

An investigation into bisphenol-A leaching from orthodontic materials

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ABSTRACT

Objective: To quantitatively determine the bisphenol-A (BPA) leached from orthodontic materials during simulated intraoral exposure.

Materials and Methods: Samples of orthodontic materials were subjected to simulated abrasion, immersion in artificial saliva, thermal shock via temperature cycling, and simulated intraoral exposure. Sample aliquots were collected for up to 2 weeks after artificial saliva immersion, derivatized, then analyzed for BPA by gas chromatography/mass spectroscopy.

Results: Quantifiable amounts of leached BPA were observed from a thermoformed orthodontic retainer material (7.63 µg/g of material) and an orthodontic adhesive (2.75 µg/g of material). BPA leaching was only observed within the first 3 days of artificial saliva immersion.

Conclusions: Under the test conditions, BPA was observed to leach from two orthodontic materials. While the quantities of leached BPA were below the reference dose for daily intake, existing data of low-dose effects and medical disorders associated with elevated urinary BPA levels suggest that BPA exposure, and thus the use of the leaching materials identified in this study, should be reduced or eliminated. (*Angle Orthod.* 2014;84:516–520.)

KEY WORDS: Bisphenol-A; BPA; Leaching; Orthodontic materials

INTRODUCTION

Bisphenol-A (BPA) is a synthetic chemical with known disruptive endocrine and weak estrogenic properties. It is produced industrially, with an estimated annual demand of up to 12 billion pounds and growing at 5% per year as of 2011.¹ BPA is a component in polycarbonate and epoxy polymers, which have applications ranging from paints, coatings, and adhesives to electrical components, food container liners, and data storage. In clinical dentistry, BPA is a precursor of the bisphenol A glycidyl methacrylate (Bis-GMA), bisphenol A dimethacrylate (Bis-DMA), and bisphenol A ethoxylated dimethacrylate (Bis-EMA) monomers found in dental sealants, adhesive resins,² and composite resins. The degradation of

these materials can leach BPA^{3–6} into the oral environment, which could be a clinical concern and could be exacerbated by temperature changes, mechanical wear,⁷ changes in pH,⁸ and bacterial or salivary enzymatic action.

BPA has been detected in many human body fluids, including urine, adult and fetal blood, amniotic fluid, placental tissue, and breast milk.⁹ Epidemiologic studies have detected BPA in the urine of 91% of Canadians aged 6 to 79 years,¹⁰ 93% of Americans aged 6 years or older,¹¹ and 99% of Germans aged 3 to 14 years.¹² The high frequency of detection and the rapid metabolism of orally ingested BPA suggests continuous exposure via multiple routes to substantial amounts of BPA.^{13–15} Many articles have been published on the potentially harmful effects of BPA, including but not limited to its weak estrogenic activity,^{3,16} proliferative effects on human breast cancer cells,¹⁷ disruptive effects on both mouse and human pancreatic cells,^{18–21} adverse effects on the fertility and reproductive system of female mice,⁴ ability to disrupt fetal mouse prostate and urethra development,²² and capacity to impair liver function in mice.²³

Many different orthodontic products are used routinely during and after orthodontic treatment, including but not limited to, brackets, adhesives, cements, ligatures, clear aligners, and retainers. In the manufacturing process of some of these products, BPA is

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Table 1. Specifications of the Orthodontic Materials Used in this Study

Material #	Material Details	Manufacturer	Item #	Batch/Lot #
1a	Prethermoformed Biocryl Essix, clear, 1 mm; 125-mm round	Great Lakes Orthodontics (Tonawanda, NY)	021-025	11-08 60793
1b	Thermoformed Biocryl Essix, clear, 1 mm; 125-mm round	Great Lakes Orthodontics	021-025	11-08 60793
2a	Prethermoformed Biocryl retainer, orange, 2 mm; 125-mm round	Great Lakes Orthodontics	021-086	11-08 61818
2b	Thermoformed Biocryl retainer, orange, 2 mm; 125-mm round	Great Lakes Orthodontics	021-086	11-08 61818
3a	Prethermoformed Dentsply Raintree Essix A+, 5" × 5" square, 0.040" (1 mm) thickness	Dentsply International (Sarasota, Fla)	10045	N/A
3b	Thermoformed Dentsply Essix A+, 5" × 5" square, 0.040" (1 mm) thickness (Clear Image Aligners)	Dentsply International	10045	N/A
4	Unused Invisalign aligner	Align Technology Inc (Santa Clara, Calif)	N/A	N/A
5	Used Invisalign aligner	Align Technology Inc	N/A	N/A
6	Energy Pak latex elastics, Skate Board 3/16", 5 oz	Rocky Mountain Orthodontics Inc (Denver, Co)	J-01141	N/A
7	Alastik Easy-to-Tie Ligatures, gray	3M Unitek (Monrovia, Calif)	406-871	N/A
8	Elastomeric Ligatures, gray	American Orthodontics (Sheboygan, Wisc)	854-674	N/A
9	Colored chain, closed, green	American Orthodontics	854-286	N/A
10	Vogue polycarbonate orthodontic brackets, MLB 18/22, 10NT, 70 FF	Dentsply GAC International (Bohemia, NY)	UR/LL6: 35-163-80	80303
11	Transbond XT light-cure orthodontic adhesive, 2 mm; 6-mm round disks	3M Unitek	712-036	BW7KS
12	Ultra Band-Lok Blue light cure compomer cement with fluoride, 2 mm/6 mm round disks	Reliance Orthodontic Products Inc (Itasca, Ill)	#UBLB	10789

^a a indicates prethermoformed material; b, thermoformed material.

utilized as a starting material. Intraorally, these materials are exposed to extreme thermal changes, mechanical wear, pH changes, and enzymatic degradation from bacterial and salivary enzymes, which can cause BPA leaching. Previous leaching studies of orthodontic adhesives^{24–26} and clear aligners,^{27,28} which failed to investigate mechanical abrasion or temperature changes, did not observe any BPA leaching or estrogenic activity. Conversely, incomplete adhesive polymerization was shown to release BPA,²⁹ and adhesive particles produced during simulated debonding demonstrated estrogenic activity.⁷ Schuster et al.²⁷ noted that mechanical wear in retrieved Invisalign aligners (Align Technology Inc, Santa Clara, Calif) led to continual particle detachment and leveling of the aligner occlusal surfaces as the aligners are replaced. Polymer particles exhibit biological activity,^{7,30} even when the respective bulk material shows no biological activity.^{25,26} The purpose of this study was to subject routinely used orthodontic materials to the vigorous mechanical and thermal conditions possibly experienced intraorally to identify whether those conditions would be responsible for stimulating BPA release.

MATERIALS AND METHODS

Sample Preparation

As-received orthodontic products (Table 1) used at home or in routine orthodontic dental treatment were obtained from the manufacturers blindly, with the

exception of Dentsply Essix materials, which were donated by Specialty Appliances (Cumming, Ga). Biocryl Essix and retainer materials (1a and 2a; Table 1) were thermoformed according to the manufacturers' instructions with a Biostar vacuum thermoforming system (Model 3010, Scheu-Dental GmbH, Iserlohn, Germany) to produce materials 1b and 2b. Materials in contact with incisal or occlusal tooth surfaces (1–5) were subjected to initial single surface abrasion with a new high-speed (330) bur. Large material samples (1–5) were cut with scissors into approximately 5 × 5-mm squares. To ensure a complete cure, eliminate an oxygen-inhibited layer, and avoid leaching of residual monomers,^{29,31,32} disks of Transbond XT and Ultra Band-Lok (materials 11 and 12) were prepared by filling a die space with the material, covering the top of the die with a clear matrix strip (Epitex finishing strips, Lot #0802041, GC America Inc, Alsip, Ill), and curing for 60 seconds with a halogen curing unit (Dentsply Caulk Limited, Model #200R, Milford, Del). The resulting disks were 2 mm in thickness and 6 mm in diameter.

Experimental Design

Artificial unstimulated saliva (AS) was synthesized by dissolving the constituent chemical components (Table 2) in 1 L of Milli-Q water (EMD Millipore Corporation, Billerica, Md) and is based on research by Dawes and Dong.³³ All commercial chemicals were purchased from Acros Organics and used as received.

Table 2. Components of Artificial Unstimulated Saliva (AS) Per Liter of Milli-Q Water

Component	Concentration (g/L)
Potassium chloride (KCl)	1.044
Monosodium phosphate (NaH_2PO_4)	0.681
Sodium bicarbonate (NaHCO_3)	0.420
Calcium chloride (CaCl_2)	0.033
Magnesium chloride (MgCl_2)	0.006

All material samples (1–12; Table 1) were immersed in a medium of 10.0 mL of AS in new glass sample vials with polytetrafluoroethylene-lined caps to prevent BPA contamination for each experimental repetition. Samples were then subjected to thermal shock treatment involving temperature cycling from hot (60°C) to cold (4°C) water baths with shaking for 5 minutes at each temperature; this was repeated for a total of 10 cycles. The samples were then shaken at normal oral temperature (37°C); 1.0-mL aliquots were removed at 24 hours, 3 days, 7 days, and 14 days and placed in new glass sample vials with tetrafluoroethylene-lined caps to prevent BPA contamination.

Sample Analysis

The sample analysis was carried out as follows: 0.5 mL of a standard BPA- d_{16} solution and 0.5 mL of the aliquot sample solution were combined with 10 mL of a 1.0 mol/L potassium carbonate (K_2CO_3) solution. The resulting solution was shaken, and 200 μL of acetic anhydride was added. After 5 minutes another 200 μL of acetic anhydride was added while shaking. Then, 2.5 mL of isooctane was added and the pH was checked. If the pH was below 10 it was titrated to 10 with 1.3 mol/L K_2CO_3 . If the pH was above 10, then 100 μL of acetic anhydride was added while shaking. The solution was left to stand for 10 minutes; then 1 mL of the top isooctane layer was pipetted into a new autosampler vial and analyzed immediately by gas chromatography/mass spectroscopy (GC-MS). A Varian 320 triple quadrupole GC-MS (Varian Inc, Palo Alto, Calif), operated in single quad selected ion monitoring mode, was used to determine BPA concentrations. A Varian VF-5ms (30-m $\times$ 0.25-mm internal diameter $\times$ 0.25- μm film thickness; part #CP8944) GC column was used. The GC oven

program was as follows: start at 100°C, hold for 0.5 minute, increase temperature at 30°C/min, hold for 7 minutes. The column flow was 2.8 mL/min (constant) with splitless injector mode and the injector temperature at 265°C. The MS conditions were as follows: electron ionization mode at ionization energy of 70 eV, emission current of 50 μA , and ion source and transfer line temperatures of 250°C and 265°C, respectively. The diacetylated BPA and BPA- d_{14} derivatives were identified by matching their retention times with those of calibration standards and by the ratio of target ions: 213.1 and 228.1 for diacetylated BPA and 224.1 and 242.1 for diacetylated BPA- d_{14} . BPA concentrations were quantified by calculating the relative response factors based on the area of the internal standard diacetylated BPA- d_{14} or by using a standard calibration curve created by a serial dilution of a BPA water solution. The level of BPA quantitation was determined to be 0.17 ppm. All GC-MS assays were performed in duplicate, and the results were averaged for each experimental repetition. Sample analysis and GC-MS assays were performed by a chemical analysis laboratory.

RESULTS

GC-MS analysis showed that two sample aliquots contained BPA (Tables 3 and 4). Thermoformed Biocryl retainer AS aliquots collected after 1 day of AS immersion from 3 of 4 experimental repetitions contained a mean of 7.63 μg of released BPA per gram of material (Table 4). No additional leaching from thermoformed Biocryl retainer material was observed thereafter on days 3, 7, or 14. Transbond XT showed no BPA leaching after 1 day of immersion in AS; however, leaching was observed after 3 days in two of three experimental repetitions with a mean of 2.75 μg of released BPA per gram of material (Table 4). No further BPA release was observed from Transbond XT on days 7 or 14. All other tested materials showed undetectable (below the level of quantitation, <0.17 ppm) levels of BPA at all time points. All samples were compared to time zero and control (AS) samples, which showed undetectable BPA levels.

The average mass of a Biocryl retainer was between 4 and 5 g, depending on factors such as arch size,

Table 3. Leached BPA Concentrations (ppm/g of Material) in Artificial Saliva

Material Tested ^a	Time (d)	Experimental Repetition #				Descriptive Statistics		
		1	2	3	4	Mean	SD ^b	Range
AS ^b	1, 3, 7, 14	ND ^b	ND	ND	ND	ND	0	ND–ND
2b (thermoformed Biocryl)	1	0.36	ND	0.6	2.09	0.76	0.92	ND–2.09
11 (Transbond XT)	3	ND	0.54	0.49	NA ^b	0.34	0.3	ND–0.54

^a Materials not listed showed undetectable levels of BPA at all time points (1, 3, 7, and 14 days).

^b SD indicates standard deviation; AS, artificial saliva; ND, not detectable (< 0.17 ppm); and NA, not applicable.

Table 4. Leached BPA Masses (mg/g of Material) in Artificial Saliva

Material Tested ^a	Time (d)	Experimental Repetition #				Descriptive Statistics		
		1	2	3	4	Mean	SD ^b	Range
AS ^b	1, 3, 7, 14	ND ^b	ND	ND	ND	ND	0	ND–ND
2b (thermoformed Biocryl)	1	3.6	ND	6	20.9	7.63	9.19	ND–20.90
11 (Transbond XT)	3	ND	4.32	3.92	NA ^b	2.75	2.39	ND–4.32

^a Materials not listed showed undetectable levels of BPA at all time points (1, 3, 7, and 14 days).
^b AS indicates artificial saliva; ND, not detectable (< 0.17 ppm); and NA, not applicable.

palate depth, etc, resulting in an average release of between 30 and 38 µg of BPA. Six disks of Transbond XT had an average mass of 0.7 g, more than the amount of adhesive typically used to bond 24 orthodontic brackets, resulting in an average release of 2 µg of BPA.

DISCUSSION

We investigated BPA leaching from a variety of routinely employed orthodontic materials whose intra-oral use ranges from weeks to years. Because the majority of orthodontic patients are teenagers, the exposure of BPA to their growing and developing bodies may be more hazardous than exposure to adults. These results reveal that thermoformed Biocryl retainers and fully cured Transbond XT orthodontic adhesive leach BPA and thus may contribute to the high frequency of detected urinary BPA in humans.^{10–12} The leached BPA likely originated from the degradation of the material components, such as with the thermoforming of the Biocryl retainer material. The conditions employed in this study represent the vigorous mechanical and thermal conditions possibly experienced intraorally.

In the United States, the Environmental Protection Agency (EPA) reference dose (and Food and Drug Administration acceptable daily intake dose), the presumed “safe” dose, is 50 µg/kg/day of BPA.^{34,35} Because the quantities of leached BPA observed in this study were below the EPA reference dose, it can be concluded that the use of thermoformed Biocryl retainers and Transbond XT is safe at this time. However, many recent studies have demonstrated observable adverse effects, such as cancer cell proliferation,³⁶ with BPA doses below the EPA reference dose.^{37–39} Furthermore, elevated human urinary BPA levels have been associated with peripheral arterial disease,⁴⁰ cardiovascular disease, diabetes, abnormal liver enzyme levels,⁴¹ and obesity in children and adolescents.⁴² Based on this evidence, it seems prudent to minimize our patients’ exposure to BPA.

Methods to reduce BPA leaching from thermoformed Biocryl retainers and Transbond XT may include soaking retainers in hot water for a few hours prior to delivery, removing any excess adhesive before curing, ensuring that all adhesive is fully cured around the bracket’s

peripheral margins, having the patient rinse with warm water after bonding, and/or using an orthodontic adhesive that does not contain a BPA derivative.

CONCLUSIONS

- Under the extreme mechanical and thermal conditions of the study, BPA was found to leach from thermoformed Biocryl acrylic resin retainer material and a fully cured Transbond XT orthodontic adhesive within 3 days of artificial saliva immersion.
- The amounts of leached BPA were below the reference dose for daily intake; however, previous evidence suggests that patient BPA exposure should be minimized and perhaps even eliminated.
- All other tested materials did not leach detectable amounts of BPA under the current experimental conditions.

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