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Release of bisphenol A and TEGDMA from orthodontic composite resins

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Abstract
Most composite resins release both bisphenol A (BPA), which disrupts the endocrine balance, and triethylene glycol dimethacrylate (TEGDMA), which has high risks for human health.
The purpose of this study was to evaluate BPA and TEGDMA leaching from orthodontic light-cured composite resins after immersion in different media and to quantify the BPA released. Dental restoration resins were used as control.
Resin samples were cured for 20 seconds and immersed in distilled water, RPMI 1640 culture medium and ethanol for 24 hours. The release of BPA and TEGDMA was then evaluate by gas phase chromatography and mass spectrometry (GC-MS). The limit of quantification was 0.01 µg/mL.
In ethanol, the eluted amounts of BPA were higher compared to eluted amounts in distilled water and RPMI 1640 culture medium.
The lowest amount (0.01 µg/mL) of BPA released was observed in distilled water and the highest (4.25 µg/mL) with ethanol.
BPA is less frequently released by orthodontic resins in distilled water and RPMI 1640 culture medium in comparison with dental restoration resins. TEGDMA was detected in all resins containing this compound except for Blugloo and Transbond XT in which it was sometimes present while their composition does not indicate the presence of this compound.

Key words: *Bisphenol A, TEGDMA, Monomer released, Light-cured composite resin, GC-MS*

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I. Introduction

The composite resins used in dentistry are complex polymers containing a variety of monomers, initiators, activators, stabilizers, plasticizers and other additives. Two monomers are mainly used in orthodontic adhesive resins: bisphenol A diglycidyl dimethacrylate (Bis-GMA) and triethylene glycol dimethacrylate (TEGDMA). Bisphenol A is used as a raw material for the formulation of Bis-GMA.

During polymerization the monomers crosslink to create a polymeric matrix. The polymerization is however, not complete, leaving up to 10% of residual monomers capable of leaching out [1]. Residual low molecular weight monomers, like 2-hydroxy ethyl methacrylate (HEMA) and TEGDMA, are relatively mobile, and may diffuse through the matrix into an immersion medium.

The unreacted monomers elute from resin-based composites as a result of chemical biodegradation in the presence of liquids such as water, saliva, ethanol, methanol, acetonitrile and bacterial enzymes [2-4].

Several studies have shown that many of residual monomers and additives are leaching from the filling materials even after adequate polymerization [5-11].

By use of chromatographic and mass spectrometric techniques, monomers and additives have been identified in aqueous and alcohol extracts of polymerized dental fillings [5-10, 12].

The relationship between dental materials and endocrine disrupting chemicals was first indicated by Olea et al [13]. There have been many investigations on the adverse reactions of residual monomer released from methacrylate-based restorative materials [14-18].

The quantity and composition of the eluted substances are key factors for the study of the toxic potential of resin composites [19].

Demands for the safety of patients have been put into law [20] because the actions of various polymer derivatives have been shown to have the potential to induce allergic, mutagenic, and carcinogenic effects at the cell and tissue levels [21-25].

In the analysis of low molecular weight monomers and additives GC-MS based methods are to be preferred [26].

The aim of this study was to evaluate BPA and TEGDMA releasing from composite resins using various immersion media and to quantify the BPA released. Three dental restoration resins were used as control.

II. Materials And Methods

Specimens preparation

Specimens (10 mm in diameter and 1 mm in thickness) were prepared from commercially composite resins (Table 1) following the International Organization for Standardization (ISO) 10993-12:2012 standard for medical-device testing in biologic systems [27]. They were then cured for 20 seconds using BA Optima 10 LED Curing Light.

Clearfil Majesty ES-2, Clearfil Majesty ES Flow and Filtek Supreme XTE were control resins.

Table 1: Characteristics of resins evaluated in the study

Manufacturer	Product (Lot)	Resin matrix
Kuraray	Clearfil Majesty ES-2 (4D0069)	Bis-GMA, Hydrophobic aromatic dimethacrylate Hydrophobic aliphatic dimethacrylate
	Clearfil Majesty ES Flow (A60239)	TEGDMA, Hydrophobic aromatic dimethacrylate
Ormco	Grengloo (6623923)	TEGDMA, UDMA, HEMA, Bis-EMA6, GMA, EO-TMPTA, 3-trimethoxysilylpropyl methacrylate
	Blugloo (6556174)	UDMA, Bis-EMA6, GMA, EO-TMPTA, 3-trimethoxysilylpropyl methacrylate
3M	Transbond XT (N921496)	Bis-GMA, Bis-MEPP
	Transbond LR (N919866)	Bis-GMA, TEGDMA
	Filtek Supreme XTE (N879475)	Bis-GMA, UDMA, TEGDMA, Bis-EMA6, PEGDMA

Monomers release

Specimens of resins were immersed in distilled water, RPMI 1640 culture medium and ethanol. The eluates of immersion media were extracted using solid phase extraction (NH_2 cartridge) and then analyzed by gas phase chromatography and mass spectrometry (Agilent 6890 Series – Agilent 7673). A capillary column 30 m in length, internal diameter of 320 µm, and film thickness of 0.25 µm was used with helium carrier gas at a flow rate of 1.2 mL per minute. The column temperature program was set as follows: initially, 80°C for 1 minute, increasing to 150°C at a rate of 20°C per minute, and then increasing to 280°C for 2 minutes at a rate of 10°C per minute. The temperature of the injector was 280°C, and the transfer line was 280°C. Mass spectra were obtained using electron impact ionization (69.9 eV, 34.6 µA, 230°C). The compounds primarily sought were BPA and TEGDMA.

Data were acquired by selected ion monitoring mode and processed with the software MSD ChemStation.

The calibration curve and response factor were computed with reference BPA in different concentrations from 0.01 to 50 µg/mL with caffeine as internal standard. Linear correlation with efficiency of 0.996 was obtained between the amount of BPA and the corresponding peak area. BPA was quantified after identification of the released compounds.

III. Results And Discussion

BPA was detected in all the orthodontic resins with ethanol but not in Transbond XT and Transbond LR with distilled water and RPMI 1640 culture medium. This compound was also present with all immersion media for all restoration resins with exception of Clearfil ES Flow with distilled water.

There was no TEGDMA in Transbond XT with distilled water and in Blugloo with ethanol. Blugloo and Transbond XT did not release TEGDMA with RPMI 1640 culture medium. Clearfil ES-2 was free of TEGDMA with all immersion media. (Table 2)

Table 2: BPA and TEGDMA detected

		Grengloo	Blugloo	Transbond XT	Transbond LR	Clearfil ES-2	Clearfil ES Flow	Filtek Supreme XTE
Distilled water	**BPA (µg/mL)**	0.19	0.59	-	-	0.01	ND	0.29
	TEGDMA	X	X	-	X	-	X	X
RPMI 1640	**BPA (µg/mL)**	0.22 ± 0.29	1.75 ± 0.87	-	-	0.64	0.53 ± 0.44	1.92 ± 0.02
	TEGDMA	X	-	-	X	-	X	X
Ethanol	**BPA (µg/mL)**	Below calibration	Below calibration	1.15	1.27 ± 1.66	4.25	0.36	0.77
	TEGDMA	X	-	X	X	-	X	X

Many studies used GC-MS analysis to evaluate residual monomers released from orthodontic adhesives (Table 3).

Table 3: In vitro studies of monomers released from orthodontic resins using GC-MS analysis

Authors	Monomers	Composite resins	Immersion media and time	Results
Eliades et al [28] 2011	BPA	Transbond XT	Double-distilled water 10, 20, and 30 days	Highest amount: 1-month group (2.9 mg/L) Control: 0.16 mg/L.
Kotyk and Wiltshire [29] 2014	BPA	Transbond XT	Artificial saliva 1, 3, 7, 14 days	Release at 3 days of 0.34 ppm
Bationo et al [30] 2016	BPA TEGDMA	Transbond XT Transbond Supreme LV Blugloo MonoLok 2	Milli-Q water 1 day	BPA detected in Blugloo; TEGDMA in all samples
Pelourde et al [31] 2018	BPA TEGDMA	Transbond XT Transbond LR	Milli-Q water 1 day	No trace of BPA; TEGDMA 31.7 mg/mL for Transbond LR and 13.12 mg/mL for Transbond XT

In this study, BPA is less frequently released by orthodontic resins in distilled water and RPMI 1640 culture medium in comparison with dental restoration resins.

Aqueous solvents are not able to extract the total amount of eluates from the cured specimens. Therefore, we have also used ethanol as an extracting solvent to be able to estimate the total amount of compounds that might leak from the actual filling materials. As expected, higher amounts of eluates were found in ethanol solutions compared to in distilled water and in RPMI 1640 culture medium.

All our resins had derivatives of bisphenol A in their composition except for Clearfil ES Flow in which BPA has however been detected. Blugloo and Transbond XT were free of TEGDMA according to the Material Safety Data Sheets (MSDS) but this compound has been found in Blugloo with distilled water and in Transbond XT with ethanol.

Elution of BPA may result from impurities left after resin synthesis [32, 33]. This compound can be a byproduct of degradation of bisphenol A-glycidyl methacrylate (Bis-GMA) or other components such as ethoxylated bisphenol A dimethacrylate (Bis-EMA), bis-dimethylaminopropyl (Bis-DMA), 2,2-bis-(4-(3-methacryloxypropoxy)phenyl)propane (Bis-PMA), and bisphenol a diglycidyl ether (BADGE) [34, 35].

As for BPA, our results match those of Bationo et al. [30] in 2016 (BPA detected from Blugloo and not from Transbond XT after 1 hour of immersion in Milli-Q water) and Pelourde et al. [31] in 2018 (no trace of BPA with Transbond XT and Transbond LR after 1 hour of immersion in Milli-Q water).

BPA is an endocrine disruptor with potential toxicity in vitro [36] and in vivo [37]. It can cause an early puberty in girls, an ovarian cancer, or a disturbance of the maturation of male reproductive organs. It is also a neurotoxic, with effects on the development of the nervous system, on the homeostasis of the skeleton, on the cardiovascular system, on the liver and on the fatty tissue. In contrast, very few contact allergies seem to be due to BPA [38-40]. Other products including TEGDMA and bis-GMA [41-49], released by the restoration and bonding composites, also present a potential toxicity. Infants, young children and pregnant or nursing women are the most sensitive [50].

IV. Conclusion

Most composite resins release both BPA which disrupts the endocrine balance and TEGDMA which has high risks for human health.

The applied GC-MS method seems well suited for analysis of small monomers and additives eluting from composites. The results allowed for a possibility to compare eluted amounts of organic compounds between various composite resins [51].

The risk of allergies and the cytotoxicity of TEGDMA are known and the probability of its release from dental composites is strong. The best way to protect yourself is to use composites without TEGDMA.

As for BPA which present potentially much more serious risk to health, especially by disturbing the endocrine balance clinical precautions should be taken to decrease its release.

BPA is less frequently released by orthodontic resins in distilled water and RPMI 1640 culture medium in comparison with dental restoration resins.

The MSDS are known to be incomplete and sometimes misguiding [52, 53]. In the MSDS, the manufacturers are obliged to give information about the main ingredients (≥1%).

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Conflict of interest

The authors declare no potential conflicts of interest.

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