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RESEARCH ARTICLE

EXPOSURE TO BISPHENOL A IN DENTISTRY – CURRENT VIEWS

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ABSTRACT

Bisphenol a is xenoestrogen synthesized in large quantities worldwide for production of polymers (polycarbonates, epoxy resins) and thermal paper. This determines its universal presence - in everyday products (packaging, containers and bottles), food and drinking water. Food is considered to be the most important source of population exposure; however, in overall exposure assessment consumption of drinking water, inhalation of dust and dermal contact with thermal paper must be taken into account. Exposure to BPA and its derivatives from dental composites and sealants is possible. High levels of BPA in saliva (especially immediately or one hour after dental treatment), decreasing over time have been found. No BPA in the blood samples of dental patients have been detected, as reported in the available studies. High urinary levels of BPA after treatment with dental composites and sealants have been reported. The degree of exposure to BPA from dental materials and the possible adverse health effects are insufficiently investigated. No data were found in the available literature concerning the urinary levels of BPA among occupationally exposed dental professionals, in comparison with those among dental patients after treatment with composites and sealants.

INTRODUCTION

This appears to be interesting field for further investigations

Bisphenol A [2, 2 b-bis (4- hydroxyphenyl) propane; CAS 80-05-7], is synthesized by condensation of two phenol groups and one molecule acetone.

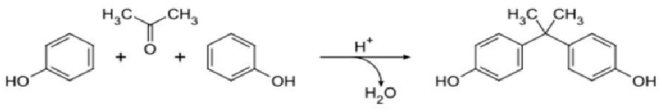

Fig. 1.

Bisphenol A (**BPA**) is a white, crystalline substance with a molecular weight of 228.29 g/cm^3, melting point 156°C and boiling point 220°C, good solubility in fats and low solubility in water. Its solubility is higher at an alkaline pH. The presence of hydroxyl groups (Fig. 1) determines the good reactivity of Bisphenol A (Flint *et al*., 2012 and Volkel *et al*., 2002). Bisphenol A was first synthesized in 1891 by the Russian chemist A. Dianin and Thomas Zincke from the university in Marburg, Germany, who published a note of its synthesis in 1905 (Zincke, 1905). In 1953, Hermann Schnell – Bayer, Germany and Dan Fox- General electric, USA developed the technology for synthesis of a new plastic material – polycarbonate, using BPA as row material. Since then, BPA has been used mainly as:

- monomer in the production of numerous polymers – polycarbonate (PC) plastics, epoxy resins, polysulfones, and polyacrylates;
- antioxidant and inhibitor in the manufacture of polyvynil chloride (PVC) plastics;
- precursor for the synthesis of tetrabromobiphenol-A (Geens *et al*., 2011).

Currently, polycarbonates are widely used for the manufacture of products intended for contact with food - plastic bottles, plates, cups, fireproof containers for microwave ovens, storage containers, etc., and epoxy resins used for internal coating of cans (EFSA, 2006). However, only 3% of totally produced polycarbonates and 10% of epoxy resins are used as materials for contact with food products (Plastics Europe, 2007). There are many other uses of polycarbonates, epoxy resins, polysulfones and polyacrylates, e.g. for manufacture of spectacle lenses, digital media (CD and DVD), mobile phones,

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electronics, computers and other electrical equipment, household appliances, building glass, safety equipment in sport, cars, construction materials, medical equipment, dental materials, thermal print paper (Geens *et al*., 2011). Thermal paper is produced in large amounts as it is used for receipts, faxes, labels, and after recycling - for brochures, tickets, envelopes, newspapers, kitchen towels, toilet paper and cardboard packaging for food (Liao and Kannan, 2011 and Nam *et al*., 2010). In addition, BPA is widely used in the production of polyacrylates, polyesters and varnishes which, after degradation, could be an important source of this compound in environment and food (Vandenberg *et al*., 2007). Through condensation of a ketone or aldehyde with phenols or by alterations of carbonyl derivatives numerous analogues of bisphenol can be synthesized. Many of them are too expensive for wide industrial applications. Among them, widely used is bisphenol-F (BPF) because of the lower viscosity and better solvent resistance compared to BPA (Danzl *et al*., 2009). Bisphenol-S (BPS) is also used as a monomer in plastics industry. Typical for polycarbonate plastics is the unique combination of properties such as optical transparency, shock-resistance and high heat resistance. These characteristics contribute for the diversity of applications of polycarbonate. It is calculated that the current annual production of BPA is about 3.8 million tons.

Routes of entry into environment and foods

The presence of BPA in the environment is associated with anthropogenic activities. It is difficult to define the most important sources for human exposure. It's considered that BPA enters the ecosystems and foods as a consequence of production, processing, and degradation (hydrolysis) of different polymers, e.g. epoxy resins and polycarbonates (Mercea, 2009).

Pharmacokinetics and metabolism

Pharmacokinetics of BPA have been studied in rodents, primates and humans (Doerge *et al*., 2010; Doerge *et al*., 2010; Völkel *et al*., 2005 and Vőlkel *et al*., 2008). After oral administration, BPA is subjected to rapid initial metabolism in the liver and intestines, and is completely absorbed in the gastrointestinal tract. In a subsequent phase, it binds to glucuronic acid to form BPA- glucuronide. Small amounts of BPA can react with sulfates to form bisphenol-sulfate. The glucoronide, a metabolite that has no known biological activity and, in particular, has been shown to be non-estrogenic, was cleared from the blood and excreted by the urine within the day of exposure (Matthews *et al*., 2001; Snyder *et al*., 2000; Völkel *et al*., 2005 and Vőlkel *et al*., 2008). The applied doses are excreted entirely; therefore, exposure to BPA may be assessed by its urinary levels (Vőlkel *et al*., 2008). Upon inhalation or skin exposure to BPA elimination is slower.

Environmental exposure

Air

BPA is presented in the atmosphere in various concentrations, mostly as a result of industrial activities. Berkner *et al*. (2004), in a study performed in the region of Bavaria established low BPA concentration (5-15 pg/m^3), while Matsumoto *et al*. (2005) established significant concentrations (10-1920 pg/m^3) in Osaka. The concentrations of BPA were found to be low in marine areas, highest being over the east coast of Asia. Significantly higher concentrations (170-880 pg/m^3) were measured over large urban agglomerations in Asia, New Zealand and USA. Highest concentrations (4.55 ng/m^3) have been measured in the urban parts of India (Bombay), resulting from the intense burning of plastic products for household use. The polar region was also found to be polluted with BPA (in concentrations 1-17 pg/m^3), most likely origination from the middle latitudes of Eurasia and North America. For the period 1991-2000, an increase in concentration in this region has been observed (Fu and Kawamura, 2010).

Water

Bisphenol A is usually presented in low concentrations in surface water. Rocha *et al*. (2013) established BPA in about half of the rivers in Portugal in concentrations 28.7-98.4 ng/dm^3. Some studies indicate higher degree of pollution of surface water. In a study conducted in Germany, the levels of BPA in the Elbe were 4-92 μg/ dm^3 and its sediments -10-380 μg/dm^3 (Stachel *et al*., 2003). It is considered that the main source of pollution is the industrial waste water (Lee and Peart, 2000). Cladiere *et al*. (2013) evaluated the impact of highly urbanized environment (Paris) for water pollution with BPA. The authors consider as main sources of BPA in urban waste water: atmospheric pollution (10-180 ng/dm^3); sewer overflows (917-2098 ng/dm^3); and effluents (287-1224 ng/dm^3). Significantly higher concentrations of BPA have been found in groundwater near contaminated landfills or such with plastic materials. The average groundwater concentration of BPA near the landfill in Osaka was 740 μg/dm^3 (Kawagoshi *et al*., 2003). High concentrations are found in industrial sewage as well. In a large-scale study of BPA contamination in Canada, Lee *et al*. (2000) measured in raw sewage sludge average BPA concentrations of 36.7 mg/kg (Lee and Peart, 2000).

Food and drinking water

The most important source of human exposure to BPA is by food. Its presence in food is in relation to the exposure of animal and vegetable raw materials, with accumulation in the environment and with the foods contact with polymers that contain it. The daily exposure to BPA with consumed food is evaluated to be 0.48-1.6 μg/kg body weight (Vőlkel *et al*., 2008). Several studies indicate that BPA can be released from polycarbonate and epoxy resins into food and drinking water. Bisphenol A is found in significant concentrations in meat products (0.49-56 μg/kg) (Shao *et al*., 2007), fish (7.1-102.7 μg/kg) (Munguıa-Lopez *et al*., 2005), vegetables and fruits (11.0-95.3 μg/kg) and cereals (1.0-3.8 μg/kg) (Niu *et al*., 2012 and Yoshida *et al*., 2001). Studies demonstrate that BPA concentrations are significantly higher in cans than in fresh food. Yonekubo *et al*. (2008) found BPA in various canned products in concentrations of 0.1 -235.4 μg / kg. Relatively high concentrations (3.7 - 265.6 μg/kg) were found in canned vegetables and fruits (Cunha and Fernandes, 2013). BPA was

also established in canned seafood in concentrations of 1.0 - 99.9 μg/kg (Cunha *et al*., 2012) and in minor concentrations (0.032-4 μg/kg) in canned soft drinks (Cao *et al*., 2009). It has also been found in samples of milk. O'Mahony *et al*. (2013) analyzed 27 samples of commercially available dairy products, including stored in cartons milk, infant formula milk and condensed milk. In just four of the samples the concentrations were above the limit (1.32 μg/kg), and one of the samples (tin of condensed milk) contained high concentration of BPA - 176 μg/kg. An overall analysis of data available from 65 scientific publications, concerning the level of BPA in drinking water, indicates that its concentrations are low in comparison with other sources. Data indicate that in North America, Europe and Asia they were as follow: 0.099, 0.014, and 0.317 μg/dm^3 (Arnold *et al*., 2013). Higher levels were found in bottled water. In a recent study, Colin *et al*. (2013) analyzed the exposure of the French population to BPA from drinking water. The concentrations ranged from 0.07 to 4.21 μg/dm^3 in PC bottles water, with levels being higher in newly produced ones.

Inhalational exposure

Other possible routes of exposure to BPA are through inhalation and the skin. Due to the migration of polymer products, BPA can be found in environmental dust. It is unlikely that inhalation exposure is significant, due to low vapour pressure and therefore low BPA concentrations in the air (Dekant and Völkel, 2008). Inhalation exposure to BPA from household dust is considered to be important for young children, frequently contacting their hands with mouth (Jones-Otazo *et al*., 2005). The use of BPA in consumer products such as epoxy based flooring, adhesives, paints, electronic equipment, etc. is widespread, so its evaporation and/or leaching from them could be a source of indoor dust pollution (Loganathan and Kannan, 2011). In a study, 56 dust samples from different parts of the United States were collected and analysed for BPA content. Significant levels, ranging from 0.5 to 10.2 mg/kg were found in 95% of them. The authors evaluated the exposure doses and concluded that they are close to those causing health effects in experimental animals (Loganathan and Kannan, 2011). Another study, conducted in Belgium showed that the concentrations of BPA in office dust were significantly higher if compared to that in house dust, probably due to the widespread use of electronic equipment in offices. It is generally considered that inhalation exposure of the population is significantly lower than exposure associated with food consumption (Geens *et al*., 2009).

Dermal exposure

Bisphenol A is used as a colour developer in thermal paper. One side of the paper is coated with a powder layer of BPA, which reacts with the ink when exposed to heat or pressure. Thermal paper is used mainly for devices such as cash registers and ATMs (Lassen *et al*., 2011). The population is in everyday contact with BPA as a component of thermal paper, which this way contributes to the overall oral (through direct contact of unwashed hands with food or the mouth) or dermal exposure. Thermal paper is the main source of contamination of recycled paper with BPA (88,102). Braun *et al*. (2011) reported increased urinary levels of BPA in cashiers with frequent dermal contact with thermal paper (Braun *et al*., 2011). More than 80% of paper products such as brochures, tickets, newspapers, and toilet paper contain BPA in concentrations up to 14.4 μg/g, i.e. 3-4 times lower than those in thermal paper (53). The average dermal exposure for general population is estimated at 17.4 ng/day, while among the occupationally exposed it is 1303 ng/day. The contact with thermal paper contributes to more than 98 % of total dermal exposure.

Medical devices and BPA

Some polycarbonate and polysulfone BPA-based polymers are used for production of medical devices - transfusion and dialysis equipment, filters, pumps, bypass devices, spectacle lenses, surgical instruments, inhalers, oxygenators, incubators etc. (Geens *et al*., 2011). Calafat *et al*. (2009) established that the urine BPA concentration among preterm infants is higher than the mean concentrations among the general population (children 6-11 years of age). BPA could be found in medicines (mostly liquid) in metal packing polycarbonate or with epoxy lining (FDA, 2009).

Dental materials and BPA

Dental composite resins are composed of different ingredients – bisphenol-A glycidyl methacrylate (Bis-GMA), bisphenol-A dimethacrylate (Bis-DMA), ethylene glycol dimethacrylate (EGDMA), urethane - dimethacrylate (UDMA) and triethylene glycol dimethacrylate (TEGDMA). Bisphenol A is a row material for production of Bis-DMA and Bis -GMA, and therefore it is possible that minor amounts of BPA are presenting in dental materials, containing such compounds (Fleisch *et al*., 2010; Fung *et al*., 2000; Nathanson *et al*., 1997 and Tarumi *et al*., 2000). These substances are main ingredients of dental restorative materials – composites, sealants, cements, crowns, orthodontic brackets etc. (Schmalz *et al*., 1999 and Tarumi *et al*., 2000). As a result of bis-DMA hydrolysis by the salivary esterases, after treatment with such materials BPA was detected in patient's saliva (Van Landuyt *et al*., 2012).

In summary, BPA may present in dental products in any of the following ways:

- As an ingredient, despite manufacturers' claims that BPA is used "rarely" in the production of dental materials;
- As by-product from the degradation of components of resin-based dental materials. These are a mixture of monomers, usually based on Bis-GMA. Some composite resins may contain other monomer, added in order to modify their properties. An example is bisphenol A dimethacrylate (Bis-DMA). Materials containing bis-DMA can release BPA after their degradation by salivary enzymes.
- In minimal quantities - "traces". As mentioned, BPA is a row material for production of Bis-DMA and Bis-GMA, so trace amounts may present in the final dental material (http://www.ada.org/271.aspx).

Currently, no studies are available to determine directly and quantitatively "the contribution" of dental composite materials for the total BPA exposure (Fleisch *et al*., 2010). The main routes of entry of BPA from dental materials are as follows: through the gastrointestinal tract, through the pulp by the dentinal tubules and through inhalation of volatile compounds (Gerzina and Hume, 1996; Reichl *et al*., 2008; Rogalewicz *et al*., 2006 and Van Landuyt *et al*., 2012). It is assumed that non-polymerized monomers are responsible for side effects manifestations among dental patients (Mohsen *et al*., 1998). The aaquatic environment in oral cavity enhances the chemical degradation thus changing the mechanical properties of dental composites (Cilli *et al*., 2012). It is assumed that, even under optimal conditions, 23-65 % of monomers are not polymerized and are free to enter the oral cavity (Polydorou *et al*., 2009). It is considered that higher amounts are released from polymerized than from non-polymerized composites (Olea *et al*., 1996 and Pulgar *et al*., 2000). Release of BPA from Bis-DMA-containing sealants was established (Fleisch *et al*., 2010 and Schmalz and Arenholt-Bindslev, 2009). Some of the analytical methods used for BPA evaluation are subjected to re-evaluation because of the conflicting results achieved (Imai and Komabayashi, 2000; Imai, 2000; Myers and Hutz, 2011; Olea *et al*., 1996 and Pulgar *et al*., 2000).

Due to its chemical structure, Bis-GMA is considered to be protected from the action of salivary esterases (Azarpazhooh and Main, 2008). The oxidation of polymer matrix, resulting in formaldehyde release, can also lead to BPA release (Bakopoulou *et al*., 2009). In vivo studies assessed salivary BPA levels after application of dental sealants. Salivary BPA levels decreased over time; highest exposures were established immediately after application. None of these studies detected BPA three hours later. A possible explanation is that analytical methods used in these studies are not sufficiently sensitive to detect the extremely low doses of BPA released from the resin.Therefore chronic exposure to low doses cannot be excluded (Fleisch *et al*., 2010). In 1996, Olea *et al*. establish high concentrations of BPA in saliva after sealant (Delton, Dentsply) application (Olea *et al*., 1996). BPA in saliva and urine of patients after application of fissure sealant was reported, with significant differences between the different brands (Joskow *et al*., 2006).

Sasaki *et al*. reported increased levels of BPA in saliva after treatment with composite dental materials, with levels turning to the baseline within 24 hours, when patients were rinsing the oral cavity with water (Sasaki *et al*., 2005). Van Landuyt investigated in vitro the levels of BPA released by dental materials (Van Landuyt *et al*., 2011). It was estimated that a molar crown can release 13 µg - 30 mg BPA after 24 hours. Release from dental materials for 24 hours may be of importance in patients with multiple or big restorations and dental resin-based materials can be a relevant source of BPA in such patients. The concentrations widely vary among manufacturers (Vandenberg *et al*., 2010). According to Von Goetz *et al*. (2010) in chronic exposure (after dental surgical procedures) the levels are 215 ng BPA/a day. This is probably the worst scenario of chronic exposure because the concentration in saliva decreases over time, and after 120 hours still detectable concentrations where found in only one person. Kingman *et al*. (2012) used liquid chromatography/ mass spectrometry to determine the concentrations of BPA and five related compounds in saliva and urine in 171 persons before and 30 hours after treatment with composite restorations. Salivary concentrations of BPA and related compounds increased immediately (within one hour) after placing the composites and returned to baseline levels within eight hours. Except for the increase in BPA, the concentrations of tested compounds in urine reached baseline levels within 30 hours after insertion of the restorations. The changes in the levels of BPA in saliva and urine were similar when anterior and posterior restorations were placed. The authors concluded that treatment with composite restorations is associated with increased levels of BPA and other similar within one hour compounds after placement in saliva, and after 9-30 hours - in urine. In another study, BPA concentration in the of 19 children was examined – before, 1 hour, 24 hours, 7 and 14 days after treatment. The results demonstrated quick increase from the baseline levels (0.26 ng/ml) after 24 hours (1.18 ng/ml), with a peak concentrations detected at 7th day (1.21 ng/ml). Concentrations have not reached the baseline yet 14 days after treatment (0.73 ng/ml) (Martin *et al*., 2005). In an in vitro study, simulating occupational environment during grinding composite materials, MCF- 7 cells were exposed to their extract for one month at 37°C. Rapid growth has been observed, suggesting estrogenic activity. The clinical significance of these findings is unclear, but according to the authors dental professionals can be occupationally exposed to such aerosols several times per day (Van Landuyt *et al*., 2012).

Preventive measures in dental practice

In dental practice, it is most likely that the exposure to potentially toxic substances will occur during processing of the surface (oxygen - inhibited) layer, where the amount of uncured monomers is higher. The removal of this layer reduces the risk of exposure for patients. Rueggeberg al. established that the use of safety "cup" with a cotton swab placed between it and the tooth and slow speed polishing are effective for removal of excess uncured monomers (Rueggeberg *et al*., 1999). Rinsing the mouth with water for 30 seconds after placement of restorations also reduces the levels of chemical agents near to the baseline. To reduce further the exposure, a rubber dam can be used (Fleisch *et al*., 2010). The implementation of good practices in dentistry adds to reduce exposure of the patients and the dentist. Below (Table 1) are presented data from studies on the levels of BPA in some dental materials and biological environment.

Biomonitoring

Since BPA is a chemically unstable compound, with several hours half-life, its concentrations in blood are lower than those in urine, and decrease rapidly after the end of exposure (Needham and Sexton, 2000). Therefore, BPA cannot be detected in most blood samples with current analytical methods (WHO, 2010). Furthermore, due to its ubiquitous presence in the environment is difficult to ignore a possible contamination of a sample with minimal amounts free BPA during its storage and analysis (Markham *et al*., 2010; Yonekubo *et al*., 2008 and Zhang *et al*., 2011). In such cases,

the established concentrations do not necessarily mean real exposure. BPA is rapidly and almost completely eliminated as bisphenol-conjugates, urine examination is the best choice for the aims of biomonitoring. The concentration of total (free plus conjugated) BPA in urine is often used to evaluate the exposure from all possible sources (Vandenberg *et al*., 2007).

Table 1. Level of BPA in dental materials and biological environments

Dental material	Data for the release of BPA
Composite restorations	Saliva 0.43 ng/mL (before restoration); 0.64 ng/mL (1hour after restoration); 0.4 ng/mL (1-30 hours after restoration). Urine 1.67 ng/mL (before restoration); 2.38 ng/mL (9-30 hours after restoration).
Fissure sealant composites	Urine (data from 495 examined children): 2.67 μg/g (children with 11 and more treated with sealer surfaces). Saliva (Delton LC, Dentsply) 3.98 ng/mL (3 hours after 1 restoration with sealer); 9.08 ng/mL (3 hours after 4 restoration with sealer); Reaching baseline levels (0.07-6 ng / mL) within 24 hours. Saliva (Delton LC): 5.8-105.6 ppb (1 hour, 3 hours after placement) 0.3-2.8 ppm (immediately after placement) Exposure to BPA (14 contestants) 110 μg BPA (Delton LC, BisDMA-based sealer); 5.5 μg BPA (Helioseal F, Ivoclar Vivadent) Saliva 90-931 μg BPA (1 hour after placement)
Orthodontic bonding	Saliva 0.8-20.88 ng/mL
Polycarbonate brackets	Saliva 38-60 μg /g material (18 months) 324-697 μg /g material (40 months).
Lingual fixator	Saliva 20.9 ng/mL (30 minutes after placement)
Composite restoration	Silux Plus (3M) 6.4 μg /g in non-polymerized resin; releases 91.4 ng/g material in phosphate buffered physiological solution(24 hours)
Fissure sealant/Composites	Concise (3M) 15.4 μg /g in non-polymerized resin; releases 19.8 ng/g material in phosphate buffered physiological solution(24 hours) Teeth Mate A (Kuraray) 20.2 μg /g in non-polymerized resin; releases освобождава 55.5 ng/g material in phosphate buffered physiological solution(24 hours)
Dental bonding	Clearfil Photo Bond (Kuraray) 18.5 μg /g in non-polymerized resin
Orthodontic bonding	Less than the detection limit 0.1 ppm (in ethanol)
Polycarbonate bracers	697 μg/ g материал (40 months in water) 37.4 μg / g материал (34 months in water) 0.01-0.4 μg / g материал (1 month in water)
Polycarbonate prosthetic plates	2.2 μg / g (34 months in water)
Polycarbonate temporary crowns	2.8 μg /g (34 months in water)
Bonding with a lingual fixator	Transbond XT (3M ESPE) 2.9 μg/mL (1 month in water)

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Studies conducted in North America, Europe and Asia indicated worldwide exposure to BPA. Two recent large-scale studies on exposure degree to BPA were conducted in the US and Canada, including respectively 2514 and 5476 participants. Ubiquitous exposure to BPA, in more than 90% of participants in both studies was established (Bushnik *et al*., 2010 and Calafat *et al*., 2008). In USA, highest concentrations in urine were detected in adolescents (12-19 years), followed by children (6-11 years) and adults (>19 years). In the Canadian study (Bushnik *et al*., 2010), higher were the levels of BPA in the youngest group (6-11 years) if compared with other groups defined by age. In a study performed in Germany, higher concentrations were established in children 3-5 years old if compared with other groups (6-8 years, 9-11 years and 12-14 years old children) (Becker *et al*., 2009). In a study conducted in seven Asian countries, BPA was detected in 94% of samples (Zhang *et al*., 2011). Practically, to perform biomonitoring studies single urine samples are used. Due to the short half-life of BPA, these samples reflect primarily the exposure over a relatively short period of time, prior to the analysis of the sample (Koch and Calafat, 2009). However, in large-scale studies this approach may be useful to evaluate the average exposure of population**.** Data on urinary levels indicate average range of exposure 0.01-0.05 μg/kg body weight per day for adults, and slightly higher (0.02-0.12 μg/kg body weight per day) for children. For the 95th percentile, exposure assessment is evaluated to be 0.27 μg/kg body weight per day for population, and to be higher for babies (0.45-1.61μg/kg body weight per day) and children 3-5-years old (0.78 μg/kg body weight per day) (Zhang *et al*., 2011).

Adverse health effects -data from epidemiological studies

Most of the conducted epidemiological studies are cross-sectional, with a single evaluation of BPA in urine. These types of studies are limited in the field of interpretation, especially for effects with long latency period (e.g. cardiovascular diseases, diabetes). Data on relationship between BPA exposure and manifestation of adverse health effects such as cancer, reproductive damage, cardiovascular disease, diabetes, and disorders of growth, pubertal and neuro-psychological development are summarized in the report of the Joint FAO/WHO Expert Meeting (WHO, 2010). Bisphenol A belongs to the group of xenoestrogens – substances with estrogen-mimicking properties. A significant number of studies have confirmed the estrogenic potential of BPA (Chapin *et al*., 2008) and define it as endocrine disruptor chemical, because of its ability to bind to and activate estrogen receptors, although with a capacity of 1000-5000 times smaller than endogenous 17β-estradiol (Roy *et al*., 2009). In addition, BPA may react with alternative endocrine receptors such as those for thyroid hormone, and peroxisome proliferator-activated receptor gamma (Diamanti-Kandarakis *et al*., 2009). BPA is classified in category 3 for reproductive toxicity, and is considered as main fertility risk factor in humans (INSERM, 2010).

Epidemiological studies demonstrated a correlation between increased urinary concentrations of BPA and poor sperm quality. There is no evidence of a correlation between urinary BPA levels and the age of puberty onset among girls. In a prospective study performed by Braun *et al*. (2009) was suggested that prenatal exposures, especially in the period of

early pregnancy, may be associated with developmental and behavioral disorders - aggression and hyperactivity, especially among girls. Reproduction of this experiment is needed, with multiple examinations of urinary levels of BPA. Basing on data concerning urine its concentration, an association between exposure to BPA and development of cardiovascular diseases (Lang *et al*., 2008; Melzer *et al*., 2012 and Melzer *et al*., 2010), diabetes (Alonso-Magdalena *et al*., 2005; Alonso-Magdalena *et al*., 2006; Alonso-Magdalena *et al*., 2011 and Alonso-Magdalena *et al*., 2010), obesity (Bhandari *et al*., 2013), chronic kidney disease (Krieter *et al*., 2013), breast and uterus cancer (Hiroi *et al*., 2004 and Smith-Bindman, 2012), immune disorders (Clayton *et al*., 2011), chronic respiratory disease and asthma (Spanier *et al*., 2012) was found. Although the short, less than six hours half-life of BPA, recent data suggest that the substance can be accumulated in adipose tissue (Stahlhut *et al*., 2009).

Confirmation of observations above is needed, with prospective studies performing numerous measurements of BPA levels of in order to clarify the duration of exposure (years or even decades) before the onset of cardiovascular diseases, diabetes and reproductive disorders. Due to the short half-life of BPA, although ubiquitously presenting, it is unsecure if epidemiological studies in humans will make it possible to establish the correlation between BPA exposure and long-term effects manifestation (Völkel *et al*., 2005 and Welshons *et al*., 2006). Prenatal exposure to BPA may have harmful cumulative effects; the National Toxicology Program and the US Food and Drug Association Risk Assessment state that "BPA exposure may lead to alterations in nervous system development, in reproduction and metabolism throughout life" (Chapin *et al*., 2008).

Conclusions

1. Bisphenol A is xenoestrogen synthesized in large quantities worldwide for production of polymers (polycarbonates, epoxy resins) and thermal paper. This determines its universal presence - in everyday products (packaging, containers and bottles), food and drinking water. Food is considered to be the most important source of population exposure; however, in overall exposure assessment consumption of drinking water, inhalation of dust and dermal contact with thermal paper must be taken into account.
2. BPA can cause numerous adverse health effects, disrupting endocrine system (e.g. affecting sex hormones, insulin, leptin, adiponectin and thyroxine), as well as immune and nervous systems. Hepatotoxic, mutagenic, and carcinogenic effects and increased risk of coronary diseases have been also discussed.
3. Exposure to BPA and its derivatives from dental composites and sealants is possible. High levels of BPA in saliva (especially immediately or one hour after dental treatment), decreasing over time have been found. No BPA in the blood samples of dental patients have been detected, as reported in the available studies. High urinary levels of BPA after treatment with dental composites and sealants have been reported.
4. The degree of exposure to BPA from dental materials and the possible adverse health effects are insufficiently investigated. No data were found in the available literature concerning the urinary levels of BPA among occupationally exposed dental professionals, in comparison with those among dental patients after treatment with composites and sealants.

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