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Bisphenol A levels in commercial milk, infant formula and dairy products

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Abstract. This paper reviews current information on milk, infant formula and dairy products contamination with bisphenol A (BPA), an ubiquitously found chemical compound originating from polycarbonate containers and epoxy resins. BPA is highly lipophilic and bioaccumulates. It leaches into food, particularly at high (>50°C) temperatures. It has been shown that BPA may mimic estrogenic effects in both animals and human, resulting in reproductive disorders and potentially increased risk of hormone-dependent cancers. Recently, BPA has been implicated in the etiology of pandemic diseases such as obesity and type 2 diabetes mellitus. Although banned for use in baby bottles by the European Commission, it remains controversial if longlife use of BPA-containing products poses significant risks for human and animals. Milk and dairy products are widely consumed however BPA levels reported in the majority of studies appear not to exceed maximum limits accepted by the European Union. Higher BPA concentrations have been constantly detected in canned milk and infant formula.
Key Words: bisphenol A, food chain, food containers, endocrine-disrupter.

Introduction. Persistent organic pollutants (POPs) define synthetic chemical substances with long remanence (for tens of years) in the surrounding environment (water, air, soil) and the property to spread within the food chains. Typically, organochlorine pesticides enter, through contaminated fodders, the animal body and concentrate in animal products and sub-products, food being the most significant way of human contamination. Lipid soluble organochlorine compounds participate in a process of bioaccumulation, particularly in fat tissue and fatty biological environments such as milk. Despite ban of use of DDT and its metabolites and further hexachlorbenzene and heptachlorine applied in Romania since 1985 and 1995, respectively, and continuous efforts of neutralization of 12 POPs of international interests as stated by the Stockholm Convention (Downie 2003), due to the long half-life and phenomenon of bioaccumulation, pesticides and other organochlorine are still detected at noticeable levels in the food chain.

Risks associated with use of bisphenol A. Among organic compounds with certified hormone-disruptive effects, bisphenol A (BPA) is widely used in the fabrication of polycarbonate plastics and epoxy-resins and enters the animal and human food chain mainly through food containers. Although, in a recent directive adopted by the European Commission, BPA use in the fabrication of baby bottles received interdiction, BPA is found in several types of food containers, water supply pipes and other plastics. Being highly lipophilic, leaching from food containers at temperatures above 50°C, BPA is rapidly dissolved in milk and dairy products. BPA residues in baby bottles were detected at concentrations up to 100-200 ng g^{-1} however presence of BPA in milk and sub-products appears to be lower, the highest levels being encountered in sterilized milk (Casajuana et al 2004). On the other hand, when whole bottles are exposed at temperatures up to 70°C, migration levels from bottles into the water ranged from 228 to 521 ng mL^{-1}; BPA migration was found to increase over the time in the quadratic equations (Cao et al 2008). On the other hand, microwave heating appears not to affect the migration of BPA into water from polycarbonate, despite the high temperatures, as shown in a comprehensive study on 18 different brands of polycarbonate baby bottles from the European market (Ehlert et al 2008).

In contrast, information on BPA migration from food containers at room temperature is limited and controversial. Analyzing canned liquid infant formula stored for a ten month period at room temperature, additional migration of BPA from can coatings to liquid formula was documented in 42% of samples, with increases in BPA levels ranging from 29.8 to 110% (Cao et al 2009).

In animals exposed i*n utero* to BPA sex reversal, structural changes of gonads, delayed breeding (Mandich et al 2007; Georgescu et al 2013) and thyroid hormone resistance (Iwamuro et al 2006) were demonstrated. In man, BPA is incriminated as a contributor to hormone-related human pathology, mainly cancer (breast, prostate), thyroid disorders, obesity, type 2 diabetes mellitus and polycystic ovary syndrome (Kandaraki et al 2007).

The mechanisms of action of BPA are not completely elucidated. In principal, BPA functions as a ligand for at least three types of nuclear hormone receptors – the estrogen receptor (ER), the glucocorticoid receptor (GR) and the thyroid hormones receptor (TR) but also interferes with several metabolic pathways. Therefore BPA is thought to act as estrogen and glucocorticoids agonist and impair thyroid hormones effects (Georgescu et al 2012).

In humans, BPA can be routinely detected in blood and urine (in the nanograms per milliliter range). Biomonitoring data clearly indicate that the general population is exposed to BPA ubiquitously, including significant internal exposures to unconjugated BPA. To be emphasized, mammalian studies suggest that a category that is particularly vulnerable to BPA is represented by fetuses and children (Eisner et al 2002). Apart from BPA, other types of bisphenol were identified in various food samples. With respect to total bisphenols, canned food contains significantly higher levels of bisphenols in comparison to foods sold in glass or paper containers.

BPA levels in milk and dairy products. One feature of pollution due to BPA is its ubiquitously presence which is directly related to the degree of industrialization and civilization and hence largely distributed in human environments. Milk (either animal or human) and animal dairy products (particularly canned products) constitute an important source of microbiological (Coroian 2009) and chemical exposure in human, including to BPA residues. As confirmed by a recent large research on BPA levels in several samples of various types of food (The 2008 Canadian total diet study), canned food was responsible for 95% of dietary BPA, with the highest concentration being observed in canned fish (>100 ng g^{-1}) whereas BPA levels in non-canned food was low (Cao et al 2011).

In 2003, a Japanese study measured BPA levels in milk, yogurt, butter, cream, condensed and flavored milk, and reported that BPA was not identified in non-canned products. In canned products, BPA levels between 21 and 43 ng g^{-1} (Kang & Kondo 2003) were identified. Using gas chromatography-mass spectrometry (GC-MS) analysis, higher BPA levels (Table 1) were reported in infant formula powders from Taiwan (Kuo & Ding 2004).

BPA was also identified in milk samples from European countries (*e.g.* Greece, Sweden, Portugal), particularly in canned milk samples or formula with levels varying between large limits (Maragou et al 2006; Cunha et al 2011). In a Canadian research, BPA was detected in all samples of canned liquid infant formula, in various concentrations (Cao et al 2008). In contrast, analysis of infant formula products from USA was able to detect BPA in only 1 of 14 samples (Ackerman et al 2010). Taking into account the much higher fat content in dairy products in comparison to milk, it is expected that lipophilic organic compounds concentrate and therefore BPA will be found at higher levels in milk subproducts. Recent analysis of BPA and nonylphenol (NP) levels from a Swedish food market basket, based on the Swedish per capita food consumption, revealed that dairy products contain BPA levels above LOQ (*limit of quantification*, *i.e.* 2ng g^{-1} fresh weight), indicating food as a significant BPA source in the Swedish population (Gyllenhammar et al 2012). As shown for milk, detection of BPA in various amounts is confined to canned dairy products (Kang & Kondo 2003).

Table 1

Reports of BPA levels in cow milk and infant formula in various countries

No.	*Animal product*	*Country*	*BPA levels*	*Method of detection*	*Reference*
1	Milk	Japan	21–43 ng g^{-1}	HPLC	Kang & Kondo 2003
2	Infant formula	Taiwan	45-113 ng g^{-1}	GC-MS	Kuo & Ding 2004
3	Milk*	Greece	<1.7 to 15.2 ng g^{-1}	LC-ESI-MS	Maragou et al 2006
4	Milk	China	1.6-2.6 ng mL^{-1}	SPME-HPLC	Liu et al 2008
5	Infant formula*	Canada	2.27-10.2 ng g^{-1}	GC-MS	Cao & Corriveau 2008
6	Infant formula	USA	0.48-11 ng g^{-1}	HPLC-MS/MS	Ackerman et al 2010
7	Infant formula	Portugal	0.23 and 0.40 µg L^{-1}	GC-MS	Cunha et al 2011

*BPA levels suit for canned products; GC-MS - gas-chromatography/mass spectrometry; LC-ESI-MS - liquid chromatography coupled with electrospray ionization mass spectrometry; SPME-HPLC - Solid-phase microextraction coupled to high-performance liquid chromatography; HPLC-MS/MS - liquid chromatography-tandem mass spectrometry.

Conclusions. To conclude, BPA is an widely spread POP with endocrine-disrupting effects. Besides direct contact with food, additional migration of BPA from food containers exposed to high temperatures into the food (e.g. milk) may increase exposure to BPA. Food represents the main source of BPA contamination in human, with newborn and children being particularly at risk. Nonetheless, there is still controverse if the BPA levels to which people are currently exposed are beyond the limit of safety; further studies on the topic are warranted.

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