (published as of 2013 and not previously
423 evaluated by EFSA) still supports the current tolerable temporary daily intake (T-TDI)

for BPA of 4 µg/kg bw per day. To pursue the opening goal, this protocol was submitted to a web-based public consultation (EFSA, 2017c). All relevant comments and feedback received through these procedures were considered in this version of the protocol that will be implemented in the next reassessment of BPA.

In January 2018, The European Chemicals Agency (ECHA) has updated BPA in the candidate list as a result of its identification as a substance of very high concern (SVHC).

The update of BPA is related to its endocrine disrupting properties causing adverse effects to the environment (ECHA, European Chemicals Agency, 2018).

6. Legal status related to BPA in FCM

In Europe, the SMLs are established based on the TDI and considering the hypothesis that a person of ~~1-60~~ kg of body weight consumes daily 1 kg of food and that the only way of exposure is from the FCMs.

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The historical evolution of the reference values including tolerable daily intakes and specific migration limits related to BPA in plastic FCMs is summarized in Table 4.

In the case of materials for use as part of the plastic infant feeding bottles, the use of BPA was banned in 2011 (Regulation (EU) No 321/2011, 2011). This restriction was applied from 1st May 2011 in relation to manufacture and from 1st June 2011 concerning its marketing and import into the EU (Regulation (EU) No 321/2011, 2011). Moreover, it is interesting to note that France published in 2012 a specific regulation in which the manufacture, import, export, and marketing of any food package containing BPA was suspended (Law No 2012-1442, 2012).

In the latest publication by the EFSA in 2015, it is concluded that the established TDI (4 µg/kg bw/day) for the population most at risk of exposure (babies, children, and

adolescents). Moreover, EFSA report states that "there are some uncertainties that need to be evaluated and studied in reference to the exposure assessment of BPA non-dietary sources, such as exposure through the thermal paper, cosmetics, and dust" as stated above (EFSA, 2015a). In the near future, it is expected to respond to some of these issues through research that is being carried out by the National Toxicology Program of the US (NTP).

During 2017, under the guidance of a panel specialization in FCMs of EFSA, a protocol project was developed by an international working group of EFSA that will re-evaluate BPA starting in 2018 (EFSA, 2017b).

The Official Journal of the European Union in 12 February 2018 published the Commission Regulation (EU) 2018/213 (Commission Regulation (EU) 2018/213, 2018), on the use of BPA in varnishes and coatings intended to come into contact with food, and revise Regulation (EU) No 10/2011 as regards the use of that substance in plastic FCMs. Therefore in the present situation, BPA migration from varnishes or coatings applied to materials and articles shall not exceed an SML of 0.05 mg BPA/kg of food ~~(mg/kg)~~ (Regulation (EU) 2018/213, 2018). No migration shall be permitted from these materials when they are intended to come into contact with food or special nutritional products for infants and young children (Regulation (EU) 2018/213, 2018)

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7. Conclusions and Future Perspectives

In the last decade, considerable advances occurred in the analytical methodologies used to determine BPA and nowadays its analysis focused on chromatography coupled with mass spectrometry. In the near future, it is foreseen that extraction methods will be as simple as possible even when complex food matrices are analyzed. Moreover, the minimum amounts of solvents will be used to analyze BPA (green chemistry). This is

also related with the capacity of mass detectors, which will continue to show progress and advances regarding resolution, accuracy, and sensitivity, allowing detecting compounds at levels as low as ng/kg or even pg/kg.

However, the problematic of contaminants as BPA is not only related to the substance itself but also with other compounds which can present additive or synergic effects regarding adverse health effects. Therefore, more large scale, in vivo studies are required, in order to clarify some of the concerns, raised in previous epidemiological studies. Namely, concerns related with the exposure to BPA (harmful effects on human development or association with chronic diseases); exposure to different doses; single or combined exposure with other food contaminants; factors related with individuals (e.g. race, age, scholar level, eating habits) and other factors such those related with the country or countries included in the study (developed or developing countries). One of the most effective measures of avoiding deleterious effects of any contaminants, including BPA, it is to avoid or minimize exposure which can be achieved through public sensitization programs. These programs enhance the awareness of the health impact of BPA and other contaminants and allow refinement of risk assessment models that can be used to generate scientific-based intervention strategies targeting human health protection. Moreover, in BPA risk assessment it is important to take into account all its sources of contamination because BPA is a ubiquitous compound.

Nowadays some compounds like bisphenol S are being used to replace BPA and the tendency will continue to appear newer compounds to substitute BPA, but these have also to be subjected to toxicological studies in order to prove their safety.

Another important advance, which is, foreseen to happen in the next following years, relates to new packaging systems. Responsive packaging systems are predicted to suffer considerable advances and massively increase in the next decade to allow food safety

monitoring (these have only information function) or remediation (they also have a corrective function) of food contaminants such as BPA.

The main challenges in the development of these systems are their efficiency, legislative restrictions, difficulties to prove their safety, the scale-up at the industrial level and to have a low environmental impact due to ecological concerns. Therefore, bio-based plastics and bio-nanocomposites are preferred over conventional non-renewable based and or non-biodegradable systems. Ideally, it would be of great interest to have a responsive bio-packaging that allowed to detect the levels of BPA and to have a corrective function if the migration levels exceeded the permitted levels.

Acknowledgments

This work was supported by FCT, through IDMEC, under LAETA, project UID/EMS/50022/2019 and National Institute of Health Dr. Ricardo Jorge through the project “Development of methodologies for the evaluation of polymeric food packaging components and determination of their structural and mechanical properties” (2016DAN 1289).

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Table 1: Methods to extract BPA and levels of migration from plastics and cans to food simulants or foods.

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
PC water carboys or baby bottles	Miglyol 812 10% (v/v) ethanol/water Infant formula Apple juice Bottled water	Bottled water: SPE Methanol and chloroform Food simulating liquids or foods: analyzed directly	July 1995/ Washington (USA)	Baby bottles: 0.03-5.9 $\mu\text{g}/\text{cm}^2$ Bottled water: 0.1 - 4.7 ng/L	In normal use conditions, there was no migration or hydrolysis in baby bottles. Under exaggerated conditions PC undergoes hydrolysis, augmenting BPA concentrations and migration to food simulants. BPA residues were found in all the waters tested.	(Biles, McNeal, Begley, & Hollifield, 1997)
PC Baby bottles	water; 10 % ethanol; 15% ethanol	Direct injection	2001, 4 different brands of PC baby bottles, manufactured and bought in Argentina.	BPA: 2.5 $\mu\text{g}/\text{L}$	An alternative procedure for BPA quantification is the use of HPLC with amperometric detection. The values are below the limit for specific migration.	(D'Antuono, Dall'Orto, Balbo, Sobral, & Rezzano, 2001)
PC baby bottles	Water	Water extraction: SPE; Methanol and acetone		New bottles: 0.11-0.43 $\mu\text{g}/\text{L}$ 51 days of use: 3.7-17 $\mu\text{g}/\text{L}$ 169 days of use: 2.5-15 $\mu\text{g}/\text{L}$	, Even with repeated use none of the bottle samples exhibited levels of migration that exceed the TDI, The increased migration levels may be due to polymer degradation.	(Brede, Fjeldal, Skjevrak, & Herikstad, 2003)
Food wrapping stretch film (7 samples): PVC or PE	Food simulants: water, 3% acetic acid, olive oil	Films: LLE, acetonitrile	Local supermarkets in Santiago de Compostela, Spain	40 - 100 mg/Kg in 3 of the 5 PVC films and 500 mg/Kg in another Migration: 3- 31 $\mu\text{g}/\text{dm}^2$	BPA was only detected in PVC. Migration was less than 0.1 mg/dm ² .	(López-Cervantes & Paseiro-Losada, 2003)
PC baby milk bottles	10 % Ethanol and corn oil	10% ethanol: injected directly in the HPLC-FL; corn oil: extracted with n-hexane and methanol: water (1:1), 30 min, the lower aqueous phase was injected into the HPLC-FL	March and April 2002/ 28 different brands of PC baby milk bottles (manufactured in China, Germany, Hong Kong, Indonesia, Italy, Japan, Korea, Malaysia, Singapore, Taiwan, Thailand and UK were bought in the Singapore market.	In 10% ethanol = 0.64 $\pm$ 0.48 $\mu\text{g}/\text{in}^2$; Incorn oil = 0.43 $\pm$ 1.25 $\mu\text{g}/\text{in}^2$	The results indicated that there is no health risk to infants from the actual use of PC milk bottles.	(Onn Wong et al., 2005)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
Bottles of PC	Water	Headspace SPME	A local store in Ottawa (Canada)	In water after being heated at 70 °C for 6 days: 228 - 521 µg/L or 0.26 - 0.90 µg/cm ²	To reduce the exposure to BPA, the contact time of infant formula should be kept to a minimum if they have to be warmed up in a microwave, and the leavings should be discarded. It is not encouraged to fill in with hot water or heating in the microwave PC reusable water bottles.	(Xu-Liang Cao & Corriveau, 2008)
PC baby bottles	Water	SPE	18 different types of bottles from different brands: 10 major brands sold across Europe, 3 local brands from the UK, 3 from the Netherlands and 2 local brands from Germany	<LOD- 0.7 µg/L	All levels were well below the specific migration limit of 0.6 mg/Kg specified for bisphenol A (Commission Directive 2004/19/EC)	(Ehlert, Beumer, & Groot, 2008)
Prepack, PP, HDPE bottles, Tetra Brik	Pure milk, soybean milk	SPME	Local supermarket in Lanzhou, China	Pure milk Prepack - < LOD - 2.6 ng/mL HDPE - 1.6 ng/mL Plastic- < LOD Soybean milk Tetra Brik - < LOD	The concentration of BPA in all milk samples studied was lower than the legislative limits recommended by the European Commission.	(Liu, Ji, Zhang, & Liu, 2008)
Baby bottles of PC (31 samples)	Aqueous food simulants (water and 3% acetic acid, w/v)	Direct injection	Greek market	2.4 - 14.3 µg/Kg when boiling water is poured into PC baby bottles, mainly during the first eight cycles of such use	Temperature is the critical factor favoring BPA migration from PC bottles to water. The values for estimated dietary exposure for infants aged up to 1 year old are far below the recently established TDI	(Maragou et al., 2008)
PC baby bottles	Water Tea	Direct injection	Baby bottles: St. Louis, USA and Avent Suffolk, UK Water: Küsnacht and Zurich, Switzerland	Microwave boiling 5 min (max): <LOD-8.1 µg/L 5 min, water previously boiled: 64 µg/L 60 min: 86 µg/L Pan boiling Tea for 5 min: 0.8 µg/L Water for 5 min: 0.8 µg/L	An increased pH resulting from the use of hard water substantially increases the liberation of BPA from the PC. With milk-type beverages, the liberation is likely to be far lower since the proteins buffer a neutral pH. Boiling in a pan does not result in as high BPA release as may result from microwave heating. Boiling water that has already been boiled before resulted in <u>the</u> highest BPA concentrations.	(Biedermann-Brem & Grob, 2009)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
PC, LDPE, HDPE, vinyl acetate, "BPA free" baby bottles Baby bottle liners	low- and high-alcoholic foods simulant: 10% ethanol/ HPLC water solution fatty foods (e.g. infant formula) simulant: 50% ethanol/ HPLC water solution	SPE with derivatization with MTBSTFA.	Baby bottles and bottle liners supplied by the Consumer Product Safety Bureau, Health Canada	PC baby bottles 40 °C - 0.12 µ/L (average) 60 °C - 1.77 µ/L (average) Non-PC baby bottles and liners: < 0.1 µ/L	BPA migration from PC bottles increased with temperature. Migration tests conducted at high temperature revealed that non-PC baby bottles and baby bottle liners contain only trace levels of BPA, constituting an alternative.	(Kubwabo et al., 2009)
PC containers	Rice Meat Water	SPE with acetonitrile	Korea	Hot rice - 6 to 18 µg/Kg Hot meat - 5 to 15 µg/Kg Boiling water - 1.3 to 2.5 µg/Kg	Only heating the rice and meat by microwave produced migration of BPA. Storing boiling water in the PC containers produced migration. In all of the cases, the levels were far lower than the legislation limits.	(Lim, Kwack, Kim, Kim, & Lee, 2009)
PC baby bottles	A solution of detergent or bleach in distilled water	Direct injection	Baby bottles bought in a local supermarket, produced in China	BPA levels detected were about 500 times higher than the control and the concentration kept high even after rinsing the PC samples 3 times.	Dishwashing detergents may increase the BPA release while the detergent is in contact with the PC. The results were in a range from 0.012 to 67 mg/L,	(Maia et al., 2009)
Plastic containers	Rice-prepared dishes	Extraction (with acetonitrile and n-hexane- used to remove fat traces) and derivatization (ethyl acetate/BSTFA/pyridine, 2 : 1 : 1; v/v/v)	Supermarkets and a production plant in Seville, Spain	10-100 ng/g	The levels of BPA in rice-prepared dishes are unlikely to be of concern to adult health.	(Zafra-Gómez, Morales, Ballesteros, & Navalón, 2009)
PC Baby bottles	Water	<i>in situ</i> derivatization with acetic acid anhydride followed by SBSE - thermal desorption	Two commercial brands of PC baby bottles were tested.	BPA (PC baby bottles): 6-13 ng/L; BPA (PC baby bottles after sterilization): 20-90 ng/L; BPA (PC baby bottles heated at 85 °C): 1.5 µg/L.	The higher the temperature, the more BPA was released from the bottle. After a few heating cycles the released concentration became constant. At a normal use of the baby bottle, the released BPA quantities are neglectable.	(De Coensel, David, & Sandra, 2009)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
Packaged milk	Bovine milk	Milk was extracted with acetonitrile followed by phase separation with NaCl. After centrifugation, the extract was purified with C18 sorbent material.	-	-	The method LC-MS/MS validated in this study showed to be rapid and simple, with the capacity for identifying and quantify BPA in bovine milk samples.	(Malone, Elliott, Kennedy, & Regan, 2010)
PC baby bottles	Distilled water	Direct injection	PC baby bottles, bought in a local supermarket, in Spain, produced in China.	Control samples: Lot A 97 µg/L; Lot B 47 µg/L	. The values founded for BPA were below the limit established by EU Legislation.	(Maia et al., 2010)
PC baby bottles	Water	Extraction with methylene chloride, hexane, acetonitrile-Anthracene-d10 used as an internal standard	Local supermarket in Hyoja-Dong, Republic of Korea	Brand-new bottles: 0.03 ppb at 40 °C; 0.13 ppb at 95 °C 6 months of use: 0.18 ppb at 40 °C; 18.47 ppb at 95 °C	The level of migration of BPA greatly increased at temperatures over 80 °C. This is caused by hydrolysis of carbonate linkage and can be avoided by sterilization under 80 °C.	(Nam et al., 2010)
Water bottles, caps, caps septa: PC, HDPE, LDPE, PET, and PS	Water	SPE Ultrasonic extraction method UNE-EN 13130 method		Bottles PET: <LOD HDPE:<LOD PC: 1.870-3.423 µg/dm ² Caps HDPE: <LOD-0.145 µg/dm ² LDPE: <LOD-0.128 µg/dm ² Septa PS: <LOD-0.136 µg/dm ²	BPA was detected in all PC bottled waters analyze but below the legislative values. Even so, it may contribute to the total daily intake of this compound considering all types of food.	(Guart, Bono-Blay, Borrell, & Lacorte, 2011)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
PC baby bottles	Simulants (3% acetic acid, 50% ethanol) and reconstituted infant formula	LLE, acetonitrile followed by SPE	2008- 2010, the Spanish market	Most of the migration results assay the results were below the LOD. In 4 commercial brands, migration into the simulant 50% ethanol was detectable and BPA was only detected in 2 samples of infant formula	Migration results complied with EU regulations.	(Santillana et al., 2011)
PC and PES baby bottles	50% ethanol	Sterilization	40 PC baby bottles from 9 European countries 30 PES baby bottles from 12 European countries November 2009–January 2011	PC bottles <LOQ in 80% 0.33-1.83 µg/Kg in 20% PES bottles	The probability of migration of BPA is very low and it remains at very low quantities from PC bottles and the results also suggest the absence of release from PES bottles.	(Simoneau, Valzacchi, Morkunas, & Van den Eede, 2011)
PCcarboys	Water	-	June 2010, 45 brands from a local store in Ankara and Istanbul, Turkey	4 °C for 60 days: Not detected 20 °C for 60 days: 0.001 mg/Kg 35 °C for 60 days: 0.003 mg/Kg	The estimated time-dependent level of BPA migration would take 1200 days (32 years) at 35 °C for reaching the BPA level to the EFSA's SML (0.6 mg/Kg). The results indicate that exposure of BPA by the consumption of bottled water would be extremely low.	(Erdem & Acar, 2012)
PC, PP, PA, Tritan TM and silicone baby bottles	50% Ethanol	Extraction with isooctane	2010, European Union, USA, Canada (provided by National Reference Laboratories)	PA baby bottles: 0.5-1000 µg/Kg Tritan TM, PP, and silicone baby bottles: BPA not detectable	The migration of BPA was identified in PA bottles in relevant amounts (up to 1 mg/Kg).	(Simoneau, Van den Eede, & Valzacchi, 2012)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
Drinking Bottled Water	Water	LLE/ dichloromethane	Seven brands of bottled drinking water in Riyadh, Saudi Arabia. A set of seven different brands of bottled water was purchased from those stored in indoors while the second set (the same brands as those in the first set) was set was purchased from those stored outdoors.	bottled water stored indoors: 4.03 ng/L bottled water stored outdoors: 7.5 ng/L	Significant amounts of BPA leached from bottle containers into the water. Long storage of bottled water under direct sunlight should be avoided to reduce the risk of human exposure to BPA.	(Elobeid et al., 2012)
Baby Bottles (PP or PC)	Distilled water; Water–acetic acid 97:3 (v/v); Water–ethanol 50:50 (v/v)	Cold and Hot Sterilization	Samples were representative of various brands of baby bottles available in the Italian market.	HPLC-MS/MS= 3.3 µg/mL; CL-ELISA = 4.5 µg/mL ; LFIA= up to 1000 µg/mL	Only one sample resulted clearly positive both in the CL-ELISA and in the LC/MS/MS assay. The positive sample was the one obtained from the third migration cycle under microwave of the PC bottle filled with the simulant C and which was not boiled for 5 min before starting the migration tests. All other samples were below the limit of quantification of the quantitative methods and then substantially below the admitted limits set by regulations in force.	(Maiolini et al., 2014)
Bottled products	-Coca-Cola -Green tea -Milk -Milk powder	UA-DLLME combined with derivatization with acetonitrile, EASC solution, sodium bicarbonate buffer (pH 10.8) and 25% acetic acid solution	purchased from a local store in Qufu City, China	Soft drinks: 5.3 to 78.9 ng/L; BPA was detectable in two milk powder samples and one milk sample, at levels of 0.8, 8.4, and 128.7 g/Kg;	According to the TDI of the EFSA, the results in this study showed that BPA, OP, and NP were present in soft drinks and dairy products but at very low levels and within the limits of the TDI.	(Lv et al., 2014)
Plastic bottles; Tetra Pak packages and Metal Cans	Soft drinks/juice and food products.	Soft drinks: Degassed in an ultrasonic bath, Centrifuged and added acid formic and IS. Condition with dichloromethane–methanol–water (1:1:1). Elution with methanol–dichloromethane (1:1), redissolved in 100 µl methanol. Canned foods: LLE	Greek market in 2014. 12 plastic bottles, 5 tetra pack packages and 10 metal cans.	Soft drinks: 0.4 to 10.2 ng/ml; Juices: 0.61 to 82.5 ng/ml; Meat products: 0.58 to 98.0 ng/ml; Seafood: 0.9 to 550.5 ng/g; Sauces: 0.2 to 21.0 ng/g; Corn: 0.9 to 230.8 ng/g; Tomatoes: 0.31 to 109.7 ng/g; Vegetables: 0.1 to 1858.7 ng/g.	Analytical methodologies were successfully applied for the determination and quantification of BPA in foodstuffs collected from the Greek market. The determined levels of BPA are below the recommended European Commission migration Limit.	(Tzatzarakis et al., 2017)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
Plastic PET bottles and Metal Cans	Water and Beverages products (cola, diet cola, ginger ale, ~~iced~~ Iced Tea).	SPE	April 2017/Ottawa (Canada)	PET bottle: [0.011, 0.031] ng/g Metal can: [0.16, 0.32] ng/g	SPE of large sample volume can improve the detection limits for the analysis of bisphenols in water and beverage products. For the more complex beverage products, improvement in detection limits may not necessarily be proportional to sample volumes for all bisphenols depending on the interferences and noise levels around the analytes.	(Xu-Liang Cao & Popovic, 2018)
Plastic packing	Milk	SPE with a porous aromatic framework (PAF-6) as solid-phase extraction sorbent.	All samples were purchased from a supermarket in Zhengzhou, China. They are the same brand and produced by the manufacturers on the same day.	0.12 µg/mL	PAF-6 exhibited high selectivity for BPA by the strong hydrogen-bonding interactions. The developed method featured good precision and accuracy, and it was successfully applied to analyze trace BPA in milk and its packing samples.	(Yin et al., 2018)
Plastic packing	Hotpot seasonings (grease-rich food).	SPE with Carb/PSA as composite fillers.	30 hotpot seasoning samples from various local supermarkets in China.	BPA not detected.	SPE with composite packings was used to remove highly oil-containing impurities. HPLC-MS/MS method was established for ~~the~~ simultaneous analysis of two bisphenols and three alkylphenols in hotpot seasoning. This method was confirmed to be suitable for the accurate determination of phenols in hotpot seasoning.	(Hao et al., 2018)
Plastic	Baby Food	SPE followed by a clean-up step with a mixture of dispersive-SPE sorbents (C18 and PSA) and magnesium sulfate.	15 ready-to-eat plastic packaged baby food samples from local supermarkets in Granada (Spain), including 12 fruit and milk-based baby foods, and 3 meat and fish-based baby foods.	BPAF and BPF: not detected. BPA quantified in one sample. BPS: 11.7 to 49.2 ng/g ⁻¹ BPB: 1.1 to 8.5 ng/g ⁻¹ BPP: 1 to 7.7ng/g ⁻¹ BPE: 1 to 2 ng/g ⁻¹	BPS was the most abundant compound found in ~~ready-ready~~ -to-eat plastic package baby food samples, which is in agreement with the replacement of BPA with BPS in industrial plants	(García-Córcoles et al., 2018)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
PP, PES, PA and PET	Baby bottles	SPE	Eleven different brands of baby bottles from the Italian market.	PES (40°C): 13.80 ng/mL PES (80°C): 23.20 ng/mL PP (microwave heating 40°C): 102.18 ng/mL PP (80°C) not detectable levels	Although our results support a low extent of leaching of BPA into the foodstuff, they highlight the need of regular and accurate monitoring of Endocrine Disrupting Chemical release even if the nature of the plastic material would not allow their release	(Russo et al., 2018)
Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
Epoxy-coated cans	Infant formula concentrates (with 7% and 8% (w/v) fat and intended for a 1:1 dilution (v/v) with water)	SPE	purchased in suburban Maryland and Virginia near Washington, DC, during January and February 1996	0.1 - 23.2 ppb	The amount of BPA detected in the samples analyzed is among 0.1 and 13.2 ppb and in 14 samples 4 presented BPA amount higher than the specific migration limit established by the UE in force at the time of the study	(Biles, McNeal, & Begley, 1997)
Cans for tuna and jalapeño pepper	Aqueous food simulant (distilled water)	Simulant evaporated to dryness and redissolved in acetonitrile	Cans from Mexican suppliers. Tuna cans - Productos Pesqueros de Guaymas, S.A. de C.V.; Jalapeño pepper cans - Herdez, S.A. de C.V.	0.6-83.4 µg/Kg	There is no effect of heat treatment on the migration but storage temperature did not show any effect in BPA migration from tuna cans, just from jalapeño pepper cans. (Different cans for different foods)	(Munguia-Lopez & Soto-Valdez, 2001)
Cans	Canned fruits and vegetables (corn, mushrooms, asparagus, oranges, peaches, pears, and pineapples)	Acetonitrile (solid portion) Solid phase extraction (SPE) (aqueous portion)	Supermarkets in Japan (products of Japan, China, United States)	Solid portion: < LOQ-95.3 ng/g Aqueous portion: < LOQ The maximum total amount of BPA in food cans: 11 µg	BPA concentrations in the solid portion were higher than in the aqueous portion. BPA might migrate from the aqueous portion to the solid portion during storage.	(Yoshida et al., 2001)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
Cans (that have highly cross-linked thermoset resins)	Canned food: Fish in aqueous media, vegetables, beverages, soup, desserts, fruit, infant formula, pasta, meat products	LLE For fatty samples: a mixture of n-heptane and acetonitrile (1:1) For non-fatty samples (vegetables, soup, desserts, pasta and infant formulae): acetonitrile	January to November 2000/retail outlets in the south of England	BPA was quantified in 37 from 62 samples at levels < 0.07 mg/Kg and one sample with 0.38 mg/Kg	The levels of BPA identified in canned foods in this study are unlikely to be of concern to health, and there is no reason for consumers to change their source of foodstuffs as a result of these findings.	(Goodson, Summerfield, & Cooper, 2002a)
Cans	Decaffeinated and non-decaffeinated instant coffee	Extraction with ethyl acetate and chloroform, dried, eluted with ethyl acetate, evaporated using a nitrogen stream and resolved with 10ml mobile phase	Cans used for containers of beverages and coffee from manufacturing plant; Coffee from a grocery in Japan	66.2- 84.0 ng/mL	Other components in coffee than caffeine, or, other mechanisms can have an effect on increasing BPA migration from the can coating.	(Kang & Kondo, 2002)
62 different canned foods	-10 different types of canned vegetables -5 different types of desserts -16 different types of miscellaneous (ex.: infant formulas, spaghetti in tomato sauce, hot dog...) -10 different types of canned fish -11 different types of beverages -10 different types of canned soup	Food with fat content: Extraction with n-heptane and acetonitrile, filtered, the second extraction with acetonitrile and filtration, the two were combined and treated with anhydrous sodium sulfate for and the solvent decanted into a 50-ml measuring cylinder. Food with low-fat content: the same but without de n-heptane	purchased from retail outlets in the UK from January to November 2000	Vegetables: 0.009 to 0.048 mg/Kg Desserts: two n.d. ; 0.007 mg/kg Miscellaneous: five n.d.; <LOQ to 0.422 mg/Kg Fish: one n.d.; 0.01 to 0.044 mg/Kg Beverages: ten n.d.; <LOQ mg/Kg Soup: Six n.d.; <LOQ to 0.021 mg/Kg	BPA was found in 38 samples, but in all cases levels of BPA found were much lower than the specific migration limit established by the UE.	(Goodson, Summerfield, & Cooper, 2002b)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
Epoxyphenolic coated cans	Canned food: soup, minced beef, evaporated milk and carrots Food simulant: 10% ethanol	LLE For cans: acetonitrile Foods and food simulant: n-heptane	Epoxyphenolic coated cans from UK supplier; Canned foods: UK supermarket	80-100% of the total BPA presented in the coating has migrated directly after can processing, sealing and sterilization.	There was no increase in BPA migration, associated with heating the food in the can, damage to the can or extended storage of food cans when the food is consumed at the end of its declared shelf life.	(Goodson, Robin, Summerfield, & Cooper, 2004)
Cans with epoxy resin protective coating	beverages, fruits, vegetables, fat containing products (like goulash)	Sol-Gel immunoaffinity chromatography	2003-2007, supermarkets in Austria	Canned beverages: <LOD-0.7 ng/mL Canned vegetables: 8.5-35 ng/g Canned fruits: 5.0-24 ng/g Canned fat-containing products: 2.1-37.6 ng/g	All samples contained BPA levels significantly lower than the limiting value.	(Braunrath, Podlipna, Padlesak, & Cichna-Markl, 2005)
Tuna cans coated with an epoxy resin or organosol and epoxy resin	Fatty-food simulant (sunflower oil); tuna in oil	Simulant evaporated to dryness and redissolved in acetonitrile	2000-2003 Local supermarkets in Hermosillo, México	Fatty food simulant (NHP): <LOQ-186.1 µg/Kg Heat process applied: 403.6-646.5 µg/Kg Epoxy resin: 11.3-138.2 µg/Kg Combination: <LOQ-21.9 µg/Kg Tuna (NHP): not detected (n.d.) -27.4 µg/Kg Epoxy resin: n.d.-105.4µg/Kg Combination: n.d.-57.7µg/Kg	Most of the BPA migrated during the heating process. No relationship between the coating type and the level of migration was found.	(Munguía-López et al., 2005)
Cans	Canned food: vegetables, fruit, fish, soup and sauces, canned meat, spaghetti and baked beans, infant foods, beverages and miscellaneous	LLE, Low-fat samples: acetonitrile and derivatization with acetic anhydride Samples with > 1% fat: acetonitrile/trimethylpentane (50:50) Soft drinks: analyzed directly	November 2003 - February 2004, retail outlets in Christchurch, New Zealand	< 10- 29 µg/Kg, except for individual samples of tuna, corned beef and coconut cream, which were 109, 98 and 191 µg/Kg	The levels of BPA identified in canned foods are unlikely to be of concern to adult health, and there is no reason for consumers to change their consumption patterns as a result of these findings.	(Thomson & Grounds, 2005a)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
Cans	Liquid formula products	SPE followed by derivatization with acetic anhydride	October 2007, local grocery in Ottawa	2.27 - 10.2 ng/g	The maximum probable daily intake was lower than the daily intake for BPA established by Health Canada. Health Canada established the provisional tolerable daily intake for BPA at 25 g/Kg of body weight per day.	(Xu-Liang Cao et al., 2008)
Cans	Canned food Fish - tuna, shrimp, mackerel, sardine, squid Vegetables - tomato, asparagus, mushroom, carrot juice Sauces - tomato, white, gratin, demi-glace Others - quail eggs and coconut milk	Extraction with acetonitrile and purification using Oasis-HLB with 15% ethanol and peritoneum ether. SPE with Oasis HLB (Waters, Milford, MA) LC-grade EtOH and acetonitrile (Wako Pure Chemicals) were used.	Supermarkets in Chiba, Japan	Fish: n.d.–30 ng/g Vegetables: n.d.–25 ng/g Sauces: 0.9–235 ng/g Others: 27–31 ng/g	BPA did not exceed acceptable levels	(Yonekubo, Hayakawa, & Sajiki, 2008)
Cans for Peeled Tomatoes (EP lining and LB- Low BADGE coating)	Canned tomato of different brands	SPE	Bought in Italian supermarkets	20.5 µg/Kg to 115 µg/Kg,	In this study, the values of the BPA levels show that all the samples are below the limit established by EU Legislation. They conclude that the quantity of BPA in the tomatoes does not necessarily arise with the time that they are packaged in cans.	(Grumetto et al., 2008)
Cans	Tuna, mackerel, sardines, mussels, meatballs and lean pork	Conservative microextraction	Supermarkets in Córdoba, Spain	Fish: 20-129 ng/g Meat: < LOD - 37 ng/g	Coacervates of decanoic acid reverse micelles constitute a valuable alternative to the current methodologies available for the extraction of BPA from canned fatty foods - simple, rapid and almost solventless. Concentrations of BPA were in all cases below the specific migration level of 600 ng/g established by the European Commission	(Pérez Bendito, Rubio Bravo, Lunar Reyes, & García Prieto, 2009)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
Cans	Soft drink products (72)	SPE followed by derivatization	April 2007, local grocery in Ottawa	0.032 - 4.5 µg/L. About 75% with < 0.5 µg/L and 85% with < 1 µg/L	Exposure to BPA through consumption of canned soft drink products is low.	(Xu-Liang Cao, Corriveau, & Popovic, 2009)
Infant formula cans with epoxy-phenolic coatings	Infant formula	SPE Chloroform, acetonitrile or methanol	December 2008 and January 2009, U.S. District of Columbia and southern California and Arizona	Powder formula: not detected Liquid formula: 0.48 -11 ng/g	Samples with different market origins demonstrated no significant difference, and concentrations in older cans were not higher. BPA was detected in only 1 of the powder formula samples and the concentrations in the liquid formula were consistent with previous studies.	(Ackerman et al., 2010)
Cans	Soft drink products (22) Beer (8) Infant formula	DLLME/acetylation procedure; T ₄ CE solvent	Local supermarkets in Porto, Portugal	Soft drinks: 0.03- 4.02 µg/L Beers: 0.29-4.70 µg/L Infant formula: 0.40 and 0.23 µg/L (present in 2 samples)	The optimized method allowed a decrease in the LODs and LOQs comparing to previous methods reported in the literature for similar matrixes. The use of a dual GC column system allowed a high sample capacity and increased robustness. Concentrations of BPA were in all cases below the specific migration level of 600 µg/L established by the European Commission.	(Cunha et al., 2011)
Canned containers	Powdered milk Infant formula	PLE	Supermarkets in Camerino (Italy) and Valencia (Spain)	Powdered milk: n.d.-0.8 mg/Kg Infant formula: n.d.- 1.29 mg/Kg	3 samples had values beyond the specific level of migration (0.6 mg/Kg), but levels were in almost all cases below concern.	(Ferrer et al., 2011)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
Cans for fruits and vegetables	-8 different vegetables -8 different fruits	DLLME (tetrachloroethylene - extractive solvent; acetonitrile extract) obtained from QuEChERS - dispersive solvent; anhydride acetic - derivatizing reagent)	Purchased in different local markets in Oporto Metropolitan Area (North Portugal)	The results obtained in this study were between 3.7µg/Kg and 265.6µg/Kg.	Canned vegetables presented the highest values of BPA, all of them below the limit established by EU Legislation. The combination of DLLME with QuEChERS to subsequent analyze with GC/MS showed to be a good method for the determination of BPA in this type of foods.	(Cunha & Fernandes, 2013)
Domestic and imported cans for foods	Canned foods (100 Domestic; 60 Imported): Fish; Meat; Vegetable; Fruit; Other cooked foods.	Extraction: MeOH Purification: hexane; NaCl; HCL; DCL Derivatization: KOH/EtOH;	Purchased from retail stores in Tokyo in 2011–2012	Domestic canned foods: <LOQ to 30 ng/g Imported canned foods:<LOQ to 390 ng/g	The range of BPA found in domestic canned foods was <LOQ to 30 ng/g and in imported canned foods the number was very different reaching 390 ng/g. Levels found were below the specific migration limit established by the UE.	(Kawamura, Etoh, Hirakawa, Abe, & Mutsuga, 2014)
Canned Tomatoes	3% acetic acid	Extracted with MeOH, homogenized; dissolved with n-hexane: acetone (97:3, v/v). Applied to a Sep-Pak light Florisil cartridge and eluted with n-hexane: acetone (80:20, v/v); dissolved in MeOH	2013, 3 different tomato tomato -based products (peeled, cherry and concentrated paste), 16 samples - 6 commercial brands - retail and Italian market	Variation of BPA levels in different canned tomato products is from 0.3 to 3.80µg/Kg. The samples subject to the heating process and/or can's damage by denting - a significant increase in the migration levels.	No sample contained BPA exceeding the European Union limit for migration, set at 600µg/Kg. The exposure to BPA through the consumption of canned tomato products is low.	(Errico et al., 2014)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
Canned foods	Canned/Non-canned foods: Vegetables; Fruit; Meat; Fish; Dairy	Extraction: acetonitrile; hexane, purification in an ENVI-Carb. The purified extracted was derivatized with BSTFA.	Sampling entailed collection of 204 samples of fresh, frozen and canned foods in Dallas, Texas, first round in March 2010 and second round August 2010.	BPA - Quantified concentration ranged from 0.24 ng/g ww in a fresh peach to 149 ng/g ww in canned cut green beans, The second and highest measurements were 121.0 ng/g ww in canned corn and 80.6 ng/g ww in canned mixed vegetables	BPA concentrations were much higher in canned foods as compared to non-canned foods. This study underscores the important role of canned foods in children and adult exposure to BPA.	(Lorber et al., 2015a)
Canned tuna	33 tuna fish samples: 24 canned in oil medium; 9 canned in an aqueous medium	Tuna: Extracted with n-hexane/acetonitrile 1:1 (v/v); Oil of canned tuna: extracted with n-hexane; extract purified in a Florisil cartridge and eluted with n-hexane/ethyl acetate 50:50 (v/v). After evaporation, it was reconstituted with acetonitrile Aqueous medium of canned tuna: centrifuged and fitted	Italian markets	The levels of BPA detected in canned tuna fish were between 25.4 ± 0.4 ng/g to 187.0 ± 4.4 ng/g and the in the medium were between 6.3 ± 0.9 ng/g to 10.2 ± 0.6 ng/g.	The objective was successfully achieved although the results all the samples presented values below the specific migration limit established by the UE	(Fattore, Russo, Barbato, Grumetto, & Albrizio, 2015)
Canned energy drinks	40 energy drinks of different brands	Degassed in an ultrasonic bath, centrifuged and added with aqueous ammonium acetate and mixed to adjust pH at about 4.0. Samples purified by Affinimip Bisphenol A SPE cartridge: elution with methanol, then acetonitrile; eluent phases were gathered up, mixed by vortex and evaporated. The residue was dissolved in methanol.	From local supermarkets in Naples and its province (Southern Italy) between June and November 2015	7 of de 40 samples analyzed were contaminated by BPA (0.1 to 3.3 ng/ml)	All samples present values of BPA below the specific migration limit established by the UE.	(Gallo et al., 2017)

Food contact material	Food or Food simulant	Extraction method /Extraction solvent	Sampling period/place	Levels of migration	Conclusions of the study	Reference
Tinplate cans sterilize (HP) and non-sterilised (NHP) samples.	Aqueous simulant (10% ethanol v/v)	SPE: washing with 5 mL of water/methanol 95:5 (v/v); elution with 5 mL of methanol; residues were recovered with 1 mL water/acetonitrile 70/30 (v/v).	Lebanese market (2017). Two types of cans: 1 st intended for packing vegetables (L), 18 cans: 10.1 cm height, 7.3 cm diameter, and 423 mL capacity, food contact surface area of 3.15 dm ² ; 2 nd smaller size and used to pack processed meat (S) (17 cans: 5.3 cm height, 7.3 cm diameter, and 222 mL capacity, food contact surface area of 2.05 dm ²	NHP (S) 10 days at 60 °C: increase 0.2 to 23 µg/Kg NHP (L) 10 days at 60°C: increase 0.1 to 45 µg/Kg HP (L) 10 days at 60°C remained constant 105 µg/Kg HP (S) 10 days at 60 °C	Sterilization, at 121 °C for 30 min, greatly increases the release of BPA into aqueous food simulant. Nevertheless, the average migration levels reached, 92 and 125 µg/Kg in large and small cans respectively, were well below the EU regulation (600 µg/Kg). There was no significant effect of short and long storage periods, under different temperatures, on sterilized cans. Unsterilized cans were significantly affected by storage time and temperature, but BPA migration levels remained below those observed in sterilized cans	(Noureddine El Moussawi et al., 2018)

BPA- bisphenol A; **BPS**- bisphenol S; **BPB**- bisphenol B; **BPP**- bisphenol P; **BPE**- bisphenol E; **BPAF**- bisphenol AF; **BPF**- bisphenol F; **BSTFA**- N-O-bis (trimethylsilyl) trifluoroacetamide;; **CL-ELISA**- indirect competitive chemiluminescence enzyme-linked immunosorbent assay ; **DCM**- dichloromethane; **DLLME**- dispersive liquid–liquid microextraction; **EASC**- 10- ethylacridone-2-sulfonyl chloride;; **EFSA**- European Food Safety Authority ; **EP**- epoxyphenolic; **EtOH**- ethanol; **GC**- gas chromatography; **GC-MS**- gas chromatography-mass spectrometry; **HCL**- hydrochloric acid ; **HDPE**- hight density polyethylene; **HP**- heat process; **HPLC**- high performance liquid chromatography; **HPLC-FLD**- high performance liquid chromatography-fluorescence detection ; **HPLC-MS/MS**- high performance liquid chromatography–tandem mass spectrometric; **KOH**- potassium hydroxide; **LB**- low BADGE; **LC-MS/MS**- liquid chromatographic–tandem mass spectrometric; **LDPE**- low density polyethylene; **LFIA**- lateral flow immunoassay ; **LLE**- liquid–liquid extraction; **LOD**- limit of detection; **LOQ**- limit of quantification; **MeOH**- metano; **MTBSTFA**- N',N'-methyl-(tert-butyl)dimethylsilyl trifluoroacetamide;; **NaCL**- sodium chloride; **NHP**- no heat process; **NP**- 4-nonylphenol;; **OP**- 4-octylphenol; **RD**- reference dose; **EPA**- Environmental Protection Agency; **PA**- polyamide; **PC**- polycarbonate; **PE**- polyethylene; **PES**- polyethersulphone ; **PET**- polyethylene terephthalate; **PLE**- pressurised liquid extraction; **PP**- polypropylene ; **PS**- polystyrene; **PVC**- polyvinyl chloride; **QuEChERS**- quick easy cheap effective rugged safe; **SBSE**- stir bar sorptive extraction ; **SE**- solvent extraction; **SML**- specific migration limit ; **SPE**- solid-phase extraction; **SPME**- solid-phase microextraction; **T₄CE**- tetrachloroethylene; **TDI**- tolerable daily intake; **UA-DLLME**- ultrasound-assisted dispersive liquid–liquid microextraction; **US FDA**- US Food and Drug Administration

Table 2: Conditions of the Gas Chromatographic methods used to determine BPA.

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Other compounds analyzed	Reference
MS/MS	Injector temperature: 280 °C; Detector interface temperature: 290 °C; Injection mode: splitless; Injection volume: 2 µL; Oven ramp: started at 100 °C and increased 10 °C/min to 280 °C, which was maintained for 3 min; Carrier gas: UHP Helium; Flow: 1 mL/min; Head pressure: 10 psi; Selected ions: m/z 119, 213 and 228	Rtx-5 FSOT (30 m x 0.25 mm i.d., 1.0 µm film thickness)	-	-	-	(Biles, McNeal, Begley, et al., 1997)
MS	Initial oven temperature: 200 °C, hold 2 min; Oven ramp: linear temperature gradient 10 °C/min to 270 °C and hold 15 min; Post-run after each analysis: raising the temperature up to 280 °C for 5 min; Injection mode: constant flow; Injection volume: 1.1 mL/min; Carrier gas: Helium; Flow: 1.5 mL/min; Selected ions: m/z 228 and 213	HP-5 MS (30 m x 0.25 mm, 0.25 µm film thickness) capillary column	-	LOD: Sim.A - 0.1 ng/g; Sim.B - 1 ng/g; SimC - 2 ng/g LOQ: Sim.A - 0.01 µg/g; Sim.B - 0.02 µg/g; Sim.C - 0.02 µg/g	BADGE	(Salafranca, Batlle, & Nerín, 1999)
MS (identification)	Injector temperature: 150 °C; Transference line temperature: 200 °C; Injection mode: Splitless; Oven ramp: 90 °C increased 30 °C/min until 300 °C, which was maintained for 10 min; Selected ions: 213, 228, 119 and 91	DB5 (30 m x 0.25 mm i.d., 0.25 µm film thickness)			BADGE	(Munguia-Lopez & Soto-Valdez, 2001)
MS	Injector temperature: 270 °C; Injection mode: Splitless; Oven ramp: 90°C hold for 2 min; ramp to 250 °C at 5 °C/min; ramp to 300 °C at 10 °C/min, hold 2 min; Carrier gas: Helium; Gas Pressure: 5 psi; Flow: 1.3 mL/min; Selected ions: m/z 228, 213 (BPA-d14 diacetyl - m/z 224)	HP-5MS (30 m x 0.25 mm i.d., 0.25 µm film thickness)	BPA-d ₁₄	LOD: 0.002 mg/Kg LOQ: 0.007 mg/Kg	BPF	(Goodson et al., 2002b)
MS	Injector temperature: 250 °C; Detector temperature: 280 °C; Injection mode: Splitless; Injection volume: 1 µL; Oven ramp: 40 °C for 4 min; increased 10 °C/min until 300 °C and held for 10 min; Carrier gas: Helium; Selected ions: 123 and 213	ZB-5 (30 m x 0.25 mm i.d., 0.25 µm film thickness)	4,4'-difluorobenzophenone	LOD: 0.1 µg/L	-	(Brede et al., 2003)(López-Cervantes & Paseiro-Losada, 2003)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Other compounds analyzed	Reference
MS	Injector temperature: 290 °C; Injection mode: Splitless; Oven ramp: 70 °C for 1 min; increased 10 °C/min until 120 °C, increased 10 °C/min until 300 °C, which was maintained for 5 min; Carrier gas: Helium; Head pressure: 8 psi; Selected ions: BPA - 213, 228, 244; BPA-d16 - 224, 242	HP-5 MS (30 m x 0.25 mm i.d., 0.25 µm film thickness)	BPA-d ₁₆	LOD: 2 µg/Kg (foods and acetonitrile) and 0.5 µg/Kg (10% ethanol)	-	(Goodson et al., 2004)
MS	Injector temperature: 250 °C; Injection mode: Splitless; Injection volume: 2 mL; Oven ramp: from 60 °C (1 min) to 175 °C at 6 °C/min, stand for 1 min, and up to 280 °C at 3 °C/min and to 300 °C at 7 °C/min; Flow: 1 mL/min; Electron ionization: 70 eV; Ionizations temperature: 270 °C; Emission current: 100 µV; Detector voltage: 380 V; Selected ions: m/z 213, 119, 228	HP 5MS fused-silica capillary column (30 m x 0.25 mm i.d., 0.25 µm film thickness)	-	LOD: 0.15 µg/Kg	BADGE, NP and five phtlates	(Casajuana & Lacorte, 2004)
MS	Oven ramp: 120 °C for 2 min; increased 10 °C/min until 280 °C; Carrier gas: Helium; Flow: 0.76 mL/min; Selected ions: 228 and 213 (confirmation)	DB-5MS (30 m x 0.25 mm i.d., 0.25 µm film thickness)	BPA-d ₁₄	LOQ: < 10 µg/Kg for foods of low fat content (<1%), < 20 µg/Kg for foods with >1% fat content	-	(Thomson & Grounds, 2005b)
MS	Injector temperature: 250 °C; Detector interface temperature: 280 °C; Detector source temperature: 230 °C; Oven ramp: 50 °C for 5 min; increased 15 °C/min until 280 °C, which was maintained for 10 min; Carrier gas: Helium; Flow: 1.5 mL/min; Selected ions: 213 and 228	Zebron ZB-5 (30 m x 0.25 mm i.d., 1.0 µm film thickness)	BPA-d ₁₄	LOD: 0.5 µg/L	-	(Xu-Liang Cao et al., 2008)
MS	Injector temperature: 280 °C; Detector interface temperature: 280 °C; Detector source temperature: 230 °C; Oven ramp: 100 °C for 1 min; increased 20 °C/min until 225 °C, which was maintained for 5 min; increased 35 °C/min until 325 °C, which was maintained for 1 min; Carrier gas: Helium; Flow: 1.1 mL/min; Selected ions: 213, 228, 270 and 312	ZB-5MS (30 m x 0.25 mm i.d., 0.25 µm film thickness)	BPA-d ₁₄	LOD: 0.1 ng/g LOQ: 0.5 ng/g	-	(Xu-Liang Cao et al., 2008)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Other compounds analyzed	Reference
MS	Injector temperature: 250 °C; Injection mode: Splitless; Injection volume: 1 µL; Oven ramp: 90 °C for 4 min, 10 °C/min to 300 °C, and held for 10 min; Carrier gas: Helium; Flow: 1.5 ml/min; Scan range: 50–600 m/z; Selected ions: 357, 368	HP-5 MS (30 m x 0.25 mm i.d., 0.25 µm film thickness)	BPA-d ₁₆	LOD: 0.1 µg/L	-	(Ehlert et al., 2008)
MS	Injector temperature: 280 °C; Detector interface temperature: 280 °C; Detector source temperature: 230 °C; Oven ramp: 100 °C for 1 min; increased 20 °C/min until 225 °C, which was maintained for 5 min; increased 35 °C/min until 325 °C, which was maintained for 1 min;; Injection volume: 1 µL; Carrier gas: Helium; Flow: 1.2 mL/min; Selected ions: 213, 228, 270 and 312	HP-5MS (30 m x 0.25 mm i.d. x 0.25 µm film thickness)	BPA-d ₁₄	LOD: 0.045 µg/L	-	(Xu-Liang Cao et al., 2009)
MS/MS- EI	Injector temperature: 250 °C; Detector interface temperature: 250 °C; Detector source temperature: 180 °C; Injection mode: Splitless; Injection volume: 1 µL; Oven ramp: 60 °C (hold 1 min) to 280 °C at 10 °C/min; Flow: 1ml/min MS/MS mode: MRM Electronic impact: 70 eV MRM transitions: BPA 357-191 m/z and BPA-c13 369-197 m/z	Zebron ZB-5HT (30 m x 0.25 mm i.d., 0.1 µm)	BPA-c13	LOD: 0.04 ng/L LOQ: 0.11 ng/L	-	(Kubwabo et al., 2009)
MS (confirmation)	Injector temperature: 225 °C; Injection mode: Split (1:30); Injection volume: 1 µL; Detector interface temperature: 200 °C; Oven ramp: isocratic, 250 °C for 20 min; Injection volume: 1 µL; Carrier gas: Helium; Flow: 0.8 mL/min; Selected ions: 213, 228	DB-5MS (30 m x 0.25 mm i.d., 1.0 µm film thickness)	-	LOD: Full-scan mode = 50 mg/L in SIM mode at m/z 213 = 0.5 mg/L	-	(Maia et al., 2009)
MS	Injector temperature: 280 °C; Detector source temperature: 250 °C; Injection mode: Splitless; Injection volume: 1 µL; Oven ramp: 150 °C, held for 0.5 min; increased to 280 °C (20 °C/min), held for 5.0 min; raised to 300 °C (40 °C/min), held for 2.5 min; Carrier gas: Helium; Flow: 1.0 ml/min; Electronic impact: 70 eV; Selected ions: 372, 357 m/z	DB-5MS (30m x 0.25mm i.d., 0.25 µm film thickness)	Bisphenol F	LOD: 0.5 ng/g LOQ: 0.8 ng/g		(Zafra-Gómez et al., 2009)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Other compounds analyzed	Reference
MS	SBSE desorption: 35°C 1min; 60 °C/min to 300 °C held 10min under a flow of 100ml/min helium ; Flow: 1.2 ml/min; Carrier gas: helium ; Injector temperature: -150 °C; Mode: Splitless; Column temperature program: 10 °C/s to 300 °C, and held for 5 min ; Oven temperature program: from 40 °C (held for 1 min) to 300 °C (held for 3 min) at 10 °C/min; Mode: SIM ; Electron ionization: 70 eV ; SIM elution: 20-30 min; Selected ions: BPA - m/z 213 and 228; d6-BPA – m/z 216 and 234	HP-5MS (30 m x 0.25 mm i.d., 0.25 µm film thickness)	Deuterated internal standard d ₁₆ -BPA	For BPA (as acetate): LOD: 0.12 ng/L LOQ: 0.40 ng/L	-	(De Coensel et al., 2009)
MS	Injector temperature: 90 °C; Detector interface temperature: 300 °C; Detector source temperature: 170 °C; Injection mode: Splitless; Injection volume: 1 µL; Oven ramp: 90 °C for 1.25 min, then at 25 °C/min to 300 °C, and held for 8 min; Carrier gas: Helium; Flow: 1.0 ml/min; Head pressure: 15 psi; Selected ions: 616 and 628	DB-5MS (30m x 0.25mm i.d., 0.25 mm film thickness)	BPA-c13	Beverages - LOQ: 0.02 ng/ml Food - LOQ: 0.10 ng/g	-	(Geens, Apelbaum, Goeyens, Neels, & Covaci, 2010)
MS	Injector temperature: 225 °C; Injection mode: Split (1:30); Injection volume: 1.0 µL; Column temperature program: Isocratic (250 °C for 20 min); Flow: 0.8 mL/min; Carrier gas: Helium; Interphase temperature: 200 °C; Electron energy: 70 eV; Electron multiplier: 1504 V; Full-scan – m/z 50-400; SIM mode: m/z 214 (base peak), 228	DB-5MS (30 m x 0.250 mm 1 µm)	-	LOD: Full-scan mode = 50 mg/L in SIM mode at m/z 213 = 0.5 mg/L	-	(Maia et al., 2010)
MS	Injector temperature: 250 °C; Injection mode: Splitless; Injection volume: ; Oven ramp: 100 °C for 4 in, increased 10 °C /min until 250 °C , which was maintained for 6 min; Carrier gas: Helium; Flow: 1.5 mL/min; Selected ions: 213 and 228	GC: HP-5 MS (30 m x 0.25 mm i.d. x 0.25 µm film thickness)		LOD: 0.1 ppb	-	(Nam et al., 2010)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Other compounds analyzed	Reference
MS	Injector temperature: 280 °C; Detector interface temperature: 280 °C; Detector source temperature: 200 °C; Injection mode: Splitless; Injection volume: 2 µL; Oven ramp: 70 °C for 2 min; increased 10 °C/min until 135 °C, 3 °C/min until 160 °C, 1 °C/min until 175 °C, 3 °C/min until 195 °C, 10 °C/min until 300 °C which was maintained for 5 min; Carrier gas: Helium; Flow: 1.2 mL/min; Cone voltage: 70 eV; Selected ions: <i>m/z</i> 60 to 400	DB-5MS (30 m x 0.25 mm i.d., 0.25 µm film thickness)	BPA-d ₁₆	LOD: 0.009 µg/L	Phthalates, alkylphenols	(Guart et al., 2011)
MS	Injector temperature: 280 °C; Detector interface temperature: 280 °C; Detector source temperature: 230 °C; Oven ramp: 100 °C for 1 min; increased 20 °C/min until 225 °C, which was maintained for 5 min; increased 35 °C/min until 325 °C, which was maintained for 1 min; Injection volume: 1 µL; Carrier gas: Helium; Flow: 1.2 mL/min; Selected ions: 213, 224, 228, 270, 312	HP-5MS (30 m x 0.25 mm i.d., 0.25 µm film thickness)	BPA-d ₁₆	Simple liquids - LOD: 0.14 ng/g Dairy products and other liquids - LOD: 0.20 ng/g Simple food matrices - LOD: 0.38 ng/g Complex food matrices - LOD: 1.0 ng/g	-	(Zhang, Cooke, Curran, Goodyer, & Cao, 2011)
MDGC-MS	Injector temperature: 280 °C; Injection mode: Splitless; Oven ramp: 140 °C held for 1 min, ramped to 280 °C at 40 °C/min and held for 3.3 min; Carrier gas: Helium; Flow: 1.0 ml/min in the first column and 2.0 ml/min in the second; Ramped pressure: 169.2 kPa, 0.31 kPa/min to 172 kPa; Cone voltage: 70 eV; Ionization source: 230 °C; Selected ions: 224, 242, 284, 326, 270, 213, 228, 312	Primary column DB-5HT (5 m x 0.32 mm i.d., 0.10 µm of film thickness) Secondary column DB-5MS (15 m x 0.25 mm i.d., 0.25 µm film thickness)	BPA-d ₁₆	Beverages: LOD: 5 ng/L; LOQ: 10 ng/L Infant formula: LOD: 60 ng/L; LOQ: 200 ng/L	-	(Cunha et al., 2011)
MS	Injector temperature: 300; Injection mode: Splitless; Injection volume: 1 µL; Oven ramp: 50 °C for 5 min; increased by 15 °C/min to 300 °C (1 min) and subsequently increased 25 °C/min to 340 °C and was kept at this temperature to the end; Carrier gas: Helium; Flow: 1.3 mL/min	HP-5MS (30 m x 0.25 mm i.d., 0.25 µm of film thickness)	Deuterated 2,6-bis(1,1-dimethylethyl)-4-methylphenol-D21	-	47 more types of migrants, like TXIB, DIPN, BHT	(Simoneau et al., 2012)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Other compounds analyzed	Reference
MS	Flow: 0.1 mL/min; Carrier gas: helium; Injector temperature: 300 °C; Split mode: splitless; Injection volume: 1 µL; Oven temperature program: 100 °C (for 2 min) and then at 300 °C; Column temperature program: 150 °C (2 min) to 5 °C/min to 270 °C (5 min); Interphase temperature: 310 °C; Ion source temperature: 150 °C; Quadrupole temperature: 150 °C	Capillary column Elite-5-MS (30 m x 0.25 mm, 0.5 µm film thickness).	d ₁₆ -BPA	LOQ ≤ 0.2 ng/L	-	(Elobeid et al., 2012)
MS	Injector temperature: 280 °C; Injection mode: Splitless; Injection volume: 1 µL; Oven ramp: 100 °C held for 1 min, ramped to 280 °C at 30 °C/min held for 5.0 min. Total run time was 12 min. The MS transfer line was held at 280 °C; Flow: 1 mL/min; Carrier gas: Helium; Electron ionization: 70 eV; Ion source temperature: 230 °C; MS quadrupole temperature: 150 °C; Retention time: d16-BPA – 7.73 min.; BPA – 7.76 min.; Selected ions: d16-BPA - m/z 224, 242, 284; BPA – m/z 270, 213, 228	DB-5MS column (30 m x 0.25 mm i.d., 0.25 µm film thickness)	d ₁₆ -BPA	LOD: lower than 0.3 µg/Kg LOQ: 1 µg/Kg	BPB	(Cunha & Fernandes, 2013)
MS	Injection temperature: 250 °C; Interface temperature: 290 °C; Injection mode: Splitless; Injection volume: 1 µL; Oven ramp: 100 °C for 1 min, then at 20 °C/min to 250 °C, at 10 °C/min to 290 °C, then held for 5.5 min; Flow: 1 mL/min; Carrier gas: Helium; MS Mode: SIM; Selected ions: BPA - m/z 269 and 284; d16-BPA - m/z 280 and 298; pyrene-d10 - m/z 212.	Inertcap17MS (30 m × 0.25 mm i.d., 0.25 µm film thickness)	d ₁₆ -BPA and pyrene-d10	LOQ: Fish - 5 ng/g Meat, vegetables, fruit and other foods- 5 ng/g Coffee, tea and other beverages: 1 ng/g	-	(Kawamura et al., 2014)
LRMS	Flow: 2.0 mL/min; Carrier gas: helium; Injector temperature: 280 °C; Split mode: splitless; Oven temperature program: 120 °C for 1 min, 10 °C/min to 240 °C, and 30 °C/min to 300 °C, then held 10 min	DB5 MS (30m x 25mm i.d., 0.25µm film thickness)	Internal standard ¹³ C-BPA	LOQ: 0.20 ng/g for food and 20 ng/L for liquids	-	(Lorber et al., 2015b)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Other compounds analyzed	Reference
MS/MS	GC: Carrier gas:helium (1.4 mL/min); Injector temperature 250 °C; Injection volume: 1 µl; Split mode: split; Oven temperature program the initial oven temperature was 150 °C (held for 1 min), followed by a ramp temperature of 20 °C min ⁻¹ to 270 °C (held for 1.67 min), and to 310 °C at 30 °C/min (held for 4.0 min). Total run time was 14.0 min. MS: electron impact (EI) mode at 70 eV; Collision gas: Argon	ZB5MS capillary column (30 m × 0.25 mm i.d.; 0.25 µm).	BPA-d ₁₄	LOQ: 0.1 to 1.2 ng/g	BPAF; BPF; BPE; BPB; BPS; BPP	(García-Córcoles et al., 2018)
MS	GC: Carrier gas: helium (1.2 mL/min); Injector temperature: 300 °C; Split mode: splitless; Oven temperature program: 100 °C for 1 min, raised to 300°C at 15°C/min and held for 4 min, with a total analysis time under 19 min. MS: electron impact ionization in selected ion monitoring (SIM) mode. The GC–MSD interface and MSD source temperatures were 280 and 230° C, respectively.	DB-5MS capillary column (30 m × 0.25 mm × 0.25 µm, Agilent Technologies)	For BPAF; BPF and for BPB: isotope BPF- ¹³ C ₁₂	LOD: 0.022 ng/g	BPAF; BPF; BPE; BPB	(Xu-Liang Cao & Popovic, 2018)

BADGE- bisphenol A diglycidyl ether; **BHT**- butylated hydroxy- toluene; **BPAF**- bisphenol AF; **BPB**- bisphenol B; **BPE**- bisphenol E; **BPF**- bisphenol F; **BPS**- bisphenol S; **BPP**- bisphenol P; **DIPN**- 2,6-di-isopropyl-naphthalene ; **GC**- gas chromatography; ; **LOD**- limit of detection; **LOQ**- limit of quantification; **LRMS**- low resolution mass spectrometry; **MDGC-MS**- multidimension gas chromatography-mass spectrometry; **MS**- mass spectrometry; **MS/MS**- tandem mass spectrometry; **MRM**- multiple reaction-monitoring mode ; **EI**- negative electro ionosation; **NP**- 4-nonylphenol; **Sim A**- simulant A; **Sim B**- simulant B; **Sim C**- simulant C; **TXIB**- 2,2,4-trimethyl-1,3-pentanediol diisobutyrate.

Table 3: Conditions of liquid chromatographic methods used to determine BPA.

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Compounds analyzed besides BPA	Reference
FLD	Mobile phase: solvent A water/methanol/acetonitrile (90:5:5); solvent B water/methanol/acetonitrile (5:90:5); solvent C water/methanol/acetonitrile (5:5:90); Elution: Gradient; Column temperature: 40 °C; Injection volume: 50 µL; Flow: 0.5 mL/min; $\lambda_{\text{excitation}}$: 235 nm; $\lambda_{\text{emission}}$: 317 nm	Shandon Hypercarb S graphitized carbon column (150 mm x 4.6 mm, 7 µm)	-	LOD: 0.9 ng/mL	-	(Biles, McNeal, Begley, et al., 1997)
FLD	Mobile phase: methanol/water/acetonitrile; Elution: Isocratic; Column temperature: 40 °C; Injection volume: 20 µL; Flow: 0.5 mL/min; $\lambda_{\text{excitation}}$: 235 nm; $\lambda_{\text{emission}}$: 317 nm	Shandon Hypercarb S graphitized carbon column (150 mm x 4.6 mm, 7 µm)	-	LOD Ethanollic simulants and water: 2 ng/mL Miglyol 812, fruit juices, infant formula: 100 ng/mL Bottled water: <0.05 ng/L	-	(Biles, McNeal, Begley, et al., 1997)
FLD	Mobile phase: acetonitrile/imidazole/HNO ₃ buffer; Elution: Isocratic; Injection volume: 5 µL; Flow: 1.0 mL/min	Daisopak-SP-120-5-ODS-BP (250 x 4.6 mm, 5 µm)	-	LOD: 0.38 ng/mL LOQ: 0.57 ng/mL	-	(Sun et al., 2000)
FLD	Mobile phase: acetonitrile/water; Elution: Gradient; Injection volume: 10 µL; Flow: 1 mL/min; $\lambda_{\text{excitation}}$: 224 nm; $\lambda_{\text{emission}}$: 310 nm; Retention time between 16.8 and 17.1 min.	Micropak C18 MCH-5-N-CAP (150 x 5 mm)	-	LOQ: 0.2 µg/L	BADGE	(Munguia-Lopez & Soto-Valdez, 2001)
UV	Mobile phase: acetonitrile/water (40:60, v/v); Elution: Isocratic; Column temperature: 40 °C; Injection volume: 20 µL; Flow: 0.8 mL/min; λ = 228 nm	Wakosil II 3C18 RS column (150 mm x 4.6 mm, 3 µm)	-	LOQ: Solid portion: 10 ng/g Aqueous portion: 5 ng/ml	-	(Yoshida et al., 2001)
ECD	Mobile phase: CH ₃ OH/OH ₂ , 60:40, containing 10 mM KNO ₃ and 0.25 mM H ₂ SO ₄ , as supporting electrolyte; Injection volume: 20 µL;	Hewlett - Packard C18 (200 x 4.6 mm, 5 µm)	-	LOD (at 1.3V): 20 ng/mL; LOD (with chemically modified electrode): 0.2 ng/mL	-	(D'Antuono et al., 2001)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Compounds analyzed besides BPA	Reference
FLD	Mobile phase: acetonitrile/water; Elution: Isocratic; Column temperature: 40 °C; Flow: 1 mL/min; λ excitation: 275 nm; λ emission: 300 nm	Symmetry Shield RP18 (150 x 4.6 mm, 5 μ m)	-	LOD: 2 ng/mL	-	(Kang & Kondo, 2002)
FLD (identification) MS (confirmation)	LC-FLD Mobile phase: water/acetonitrile (70:30); Elution: Isocratic; Column temperature: 40 °C; Injection volume: 10 μ L ; Flow: 1.0 mL/min; λ excitation: 275 nm; λ emission: 300 nm LC-MS Mobile phase: Acetic acid/water (A); Acetonitrile (B); Elution: Isocratic (70 A: 30 B); Column temperature: 40 °C; Injection volume: 5 μ L; Flow: 300 μ L/min; Ionization mode: negative; Probe temperature: 350 °C; Capillary potential: 3.5 KV; Fragmentor voltage: 140V; Investigation of fragment ion: 220V ; Selected ions: m/z 100 and 300	Capcell Pak C18 (150 mm x 4.6 mm, 5 μ m)	-	LOD: 20 ng/mL	BPF	(Inoue et al., 2003)
MS (confirmation) FLD UV	LC-MS Mobile phase: A- acetonitrile B- Milli-Q water; Elution: Gradient; temperature: 500 °C;; Flow rate: 1 ml min ⁻¹ ; APc Ionization; Ionization mode: Negative; Ionization source temperature: 125 °C; Cone voltage: 50 eV; Electron multiplier voltage: 700V; Drying gas: N ₂ at 175 l h ⁻¹ ; Selected ion: m/z 213 base peak, 227 HPLC-FLD Mobile phase: A - acetonitrile; B - Milli-Q Water; Elution: Gradient; Column: Kromasil 100 C18 5 μ m (15 cm x 0.4 cm); Injection volume: 50 μ L; Flow: 1 mL min ⁻¹ ; λ excitation: 225 nm; λ emission: 305 nm UV λ = 225 nm	Kromasil 100 C18 (150 mm x 4 mm, 5 μ m)	-	LOD: LC-MS - 500 μ g/L; HPLC-FL - 3 μ g/L; and HPLC-UV - 30 μ g/L (UV)	-	(López-Cervantes & Paseiro-Losada, 2003)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Compounds analyzed besides BPA	Reference
FLD	Sol-gel immunoaffinity chromatography Gel: PBS containing BPA antibody with pre hydrolyzed TMOS; Column: 3 mL glass with a polytetrafluorethylene frit; Flushing: PBS, ACN-water (40:60, v/v) and PBS HPLC-FLD system 1 Mobile phase: sodium acetate buffer/acetonitrile (60:40); Elution: Isocratic; Flow: 1.0 mL/min; λ excitation 275 nm; λ emission 305 nm HPLC-FLD system 2 Mobile phase: sodium acetate buffer/acetonitrile (65:35); Elution: Isocratic; Flow: 0.3 mL/min; λ excitation: 275 nm; λ emission: 305 nm HPLC-FL system 3 and 4 similar to system 1, but with gradient	HPLC systems 1, 3, 4 Spherisorb S ODS1 (250 x 4.6 mm i.d., 5 μ m) HPLC system 2 Intersil ODS-2 (150 x 2.1 mm i.d., 5 μ m)	-	LOD system 1: 0.2 ng/mL system 2: 0.8 ng/mL system 3: 0.5 ng/mL system 4: 0.4 ng/L	-	(Braunrath & Cichna, 2005)
FLD	Mobile phase: acetonitrile/water; Elution: Gradient; Injection volume: 10 μ L; Flow: 1 mL/min; λ excitation: 224 nm; λ emission: 310 nm	Micropak C18 MCH-5-N-CAP (150 x 5 mm) protected by a C18 guard column	-	LOD: 5.0 μ g/L LOQ Fatty-food simulant: 10.0 μ g/L Tuna fish: 7.1 μ g/L	-	(Munuguía-López et al., 2005)
FLD	Mobile phase: Acetonitrile - water (65:35) with 0.1% trifluoroacetic acid; Flow rate: 0.6 ml/min; Temperature: 35 °C; λ excitation: 235 nm; λ emission: 327 nm; Gain: 1000; Run length: 20 min	HPLC-FL: reversed-phase column Hypersil C18 (250 x 4.6 mm, 5 μ m)	-	LOD (10% ethanol): 0.05 μ g/in ² ; LOD (corn oil): 0.05 μ g/in ²	-	(Onn Wong et al., 2005)
HPLC-FLD (system 1 - determination) HPLC-CoulArray (system 2 - confirmation)	Sol-gel immunoaffinity chromatography Gel: PBS containing BPA antibody with pre hydrolyzed TMOS; Column: 3 mL glass with a polytetrafluorethylene frit; Flushing: PBS, ACN-water (40:60, v/v) and PBS HPLC system 1 Mobile phase: water/acetonitrile (70 : 30, v/v); Elution: Isocratic; Injection volume: 100 μ L; Flow: 1.0 mL/min; λ excitation = 275 nm; λ emission = 305 nm HPLC system 2 Mobile phase: A-0.01 M sodium acetate buffer; B – acetonitrile; Elution: Gradient; Injection volume: 100 μ L; Flow: 0.6 mL/min	System 1 LiChrospher 60 RP-Select B (250 x 4.0 mm i.d., 5 μ m) System 2 HP-Hypersil PDS (250 x 4.0 mm i.d., 5 μ m)	-	LOD: 0.1 ng/mL LOQ: 0.2 ng/mL	-	(Brenn-Struckhoffova & Cichna-Markl, 2006)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Compounds analyzed besides BPA	Reference
MS/MS	Mobile phase: A - Methanol; B - water with 0.1% ammonia; Elution: Gradient; Column temperature: 40 °C; Injection volume: 10 µL; Flow: 0.2 mL/min; Electrospray ionization (ESI); Ionization mode: Negative; Capillary potential: 3.5 kV; Cone voltage: 70 V; Multiplier voltage: 650 V; Nebulizing, desolvation and cone gas: nitrogen; Flow of desolvation gas: 550 l/h; Desolvation gas temperature: 300 °C; Source temperature: 100 °C; RF lens: 1 – 50 V ; 2 – 0.5 V; Entrance voltage: 0 V; Exit voltage: 0 V; Collision gradient: 3.2; Collision gas: UHP argon; Pressure of collision chamber: 3.0 x 10 ⁻³ mbar	Symmetry C18 column (150 mm × 2.1 mm, 3.5 µm)	-	LOD: Eggs and milk - 0.10 µg/Kg	NP and OP	(Shao, Han, Tu, & Huang, 2007)
FLD	Mobile phase: acetonitrile/water; Elution: Isocratic; Column temperature: 25 °C; Flow: 0.8 mL/min; λ excitation: 275 nm; λ emission: 315 nm	C18 column (250 mm x 4.5 mm, 5 µm) RF-530	-	LOD: 0.2 ng/mL LOQ: 0.5 ng/mL	-	(Liu et al., 2008)
FLD and MS (confirmation)	LC-FLD Mobile phase: methanol/water (70:30, v/v); Elution: Isocratic; Injection volume: 25 µL; Flow: 1.3 mL/min; λ excitation: 235 nm; λ emission: 317 nm LC-MS Mobile phase: methanol/water (70:30, v/v); Elution: Isocratic; Injection volume: 25 µL; Flow: 0.9 mL/min; Ionization mode: negative; Capillary potential: 3.5 KV; Cone voltage: 70 V; Ionization source: 500 °C; Selected ion: m/z 227	Inertsil ODS-2 (250 mm x 2.1 mm, 5 µm)	-	LOD for water: 2.4 ng/mL and LOD for 3% acetic acid: 1.8 ng/mL	-	(Maragou et al., 2008)
FLD UV	Mobile phase: acetonitrile/water 50:50 (v/v); Elution: Isocratic; Column temperature: 20 ± 2 °C; Injection volume: 20 µL loop; Flow: 1.0 mL/min; λ excitation: 273 nm; λ emission: 300 nm; UV λ: 228 nm	Stainless-steel column reversed-phase Synergi 4 µ Fusion-RP80A (250 × 4.6 mm, 4µm) equipped with a reversed-phase Synergi 4 µ guard column	-	LOD UV detection: 20.0 µg/Kg FL: 1.1 µg/Kg LOQ: UV detection: 66.9 µg/Kg FL: 3.7 µg/Kg	BPB	(Grumetto et al., 2008)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Compounds analyzed besides BPA	Reference
MS MS/MS	HPLC-MS Mobile phase: acetonitrile/water (40:60, v/v); Elution: Isocratic; Column temperature: 40 °C; Injection volume: 10 µL; Flow: 0.25 mL/min; Ionization mode: negative; Source temperature: 130 °C; Dissolution temperature: 390 °C; Capillary potential: 3.5 KV; Cone voltage: 39 V; Selected ion: m/z 227 HPLC-MS/MS Mobile phase: water/acetonitrile; Elution: Gradient; Column temperature: 40 °C; Injection volume: 5 µL; Flow: 0.35 mL/min; Electrospray ionisation source; Ionization mode: Negative; Cone voltage: 37 V; Collision energy: 20 eV; Source temperature: 130 °C; Desolvation temperature: 390 °C; SRM transitions: BPA- m/z 227-212	LC-MS: Symmetry C18 (150 mm × 2.1 mm, 3.5 µm) LC-MS/MS: Acquity BEH C18 (50 mm × 2.1 mm, 1.7 µm)		LC-MS LOD: 0.3 ng/mL	BADGE, BADGE·2H ₂ O, BADGE· HCl ·H ₂ O, BADGE· HCl, and BADGE· 2HCl	(Yonekubo et al., 2008)
FLD	Mobile phase: water/acetonitrile; Elution: Gradient; Injection volume: 20 µL; Flow: 1 mL/min; λexcitation: 276 nm; λemission: 306 nm	Hypersil ODS C18 column (4.6 x 150 mm, 5 µm)		LOD: 9 ng/g LOQ: 14 ng/g (the minimum for the method)	-	
FLD	Mobile phase: methanol/water (70:30); Elution: Isocratic; Injection volume: 200–500 µL; λexcitation: 226 nm; λemission: 296 nm	Spherisorb ODS-2 (250 x 4.5 mm, 5 µm)		LOD: 0.5 ng/mL	-	(Biedermann-Brem & Grob, 2009)
FLD	Mobile phase: acetonitrile/water (60:40 v/v); Elution: Isocratic; Injection volume: 20 µL ; Flow: 1 mL/min; λexcitation: 275 nm; λemission: 315 nm	ATRAPANTIS dC-18 (250 x 4.6 mm, 5 µm)		LOD: 1 ng/mL	-	(Lim et al., 2009)
FLD	Mobile phase: acetonitrile and water; Elution: Gradient; Column temperature: 25 °C; Injection volume: 25 µL ; Flow: 0.5 mL/min; λexcitation: 225 nm; λemission: 305 nm	Kromasil C18 (250 x 3.6 mm, 5 µm)		LOD: 5.0 ng/mL	-	(Maia et al., 2009)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Compounds analyzed besides BPA	Reference
MS/MS	Mobile phase: methanol/water; Elution: Gradient; Column temperature: 60 °C; Injection volume: 20 µL; Flow: 0.4 mL/min; Ionization mode: Negative; Capillary potential: 4.5 KV; Selected ion: BPA - m/z 227.1 to 133.1 and 212; d6-BPA - m/z 233.1 to 138.1 and 215.1; d16-BPA - m/z 241.1 to 142.1 and 223.1	Varian Pursuit XRs C18 column (150 mm x 2 mm, 3 µm)	BPA-d16 and BPA-d6	LOD: 0.15 ng/g LOQ: 0.5 ng/g		(Ackerman et al., 2010)
FLD	Mobile phase: (A) Milli-Q water; (B) Acetonitrile; Elution: Gradient; Column temperature: 25 °C; Injection volume: 20 µL; Flow: 0.5 mL/min; Scan excitation range: 200-280 nm; λ_{ex} : 225 nm; λ_{em} : 305 nm	Kromasil C18 (25 x 0.36 cm i.d., 5 µm)	-	LD: 50 ng/mL	-	(Maia et al., 2010)
MS/MS	LC-MS Mobile phase: (A) 0.5mM ammonium acetate:methanol (70:30, v/v) (B) ammonium acetate:methanol (5:95, v/v); Elution: Gradient; Column temperature: 55 °C; Injection volume: 15 µL; Flow: 0.5 mL/min; Ion Electrospray (ESI); Ionization mode: positive and negative; Ion spray voltage: 1500 V; Ion source gas: 1- 50 psi; 2- 60 psi; Temperature: 650 °C; Curtain gas: 15 psi; Collision gas pressure: 8; Entrance potential: 10; Selected ion: m/z 227 > 133 (quantification) and 227 > 212; Retention time: 3.05 min	Agilent Eclipse Plus C18 column (50mm x 2.1 mm, 1.8 µm)	d16- BPA	-	-	(Malone et al., 2010)
MS/MS	Mobile phase: A: 0.001 mM ammonium formate and B: methanol; Elution: Gradient; Column temperature: 40 °C; Injection volume: 10 µL; Flow: 0.2 mL/min; Electrospray ionization (ESI); Ionization mode: Positive and Negative; Capillary potential: 3 kV; Nozzle voltage: 1.5 kV; Dry gas temperature: 220 °C; Dry gas flow: 14 L/min; Nebulizing gas pressure: 20 Psi; Sheath gas temperature: 300 °C; Dry gas flow: 11 L/min; Dwell time: 20 ms; SRM transitions: BPA - m/z 227.2 > 212.2	ACQUITY UPLC BEH C18 (50 x 2.1 mm i.d., 1.7 µm)	BPA-d4	LOD: 0.08 µg/kg LOQ: 0.5 µg/kg	BPF, BPB, BPS, BPC, BPZ, DMBPS, BPP, BPAP, BPAF, TCBPA, TBBPA, BADGE, BFDGE,	(Cheng et al., 2017)(X.-L. Cao et al., 2011)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Compounds analyzed besides BPA	Reference
MS/MS	Mobile phase: water and methanol/acetonitrile (90/10 v/v); Elution: Isocratic; Column temperature: 60 °C; Injection volume: 20 µL; Flow: 0.4 mL/min; Ionization mode: Negative; Electrospray ionisation source; Capillary potential: 3.5 KV; Extractor: 5 V; RF lens: 0.5 V; Source temperature: 100 °C; Desolvation temperature: 300 °C; Desolvation gas: nitrogen; SRM transitions: BPA- m/z 205-106	Gemini C-18 (250 mm x 4.6 mm, 5 µm)	-	LOD: 0.005 mg/Kg LOQ: 0.016 mg/Kg	OP and NP	(Ferrer et al., 2011)
FLD and MS (confirmation)	HPLC-FLD Mobile phase: acetonitrile/water; Elution: Gradient; Column temperature: 25 °C; Injection volume: 20 µL; Flow: 0.9 mL/min; $\lambda_{excitation} = 227$ nm; $\lambda_{emission} = 313$ nm LC-MS Mobile phase: acetonitrile/water; Elution: Gradient; Column temperature: 25 °C; Injection volume: 50 µL; Flow: 0.6 mL/min; Ionization mode: negative; Probe temperature: 400 °C; Cone voltage: 25 V; Ionization source: 120 °C; Selected ion: m/z 227	HPLC-FL: Hypersil C18 (250 x 4.6 mm, 5 µm) HPLC-MS: Xterra RP18 (150 x 4.6 mm, 5 µm)	-	LOD: 0.004-0.007 mg/Kg LOQ: 0.03 mg/Kg	-	(Santillana et al., 2011)
FLD	Mobile phase: methanol/water (68:32); Elution: Isocratic; Column temperature: 30 °C; Injection volume: 20 µL; Flow: 0.27 mL/min; $\lambda_{excitation}$: 235 nm; $\lambda_{emission}$: 317 nm	HPLC-FL: Phenomenex C18 (150 mm x 3 mm i.d., 2.6 µm)	-	LOD: 0.1 µg/Kg LOQ: 0.3 µg/Kg	BPS, DCPS, DHPS	(Simoneau et al., 2011)
HPLC-FLD UPLC-MS (both for detection)	HPLC-FLD Mobile phase: methanol/water (68:32); Elution: Isocratic; Column temperature: 30 °C; Injection volume: 20 µL; Flow: 0.27 mL/min; $\lambda_{excitation}$: 235 nm; $\lambda_{emission}$: 317 nm UHPLC-MS Mobile phase: aqueous ammonium acetate 1mM/methanol; Elution: Gradient; Column temperature: 30 °C; Injection volume: 7.5 µL; Flow: 0.3 mL/min; Transition reactions: m/z 227-133; m/z 227-212; Cone voltage: 39	HPLC-FL: Phenomenex C18 (150 mm x 3 mm, 2.6 µm) UHPLC-MS: Waters Acquity BEH C18 (100 mm x 2.1 mm, 1.7 µm)	-	LOD: HPLC-FL = 0.1 µg/Kg ; UPLC-MS = 0.1 mg/Kg LOQ: HPLC-FL = 0.3 µg/Kg; UPLC-MS = 0.3 mg/Kg	DEP, DIBP, DBP, DEHP	(Simoneau et al., 2012)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Compounds analyzed besides BPA	Reference
MS/MS	HPLC Mobile phase: Methanol/Water; Elution: Gradient; Injection volume: 10 µl; Flow: 300 µl/min MS/MS Curtain gas: 10 psi; Collision energy: 3 psi; Ion spray voltage: -4500 V; Temperature: 700 °C; Ion source gas: 1- 55 psi; 2- 60 psi; Declustering potential: -48 V; Entrance potential: -3 V; Collision energy: -32 V; Collision cell exit potential: -1 V; Electrospray ionization (ESI); Ionization mode: Negative; SRM transitions: m/z 227>212; BPA retention time: 10.1 min	Betasil C18 (100 mm x 2.1 mm, 5 µm) from Thermo Electron Corporation, Waltham, MA, USA) connected to a guard column	¹³ C ₁₂ -BPA	LOQ: 0.01 ng/g	BPAF, BPAP, BPB, BPF, BPP, BPS, BPZ	(Liao & Kannan, 2013)
MS/MS	Mobile phase: A= Desmineralized water MilliQ; B= A solution of 0.1% (v/v) of ammonia in methanol; Elution: Gradient; Flow rate: 200 mL/min; Column temperature: 30 °C	Supelco Discovery C18 (150mm x 2.1 mm, 5 µm)	d16-BPA	LOD 5.8 ng/mL; LOQ 17.4 ng/mL		(Maiolini et al., 2014)
DAD	Mobile phase: acetonitrile/water (40:60, v/v); Injection volume: 100µL; Flow: 1 mL/min; Column temperature: 40 °C	Column Inertsil ODS (250 mm x 4.6 mm, 3.5 µm)	-	LOQ ≤0.05 µg/mL	-	(Sungur, Koroğlu, & Özkan, 2014)
DAD FLD MS-MS (for confirmation)	Mobile phase: (A) Water; (B) Acetonitrile; Elution: Gradient; Injection volume: 20 µL; Separation: Reversed-phase; Temperature: room temperature; Flow: 1 mL/min; Retention time: 4.60 ± 0.05 min; λ _{excitation} : 230 nm; λ _{emission} : 315 nm UV detector λ: 230 and 254 nm	Reverse-phase Microsorb 300-C18 stainless-steel column (250 x 4.6 mm, 5 µm)	-	LOD: 0.01 µM (0.09 µg BPA/Kg tomato); LOQ: 0,03 µM (0.26 µg BPA/Kg tomato)	-	(Errico et al., 2014)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Compounds analyzed besides BPA	Reference
MS/MS	Mobile phase: (A) 2 mM ammonium acetate in water (B) acetonitrile Elution: Gradient; Column temperature: 40 °C; Injection volume: 50 µL; Electrospray ionization (ESI); Ionization mode: Negative; SRM transitions: 227→212 (quantifier), 227→133 (qualifier) and 241→142; BPA retention time: 4.63 min	BEH C 18 column (100 mm × 2.1 mm, 1.7 µm)	d16-BPA	LOQ: High and low fat food samples - 0.10 µg/Kg Beverages - 0.02 µg/L	DEP, DiBP, DnBP, BBzP, DEHP, DCHP, DnOP, DiNP, DiDP	(Sakhi et al., 2014)
FLD	Mobile phase: (A) acetonitrile 30% v/v; (B) acetonitrile; Elution: Gradient; Column temperature: 30 °C; Injection volume: 10 µL; Flow: 1.0 mL/min; λexcitation: 270 nm; λ emission: 430 nm	RP Agilent Zorbax SB-C18 column (150 mm x 4.6 mm, 5 µm)	-	LOD: Soft drinks - 0.5 ng/L Dairy products - 0.01 µg/Kg LOQ: Soft drinks - 1.6 ng/L Dairy products - 0.03 µg/Kg	OP and NP	(Lv et al., 2014)
FLD MS/MS	LC-FLD Mobile phase: acetonitrile/water 60:40 (v/v); Elution: Isocratic; Column temperature: 20 ± 2 °C; Injection volume: 20 µL; λexcitation: 273 nm; λemission: 300 nm MS/MS Flow: 8 mL/min; Ionization mode: Negative; Capillary potential: -4 kV; Declustering potential (DP): -60V; SRM transitions: m/z 227.2, 212.2, 133.2	Stainless steel column - reversed-phase Ascentis C18 HPLC column (250 mm x 4.6 mm, 5 µm) with a Supelguard Ascentis C18 guard column	-	LOD: Tuna fish - 1.3 ng/g Oil medium - 1.1 ng/g Aqueous medium - 1.1 ng/g LOQ: Tuna fish - 4.3 ng/g Oil medium - 3.7 ng/g Aqueous medium - 3.9 ng/g	BPB, BADGE, BFDGE	(Fattore et al., 2015)
MS/MS -ESI	Mobile phase: (A) milli-Q water; (B) Methanol; Injection volume: 3 µL; Column temperature: 40 °C; Elution: gradient; Capillary voltage: +3kV; Desolvation temperature: 400 °C; Cone voltage: 40 V; SIM mode: m/z 227.1 > 212.1 and 227.1 > 133.1 for BPA	Reverse-phase Xterra CSH C18 column (100 mm x 2.1 mm, 2.6 µm)	BPA-d16 in ethanol	LOD: 0.02 µg/g	BPS, BPE, BPB, BPF and HPP	(K. Pivnenko et al., 2015)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Compounds analyzed besides BPA	Reference
MS/MS	Mobile phase: A: water/formic acid (99.8:0.2, v/v) and B: acetonitrile/water/formic acid (97.8:2:0.2, v/v/v); Elution: Gradient; Column temperature: 25 °C; Injection volume: 10 µL; Flow: 240 µL/min; Ionization mode: Positive; Capillary potential: 3.60 kV; Cone voltage: 70 V; RF lens: 1-10V and 2-0.4V; Source temperature: 130 °C; Desolvation temperature: 350 °C; Desolvation gas: nitrogen; Desolvation gas flow 750 L/h; Cone gas: nitrogen; Cone gas flow: 80 L/h; Multiplier voltage: 650 V and the ion energies 1 and 2 were both 0.5V Entrance voltage: -2; Exit voltage: 1 V; SRM transitions: BPA-m/z 511.3 > 354.2	Pentafluorophenylpropyl Ascentis Express F5 column (100 mm x 2.1 mm, 2.7µm), equipped with a F5 guard column (5 mm x 2.1 mm, 2.7 µm); and XBridge C18 column (50 mm x 2.1 mm, 2.5 µm) and an Ascentis Express C18 column (100 mm x 2.1 mm, 2.7 µm)	BPA- ¹³ C ₁₂	LOD: 0.073 µg/Kg LOQ: 0.243 µg/Kg	BPA analogs: BPS, DMBPS, BPF, BPE, BPB, BPZ, BPAF, BPAP, TBBPA and BPP	(Regueiro & Wenzl, 2015)
MS/MS	Mobile phase: A - water/formic acid (99.8:0.2, v/v) and B - acetonitrile/water/formic acid (97.8:2:0.2, v/v/v); Elution: Gradient; Flow: 240 µL/min; Injection volume: 10 µL; Ionization mode: Positive; Capillary voltage: 3.60 kV; Desolvation temperature: 350 °C; Source temperature: 130 °C; Cone gas flow: 80 L/h; Desolvation gas flow: 750 L/h; Nebulizer, desolvation and cone gas: Nitrogen; RF lens voltages: (1) 10V; (2) 0.4 V; Multiplier voltage: 650 V; Ion energies: 0.5 V; Entrance voltage: (1) -2V; (2) 1V; Collision gas: Argon; Collision gas pressure: 4.5 x 10 ⁻³ mbar; SIM mode: MRM1 511.3 > 354.2 and 523.2 > 366.2 m/z; MRM2 511.3 > 290.1 and 523.2 > 302.1 m/z; CL-ELISA were 0.2 mg/mL of both OVA-BPAB conjugate and BPAB 11 antibody.	Pentafluorophenylpropyl Ascentis Express F5 column (100 mm x 2.1mm, 2.7 µm) with F5 guard column (5 mm x 2.1 mm, 2.7 µm)	-	LOD (non-alcoholic) = 1.8 ng/L; LOD (alcoholic): 7.1 ng/L	BPS, DMBPS, BPF, BPE, BPB, BPZ, BPAF, BPAP, TBBPA and BPP	(Regueiro & Wenzl, 2015)
UV	Mobile phase: (A) water (35%); (B) acetonitrile (65%); Elution: Isocratic; Injection volume: 10 µL; Flow: 1.0 mL/min; λ: 226 nm	LiChrosorb® C18 column (4.6 x 250 mm x 4.6 mm, 5 µm)	-	LOD: 3.05 µg/L LOQ: 10.16 µg/L	-	(Reyes-Gallardo, Lucena, Cárdenas, & Valcárcel, 2016)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Compounds analyzed besides BPA	Reference
UV	Mobile phase: acetonitrile/water (67:33, v/v); Elution: Isocratic; Column temperature: room temperature; Injection volume: 20 µL; Flow: 1.0 mL/min; UV detector λ : 230 nm; Operating pressure: 200 bar; Retention time: 2.96 min	Intertsil C8 column (250 mm $\times$ 4.0 mm, 5 µm)	-	LOD: 0.75 µg/L LOQ: 2.5 µg/L	-	(Filippou, Deliyanni, & Samanidou, 2017)
MS	LC: Mobile phase: (A) MilliQ water; (B) methanol; Flow: 0.6 mL/min. Retention time for BPA was 14.1 min and 12.26 min for the IS MS: Coupled with an APCI interface. BPA monitoring was achieved in selected ion monitoring negative mode, with ions m/z 271.15, 133.90, 259.15 and 273.20 for BPA and 236.15 for the IS.	Discovery C18 column (250 mm $\times$ 4.6 mm, 5 µm)	Phenobarbital-D5	LOD: Soft drinks - 0.1 ng/ml Canned food (solid phase) - 0.6 ng/g Canned food (liquid phase) - 0.2 ng/ml LOQ: Soft drinks - 0.4 ng/ml Canned food (solid phase) - 1.9 ng/g Canned food (liquid phase) - 0.8 ng/ml	-	(Tzatzarakis et al., 2017)
UV	Mobile phase: (A) Water (B) Methanol; Elution: Gradient; Column temperature: 30 °C; Injection volume: 20 µL; Flow: 1.0 mL/min; UV detector λ : 276 nm	Dionex Acclaim™ 120 C18 column (250 mm $\times$ 4.6 mm, 5 µm)	-	LOD: 0.3 ng/mL LOQ: 1 ng/mL	-	(Wu et al., 2017)
FLD	Mobile phase: (A) MilliQ water; (B) Acetonitrile; Elution: Gradient; Column temperature: 25 °C; Injection volume: 5.0 µL; Flow: 0.500 mL/min; λ_{ex} : 275 nm; λ_{em} : 305 nm	Ascentis Express RP-Amide stainless steel column (75 mm $\times$ 4.6 mm, 2.7 µm)	-	LOD: 0.50 ng/mL LOQ: 0.15 ng/mL	BPB, BPF, BADGE, BFDGE	(Gallo et al., 2017)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Compounds analyzed besides BPA	Reference
FL MS	UPLC/FL: Mobile phase: (A) water (B) acetonitrile; Column temperature 25 °C; Injection volume: 20 µL; Flow rate: 0.4 mL/min; Gradient: binary, 0–5 min – 30% B, 8 to 12 min – 40% B, 14 to 17 min – 100% B, and 17 to 20 min – back to 30% B. λ_{ex}: 230 nm; λ_{em}: 316 nm UPLC/MS: electrospray ionisation mode switching (ESCI) source, operating in negative mode (ESI⁻); Mobile phase: (A) water+ammonium (B) methanol; Flow rate: 0.3 mL/min; Injection volume: 10 µL; gradient: 0 to 5 min – 50% B, 8 to 12 min – 60% B, 14 to 17 min – 100% B and 17 to 20 min – back to 50% B; capillary voltage 1 kV; sample cone and source offset 65 and 45 a.u, respectively. Desolvation and cone gas flow were respectively 600 and 20 L/min, while desolvation and source temperature were set at 500 and 130°C.	Pentafluorophenyl-grafted octadecyl silica column (C18-PFP, 150 x 2.1 mm ID, 2 µm)	-	LOD: 0.1 µg/L LOQ: 0.25 µg/L	-	(Noureddine El Moussawi et al., 2018)
FL	Mobile phase: acetonitrile/ water (62:38, v/v); Injection volume: 20 µL; Column temperature 35 °C; Flow rate: 0.5 mL/min; λ_{ex} : 227 nm; λ_{em} : 313 nm	Waters XBridge C18 column (250 × 4.6 mm i.d., 5 µm)	-	LOD: 0.1 ng/mL LOQ: 0.33 ng/mL	-	(Yin et al., 2018)
MS/MS	HPLC: Mobile phase: (A) water with 0.05% ammonium hydroxide (B) methanol; Injection volume: 20 µL; Column temperature 35 °C; Flow rate: 0.5 mL/min; Gradient elution: 0–3.0 min, 35–95% B; 3.0–9.0 min, 95% B; 9.0–9.1min,95–35% B; 9.1–15.0min,35%B. MS/MS: ESI; Electrospray voltage: – 4500 V; Ion source temperature: 500 °C; Nebulizer gas: 50 psi; Heater gas: 60 psi; Curtain gas:20 psi.	Waters XBridge C18 chromatographic column (150 mm × 4.6 mm, 5 µm)	BPA-d ₄ ; 4-n-nonylphenol-d ₄	LOD: 0.3 µg/L LOQ: 1.0 µg/Kg	BPF; 4-Nonylphenol, 4-n-Nonylphenol, and Octylphenol	(Hao et al., 2018)
FL	LC Mobile phase: (A) formic acid 0.1% acetonitrile (B); Flow rate: 1.0 mL/min; Gradient elution: initially 55% A and 45% B, decreased linearly to 45% A from 0.0 min to 7.0 min, held there for 17.0 min from 7.0 min to 24.0 min, and finally recovered to 55% A and held for 4.0 min. FL Mobile phase: (A) water (B) acetonitrile; Column temperature 35 °C; Injection volume: 20 µL; λ_{ex}: 215–245 nm; λ_{em}: 295–315 nm.	Waters, C18 column (250 mm×4.6 mm, 5µm, 100Å)	-	LOD: 3.1 µg/Kg LOQ: 9.8 µg/Kg	BPA, BPB, BPC, BPE, BFDGE·2H ₂ O, BFGDGE·H ₂ O, BADGE·2H ₂ O and BADGE.	(Xiong et al., 2018)

Detector	Conditions	Analytical Column	Internal Standard	LOD and LOQ	Compounds analyzed besides BPA	Reference
FL	LC Loop: 20 µL; Elution: isocratically; Mobile phase: acetonitrile/ water 50:50 (v/v); Flow rate: 0.5 mL/min FL λ _{ex} : 273 nm; λ _{em} : 305 nm.; Retention time: 14.90 ± 0.50 min	reversed-phase Supelco Ascentis C18 (250 x 4.6 mm, 5µm) with a Supelguard Ascentis C18 guard column (Supelco, Bellefonte, PA, USA)	-	LOD: 3.75 ng/mL LOQ: 12.51 ng/mL	-	(Russo et al., 2018)

BADGE- bisphenol A diglycidyl ether; **BADGE.2H₂O**- bisphenol A bis(2,3-dihydroxypropyl) ether; **BADGE.2HCL**- bisphenol A bis(3-chloro-2-hydroxypropyl) ether; **BADGE.HCL**- bisphenol A (3-chloro-2-hydroxypropyl) glycidyl ether; **BADGE.HCL.H₂O**- bisphenol A (3-chloro-2-hydroxypropyl) (2,3-dihydroxypropyl) ether; **BBzP**- phthalate butyl benzyl; **DCPS**- 4,4'-dichlorodiphenyl sulphone ; **BFDGE**- bisphenol F diglycidyl ether;; **BPA**- bisphenol A; **BPAF**- bisphenol AF; **BPAP**- bisphenol AP; **BPB**- bisphenol B; **BPC**- bisphenol C; **BPE**- bisphenol E; **BPF**- bisphenol F; **BPP**- bisphenol P; **BPS**- bisphenol S; **BPZ**- bisphenol Z; **CoulArray**- coulometric electrode array detector; **DAD**- detector diode array ; **DCHP**- dicyclohexyl phthalate ; **DEHP**- bis(2-ethylhexyl) phthalate ; **DEP**- diethylphthalate ; **DHPS**- 4,4'-dihydroxydiphenyl sulphone; **DiBP**- di-isobutyl phthalate ; **DiDP**- di-isodecyl phthalate ; **DiNP**- di-isononyl phthalate ; **DMBPS**- 4,4'-Sulfonylbis(2-methylphenol) ; **DMP**- dimethyl phthalate ; **DnBP**- di-n-butyl phthalate ; **DnOP**- di-n-octylphthalate ; **DPS**- diphenyl sulphone ; **ECD**- electrochemical detector ; **FL**- fluorescence; **FLD**- fluorescence detection; **H₂O.BADGE**- bisphenol A (2,3-dihydroxypropyl) glycidyl ether ; **HPLC- CoulArray**- high-performance liquid chromatography-coulometric electrode array detector; **HPLC**- high-performance liquid chromatography; **HPLC-FLD**- high-performance liquid chromatography- fluorescence detection; **HPLC-MS**- high-performance liquid chromatography- mass spectrometry; **HPLC-MS/MS**- high performance liquid chromatography–tandem mass spectrometric; **HPP**- 4-cumylphenol; **LC**- liquid chromatography; **LC-ESI**- liquid chromatography negative electrospray ionosation; **LC-FLD**- liquid chromatography- fluorescence detection; **LC-MS**- liquid chromatography- mass spectrometry; **LC-MS/MS**- liquid chromatography–tandem mass spectrometric; **LOD**- limit of detection; **LOQ**- limit of quantification; **NP**- 4-nonylphenol ; **OP**- 4-octylphenol ;; **TBBPA**- tetrabromobisphenol A; **TCBPA**- Tetrachlorobisphenol A; **UHPLC**- ultra- performance liquid chromatography; **UPLC-MS**- ultra- performance liquid chromatography-mass spectrometry ; **UV**- ultraviolet detector

Table 4: Evolution history of the reference values: TDI and SML related to BPA in plastic FCMs.

Year	TDI ¹ (mg/kg bw/day)	SML ² (mg/kg food or food simulant)	References
1990	0.05	3.0	(<i>Directive 90/128/EEC</i> , 1990)
2004	0.01 (t-TDI) ³	0,6	(<i>Directive 2004/19/EC</i> , 2004)
2006	0.05	0.6 SML (T) ⁴	(European Food Safety Authority, 2006)
2011	0.05	0.6	(<i>Regulation (EU) No 10/2011</i> , 2011)
2011	0.05	0.6 SML (T) *	(<i>Directive 2011/8/EU</i> , 2011), (<i>Regulation (EU) No 321/2011</i> , 2011)
2015	4 µg/Kg bw/day (t-TDI)	0.6 *	(<i>Regulation (EU) No 321/2011</i> , 2011) (EFSA, 2015b) (<i>Directive 2006/141/EC</i> , 2006)
2018		0.05 SML	(<i>Commission Regulation (EU) 2018/213</i> , 2018)

*Restriction: BPA not to be used for the manufacture of polycarbonate infant (Directive 2006/141/EC, 2006) feeding bottles

¹ TDI (Tolerable Daily Intake) is an estimate of the amount of a substance, expressed in milligrams on a body weight that can be ingested daily over a lifetime without appreciable risk. The TDI has been set to protect all human populations for lifetime exposure, including the most vulnerable groups such as pregnant and lactating women, infants and young children.

² SML - specific migration limit for individual substance fixed on the basis of a toxicological evaluation. It is set according to the TDI established by the SCF/EFSA. To set the limit, it is assumed that, every day throughout a lifetime, a person of 60 Kg body weight consumes 1 Kg of food packed in plastics containing the substance at the maximum permitted quantity. (*Regulation (EU) No 10/2011*, 2011).

³ t-TDI (temporary Tolerable Daily Intake) is allocated if there are uncertainties in the data that may be resolved by further studies and it is known that significant new data will be available in the near future.

⁴ SML (T) - specific migration limit (total) in food or food simulant expressed as a total of a substance indicated

Figures

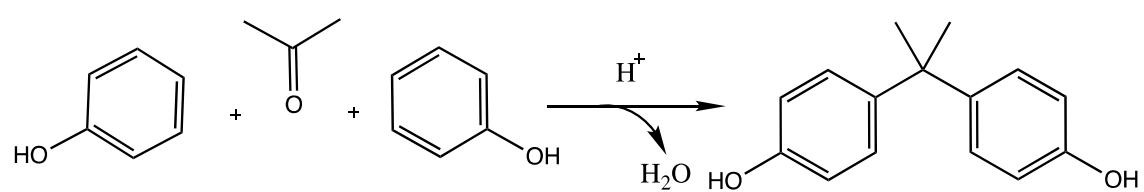


Figure 1

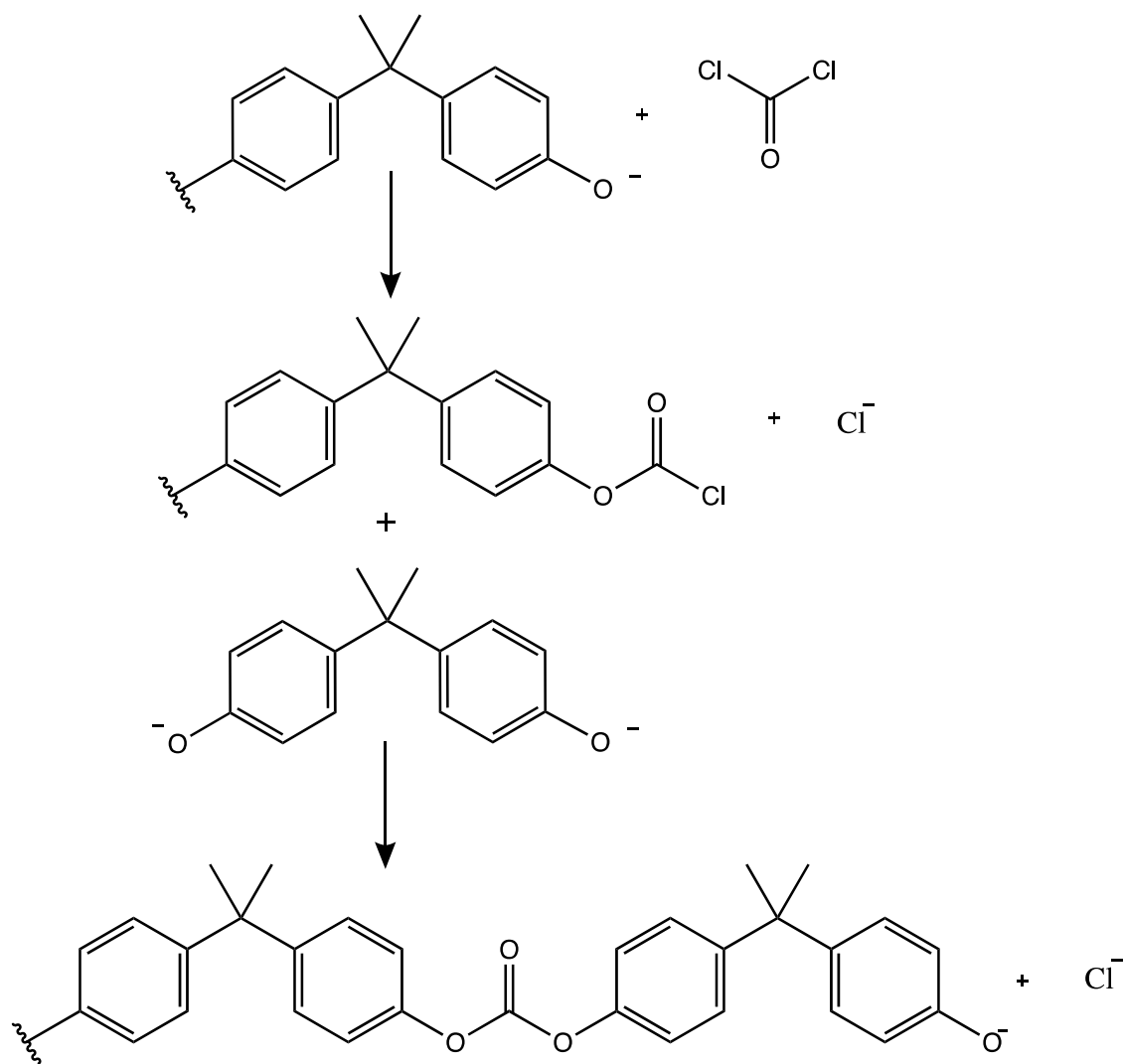


Figure 2

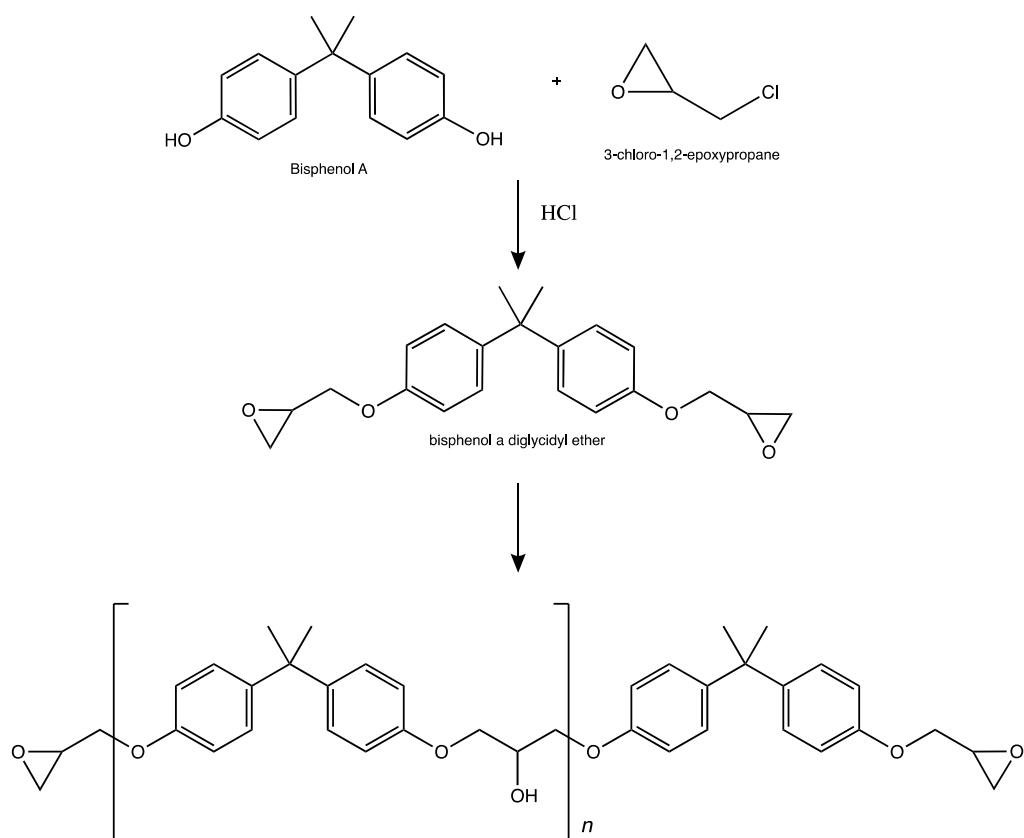


Figure 3

Figure captions

Figure 1 – Synthesis of bisphenol A from the reaction of phenol with acetone in the presence of an acid catalyst.

Figure 2 - Production of polycarbonate by the condensation polymerisation reaction of BPA and carbonyl chloride.

Figure 3 - Production of epoxy resins.