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Research Article

Bisphenol A in Dental Materials: A Review

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Abstract

Objective: To review scientific literature on BPA in dental materials, introducing the chemistry of BPA and its derivatives, and evaluating the BPA release and exposure from dental materials and the potential human health risks.

Materials & methods: A search of English peer-reviewed dental literature from Pub Med and MEDLINE databases was conducted, and the key words included bisphenol A and BPA.

Results & discussion: Most modern dental resin materials contain BPA-derivatives (but not pure BPA), such as BisGMA, BisEMA, and BisDMA. Unlike BisGMA and BisEMA, BisDMA has an ester linkage connecting bisphenol A molecule to resin. The ester linkage of BisDMA undergoes hydrolysis reaction in saliva to convert BisDMA into BPA. In contrast, neither BisGMA or BisEMA is converted into BPA in saliva. The dental materials containing BisGMA or BisEMA release the amount of BPA far below (0.1%) the daily BPA intakes in people from other sources (dust, air, water, etc.), which poses no human health risks. The dental materials containing BisDMA or polycarbonate has not been found to pose any adverse human health risks, but more studies should be conducted to evaluate the potential adverse human health effects of BisDMA and polycarbonate-based dental materials.

INTRODUCTION

Bisphenol A (BPA) has been present in many plastic polymers since the 1960s. Studies have suggested that BPA has the potential effects on the brain and behavior in infants and young children [1]. In July 2012, the U.S. Food and Drug Administration (FDA) started to ban BPA-containing resins in infant feeding bottles (baby bottles) and spill-proof cups (sippy cups). Many modern resin-based dental restorative materials are composed of BPA derivatives, which has attracted attention and caused people to be concerned about the potential human health risk of dental resin materials.

A lot of literature is now available investigating the BPA release from dental restorations and its potential harm to human health. This paper is a review of the scientific literature on BPA in dental materials, introducing the basic chemistry of BPA and its derivatives, and evaluating the BPA release and exposure from dental materials and the potential human health risks.

MATERIALS AND METHODS

A search of English peer-reviewed dental literature from Pub Med and MEDLINE databases was conducted and limited to dental journals. Key words included bisphenol A and BPA. Titles, abstracts and full articles were reviewed and evaluated.

RESULTS AND DISCUSSION

Chemistry of BPA and BPA-derivatives

Bisphenol A (BPA) (CAS Number: 80-05-7) is an organic white solid compound with two hydroxyphenyl functional groups. It is soluble in organic solvent, but almost insoluble in water. Its chemical structure is shown in Figure 1. BPA is used primarily in the production of polycarbonate (plastic containers, water bottles, and water pipers) and epoxy resins. More than 2 million tons of BPA are currently produced every year [2].

Pure BPA is not a component of dental products. In dentistry, the most commonly used BPA-derivatives include bisphenol A diglycidyl methacrylate (BisGMA), ethoxylated bisphenol A glycol dimethacrylate (BisEMA), and bisphenol A dimethacrylate (BisDMA) (Figure 1). The BPA-derivatives are synthesized from BPA, so they may contain a trace amount of (ppm or ppb level) [3] of BPA. Some BPA-derivatives with ester bond (-O-CO-) linking BPA molecule to resin, such as BisDMA and polycarbonate, have been shown to hydrolyze into BPA (Figure 2) [3-5]. However, the BPA-derivatives with ether (-O-) linkage, such as BisGMA and BisEMA, do not undergo this type of hydrolysis reaction to form BPA (Figure 2) [3-5].

Baseline level of BPA in human and potential health risks

For most people, the primary source of exposure to BPA is

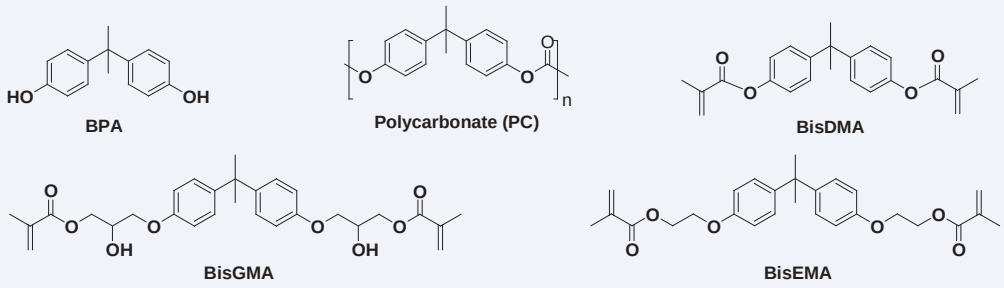

Figure 1 Chemical structures of BPA, polycarbonate, and the BPA-derivatives commonly used in dental materials, such as BisGMA, BisEMA, and BisDMA.

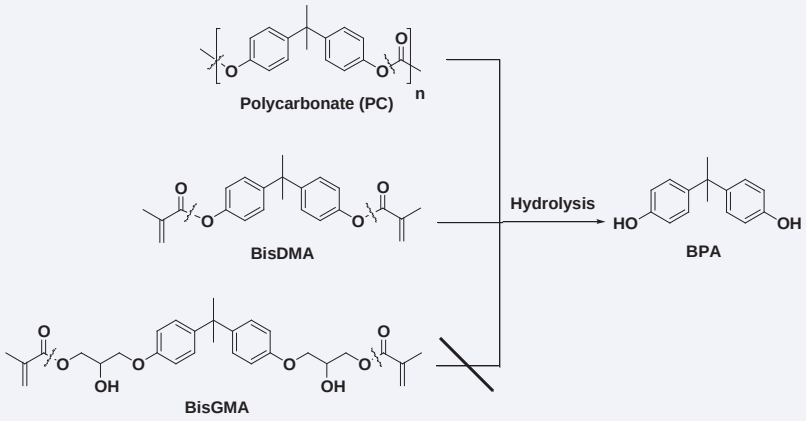

Figure 2 Both polycarbonate and BisDMA have been shown to hydrolyze into BPA at the ester linkage, while BisGMA does not hydrolyze to BPA, because its ether linkage is resistant to hydrolysis [3-5].

through diet. Other source of BPA could include air, dust and water/drinks. BPA has been found in human blood, urine (2.6 ng/mL), breast milk (1.3 ng/mL), and other tissues [6]. The estimated daily intakes of bisphenol A in people (United State) based on the "back calculation" from urinary concentration are about 0.05 μg/kg body-weight/day for people 6 years and older [6]. For infants and children 6 years and younger, the estimated daily intakes based on source of exposure are from 0.04 to 14.7 μg/kg body-weight/day [1].

BPA is considered weakly estrogenic, which can mimic the actions of the hormone estrogen and has some other negative human health effects [7,8]. Studies suggest that BPA has potential effects on obesity [9], fetal and infant brain development [1], dopaminergic system [10], and reproductive system and sexual behavior [11,12].

Although the United States Environmental Protection Agency's (EPA) maximum safe dose of BPA is 50 μg/kg body-weight/day, animal studies indicate that even low-dose exposure (0.025 – 2.5 μg/kg body-weight/day) could have long-term adverse reproductive, carcinogenic, and other effects [13-15].

A National Toxicology Program (NTP) report concludes that NTP has "negligible concern that exposure to bisphenol A will cause reproductive effects" and has negligible concern "that exposure of pregnant women to bisphenol A will result in fetal or neonatal mortality, birth defects" [1]. The NTP has "some concern for effects on the brain, behavior, and prostate gland in fetuses, infants, and children" [1].

BPA release from dental materials

Modern resin-based dental materials play an important role in preventing tooth decay and in promoting oral health [16,17]. They include resin composites (also known as "white fillings"), dental adhesives, dental sealants, resin-modified glass ionomer cements and other resin cements, liners, and pulp-capping materials. They can be immediately polymerized or hardened with a light treatment (LED light or other visible light). Resin-based dental materials are composed of organic resins and some other components such as solvents or reinforcing inorganic fillers, depending on the type of product. The organic resins are formulated with a variety of mixture of monomers and, most importantly, BisGMA. In addition to BisGMA, other monomers are generally included to modify the viscosity, handling and other properties, such as the BisEMA, BisDMA, triethylene glycol dimethacrylate (TEGDMA), and 2-hydroxyethyl methacrylate (HEMA).

Modern resin-based dental materials are not composed of pure BPA. The sources of BPA that leach from dental materials includes trace levels of BPA from the impurity of BPA-derivatives, and the degradation/hydrolysis of dental resin restorations (Table 1). The amount of BPA from the impurity of BPA derivatives (such as BisGMA or BisEMA) is usually very low and not detectable (<2 ppm) [3]. Some older dental resin materials might contain 1.5-20

ppm of BPA in their unpolymerized resin [18,19]. Therefore, a typical dental restoration (0.25 gram material) contains less than 5 μg of BPA for older materials and less than 500 ng of BPA for current materials. Even if all of the BPA is leached out in 1 year, the annual release is still less than 1% or 0.1% of the baseline of BPA intake in the United States (from air, dust, water, and food), and is 100,000 ~ 1,000,000 times lower than the EPA maximum safe dose of BPA. The degradation/hydrolysis of BisDMA and polycarbonate could lead to a much higher amount of BPA release. Studies showed no BPA could be detected for BisGMA sample under any hydrolytic conditions chosen (in methanol at pH values of 0-11 for 30 minutes/50ºC, porcine liver esterase for 24 hours, or in saliva for 24 hours) [3]. However, there is a significant amount of conversion of BisDMA to BPA under those conditions (100% conversion at pH11, 82.5% when subjected to esterase, and 81.4% in saliva) [3]. Other studies demonstrated similar results. For instance, one study showed an 89% conversion of BisDMA to BPA in saliva within 24 hours [4]. Another study showed BisDMA was completely converted to BPA in sodium hydroxide solution within 1 day and was partially converted to BPA in an acidic solution, while BPA was not formed by BisGMA monomer through those chemical-induced hydrolysis [5].

Many *in vivo* and *in vitro* studies show dental restorations release a small amount of BPA, as shown in Table 2 and Table 3. The BPA concentration in saliva was found to peak over the first several hours after restoration with resin materials but returned to baseline levels within 24 or 30 hours [20,21]. The urinary BPA concentration started to increase 9-30 hours after restoration placement [21]. BisDMA-based sealant (Delton LC) released a

Table 1: Source of BPA that leaches from dental materials.

BPA Source	Dental Products	BPA level
Pure BPA as an ingredient	None	N/A
Trace level BPA from the impurity of BPA-derivatives	Resin-based dental products containing BisGMA, BisEMA, etc.	Less than detection limit (2ppm) in raw chemicals [3]
Degradation/hydrolysis of dental materials	Dental products containing BisDMA, polycarbonate. Examples include Delton LC sealant (Dentsply) and polycarbonate bracket	80-90% conversion of BisDMA to BPA in the presence of saliva or esterase after 24hrs [3,4]

Table 2: Reported values of BPA release from dental materials (*in vivo* studies).

Restoration/Products	Reported data of BPA Release
Resin composite restoration	Saliva (172 participants) [21] : 0.43 ng/mL (before restoration); 0.64 ng/mL (1 hour after restoration); 0.4 ng/mL (after 1-30 hours). Urine (172 participants) [21]: 1.67 ng/mL (before restoration); 2.38 ng/mL (9-30 hours after restoration).
Pit & Fissure Sealant/Composite	Urine (495 children) [23]: 2.67 μg/g creatinine (children with 11 or more sealant surfaces). Saliva (Delton LC, Dentsply; 30 participants) [20]: 3.98 ng/mL (3 hours after 1 sealant restoration); 9.08 ng/mL (3 hours after 4 sealant restorations); Returned to baseline levels (0.07-6 ng/mL) within 24 hrs. No BPA in the blood serum. Saliva (Delton LC): 5.8-105.6 ppb (1hrs, 3hrs after placements) [24] 0.3-2.8 ppm (immediately after placement) [25] < 0.1 ppm detection limit (1 hrs and 24 hrs after placement) [25] BPA exposure (14 participants) [22]: 110 μg BPA (Delton LC, a BisDMA based sealant); 5.5 μg BPA (Helioseal F, Ivoclar Vivadent) Saliva [26]: 90-931 μg BPA (1 hour after placement)
Orthodontic bonding resin	Saliva [27]: 0.8-20.88 ng/mL
Polycarbonate bracket	Saliva [28]: 38-60 μg /g material (18 months); 324-697 μg /g material (40 months).
Lingual retainer bonding	Saliva (22 participants): 20.9 ng/mL (30 minutes after placement) [29]

Table 3: Reported values of BPA release from dental materials (in vitro studies).

Restoration/Products	Reported data of BPA Release
Resin composite restoration	Silux Plus (3M) [18]: 6.4 μg /g in unpolymerized resin; released 91.4 ng/g material in phosphate buffered saline (24 hours).
Pit & Fissure Sealant/Composite	Concise (3M) [18]: 15.4 μg /g in unpolymerized resin; released 19.8 ng/g material in phosphate buffered saline (24 hours). Teeth Mate A (Kuraray) [18]: 20.2 μg /g in unpolymerized resin; released 55.5 ng/g material in phosphate buffered saline (24 hours).
Dental Bonding Agent	Clearfil Photo Bond (Kuraray) [18]: 18.5 μg /g in unpolymerized resin
Orthodontic bonding resin	less than detection limit 0.1 ppm (in ethanol) [35]
Polycarbonate bracket	697 μg/ g material (40 months in water) [25] 37.4 μg / g material (34 months in water) [28] 0.01-0.4 μg / g material (1 hrs in water) [36]
Polycarbonate denture plate	2.2 μg /gram (34 months in water) [28]
Polycarbonate temporary crown	2.8 μg /gram (34 months in water) [28]
Lingual retainer bonding	Transbond XT (3M ESPE) [37]: 2.9 μg/mL (1 month in water), and the control (tooth only) was 0.16 μg/mL

significantly higher amount of BPA (110 μg) than other sealants, such as Helioseal F (5.5 μg), due to the hydrolysis of BisDMA [22].

Potential human health risks of BPA from dental materials

BPA content in modern dental materials is very low (less than several ppm). Even if all of the BPA is released into saliva, the BPA-release is still far lower than the baseline of BPA intake from other sources (air, dust, water). For instance, a study showed the maximum BPA release is less than 1/1000 of the reported dose (2 micrograms/kg body weight/day) required for xenoestrogenisity *in vivo* [18]. However, dental materials containing BisDMA and polycarbonate release a much higher amount of BPA, due to the hydrolysis reaction in saliva. A recombinant yeast cell assay study showed significantly increased estrogenic activity in saliva samples collected immediately after placement of Delton LC Sealant (a BisDMA-based sealant) [25]. However, even a restoration with BisDMA-based resin, the BPA level in saliva returns to baseline levels within several hours or a couple days [20,25]. An animal study with pregnant mice confirmed that BPA did not accumulate in the body and was discharged within 5 days [30]. BPA was not transferred to the newborn mice, either [30]. Many other studies demonstrated that human exposure to BPA from dental materials was minimal, and posed no known adverse health effects [31-34].

CONCLUSIONS

Modern dental materials contain BPA-derivatives, not pure BPA. There are two types of BPA-derivatives: ones that cannot be hydrolyzed into BPA, such as BisGMA and BisEMA, and others that can be hydrolyzed into BPA in saliva, such as BisDMA and polycarbonate. Dental materials containing BisDMA or polycarbonate have not been found to have any adverse human health risks, but more studies should be conducted to evaluate the potential adverse effects of BisDMA or polycarbonate-based dental materials, since they can be converted into BPA in the oral environment. Dental materials containing BisGMA or BisEMA release BPA far below (0.1%) the daily BPA intake from the environment (dust, air, water) and far below (100,000 ~ 1,000,000 times lower) the EPA maximum safe dose of BPA (50 μg/kg body-weight/day), and pose no human health risks. On the basis of the huge benefits of resin-based dental materials and negligible BPA-release after resin application, we recommend continuing application of resin-based dental materials.

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