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ORIGINAL RESEARCH

Bisphenol A (BPA) release from pediatric dental restorative materials under varied pH and temperature conditions: an *in vitro* study

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Abstract

Background: Bisphenol A (BPA) is a chemical compound of concern in pediatric dentistry. Demand for BPA-free dental materials reflects concern about BPA health risks for children. In this study, seven different dental pediatric restorative materials (Cention Forte Filling Material, Equia Forte HT Fil, Stela Self Cure, Riva Light Cure, Riva Self Cure, Fuji IX GP Fast and Cention Primer) were evaluated for BPA release. **Methods**: Disks (10 mm diameter and 2 mm thickness; n = 3 for each material) were prepared following the manufacturers' instructions and immersed in buffer solutions at pH 4.8, 6.8, and 8.8. Samples were stored at 37 °C and 44 °C for 1, 7, and 28 days and then analyzed using high-performance liquid chromatography (HPLC) coupled with mass spectrometry (MS). **Results**: BPA release was highest under acidic conditions at 44 °C, particularly after 1 day of exposure. Cention Primer exhibited the highest BPA release, with a peak concentration of 1.31 ± 0.17 μg/L after 1 day at 44 °C in acidic conditions. Stela Self Cure followed, with 0.51 ± 0.10 μg/L under the same conditions. Under neutral and basic conditions, no BPA release was observed, except for Cention Primer. **Conclusions**: Within the limitations of this *in vitro* study, BPA release from pediatric restorative materials is time- and pH-dependent. The results reflect short- to medium-term behavior (up to 28 days) and cannot be extrapolated to long-term clinical safety. These findings underscore the clinical importance of minimizing BPA exposure in children by preferring BPA-free restorative options whenever possible.

Keywords

Bisphenol-A (BPA); Dental materials; Pediatric dentistry; Resin-based dental materials; LC-MS/MS; Polymers; Release; Materials testing

1. Introduction

Resin-based dental filling composites are polymeric restorative materials that are commonly employed for a range of different applications in pediatric dentistry [1, 2]. Indeed, modern tooth-colored resin composites have fully replaced silver amalgam fillings in posterior teeth [3]. Despite this, the incomplete photopolymerization of these materials associated with shrinkage and risk of debonding under functional loading and secondary caries are not still minor problems [4].

Adhesive interfaces gaps of dental restorations occur due to volumetric polymerization shrinkage, which ranges from 1% to 4.5% [5]. In addition, several factors contribute to the prevalence of residual stresses during the composite cure [6].

Resin-based dental filling composites consist of various molecular weight monomer's mixture integrated with inorganic nano-filler particles [7, 8]. Research has shown that they are susceptible to biodegradation. Bacterial enzymes found in saliva can break the ester bond in acrylic polymers, a crucial process at the resin-dentin interface [9–11]. Due to irreversible hydrolysis, the resin-dentin interface may break down, leading to the potential development of secondary caries, early restoration failure, and dental restorations replacement [12, 13].

Despite the increasing popularity of resin-based dental filling composites, concerns about the release of toxic molecules such as Bisphenol-A (BPA) and its derivatives have attracted the attention of scientists, pediatrics, and patients [14–16]. After light curing, residual methacrylate monomers are released from these dental materials mainly within the first 1 day in the local environment [17, 18]. Chemical degradation occurs due to hydrolysis and enzyme-induced catalysis by human salivary esterases and dietary oral fluids [19, 20]. Brushing, occlusal sliding, and abrasion are the main wear paths of resin-based dental filling composites. In addition, the incomplete polymerization of resin-based composites can increase these adverse physic-chemical effects mainly in posterior areas [21].

At the cellular level, toxic substances can trigger oxidative stress, impair mitochondrial function, and promote inflammatory pathways, ultimately compromising cell viability and tissue homeostasis [22]. BPA is an organic compound used in the synthesis of polycarbonate, epoxy, and methacrylate matrix materials for a variety of industrial and domestic plastic applications [23, 24]. Resin-matrix composites used in dentistry contain BPA derivatives in their organic matrix components, such as bisphenol A diglycidyl-methacrylate (Bis-GMA), bisphenol A dimethacrylate (Bis-DMA), 2,2-bis(4-(2-Methacryl-oxyethoxy) phenyl) propane (Bis-EMA), and propoxylated bisphenol A dimethacrylate (Bis-PMA).

Due to its structural similarity with some hormones, BPA can bind to various receptors [25, 26] and acts as an endocrine disruptor [27]. Therefore, it has been associated with reproductive, developmental, metabolic, and other disorders [28–30]. Exposure to BPA during prenatal and in pediatric stages may be linked to the development of neurobehavioral traits in children [31]. In addition to the exposure duration, the exposure dose must also be considered, as BPA may have greater effects at low doses than at high doses, without a threshold dose, contrary to the traditional toxicological model [32]. Bis-GMA is a major source of BPA release from resin-based composite materials used as dental fillings products [33]. Lopes-Rocha *et al.* [33] investigated the BPA and Bis-GMA residual release from various polymeric cured dental filling materials. The importance of BPA release from Bis-GMA has also been studied by Berge *et al.* [34]. Several studies proposed new formulations (utilizing non-BPA dimethacrylates) to replace Bis-GMA monomers in resin composites to reduce human exposure to BPA derivatives [8]. Therefore, urethane-dimethacrylate (UDMA), a dimethacrylate monomer commonly used in dentistry, has focused as an alternative to Bis-GMA in resin-based composite materials for dental fillings in anterior and posteriors [35, 36]. In alternative, acid-base dental filling materials, partially resin modified, such as GIC (glass ionomer cement) and Alkasite named, have been introduced to reduce the presence of Bis-GMA and the risk of BPA release [37]. In addition to BPA release, recent studies have demonstrated that these materials are also capable of releasing bioactive ions (Ca^{2+}, F^{-}, PO_4^{3-}, Sr^{2+}), which may contribute to remineralization processes and enhance the protection of dental hard tissues [38, 39].

The European Food Safety Authorities (EFSA) reduced the Tolerable Daily Intake (TDI) from 4 μg/kg/day to 0.2 ng/kg/day (20,000 times less than the last TDI) because of possible BPA low-dose effects [16].

BPA is already abundantly present in the human environment, *e.g.*, in food containers, mineral water bottles, thermal papers, toys, medical devices. All the above-mentioned sources can contribute to unintentional BPA ingestion under the physical or chemical factors which can accelerate the release of BPA into food and beverages [40].

Pediatric patients represent a particularly vulnerable group about BPA exposure, as children have higher metabolic sensitivity to endocrine-disrupting compounds and lower body mass, which may amplify systemic effects. Moreover, restorative procedures are frequent in pediatric dentistry, and materials such as glass ionomer cements and resin-modified alternatives are routinely used in children. These factors justify the importance of specifically assessing BPA release from pediatric restorative materials.

To study the BPA release of different polymeric and acid-base filling dental materials employed in dentistry and mainly in pediatric dentistry [41], it is necessary to conduct *in vitro* experiments over extended times, as these materials are anticipated to remain intact in the mouth for many years.

This *in vitro* study evaluated the short and long-term release of BPA from differently formulated chemical restorative materials used to restore decayed teeth by means of a sensitive liquid chromatography-tandem mass spectrometry (LC-MS/MS) quantification method. The null hypothesis considered in the present investigation was that only polymeric based dental filling materials and not acid-based ones release BPA-derivates under the test conditions.

2. Materials and methods

2.1 Sample type

Seven types of different dental restorative materials daily used also in pediatric dentistry conveyed by specific capsules and available on the market were analyzed. Details regarding the selected materials and their compositions are outlined in Table 1. Specimens were prepared according to the manufacturers' instructions: Cention Forte Filling Material (Ivoclar), Equia Forte HT Fil (GC Europe), Stela Self Cure (SDI), Riva Self Cure (SDI), and Fuji IX GP Fast (GC) were prepared using self-curing methods. Riva Light Cure HV (SDI), Cention Primer (Ivoclar) were prepared using light curing (RADII-CAL CX Collimated Led Curing Light SDI Germany GmbH) for 20 seconds. The curing light unit had an irradiance of 1200 mW/cm^2 and was calibrated prior to use according to the manufacturer's recommendations. Cention Primer (Ivoclar) was also included in the analysis, even though it is a primer rather than a restorative filling material. Its inclusion was justified by the fact that it contains Bis-GMA, unlike the other tested products, and therefore was expected to release measurable amounts of BPA. This material was therefore used as an a priori positive control to confirm analytical method sensitivity, validate BPA detection at low concentrations, and provide a direct comparative reference for materials marketed as "BPA-free".

All materials were prepared using a stainless-steel cylinder with a 10 mm diameter and a 2 mm thickness. Each specimen was mixed by a 3M™ ESPE™ CapMix™ mixer (3M ESPE, Seefeld, BY, Germany) for 10 s and immediately applied to the cylinders. The samples were gently compressed with a celluloid strip and a smooth condenser to prevent the formation of air bubbles and to obtain a smooth and flat surface. After 5 minutes, they were removed, and the surface was polished with 800 grit abrasive paper using a water-cooled rotating polishing machine (Ecomet 30, Buehler Ltd., Lake Bluff, IL, USA).

2.2 Testing conditions of the materials

The analysis was carried out using a procedure outlined in a previous study [42]. Briefly, samples (n = 3 for each material) were submerged in 50 mL of buffer solution at three different pH values (4.8, 6.8, and 8.8) and incubated in

TABLE 1. Composite tested materials specifications.

Material	Manufacturer	Type	Curing mechanism	Composition
Cention Forte Filling Material (LT n. ZL08SR)	Ivoclar (Schaan, Liechtenstein)	Alkasite	Self-curing with light-curing option	Ca-fluorosilicate glass, Ba-Al silicate glass, copolymer, Ca-Ba-Al fluorosilicate glass, 25–50% UDMA, 2.5–10% ytterbium trifluoride, 10–25% aromatic aliphatic UDMA, DCP and PEG-400-DMA
Cention Primer (LT n. Z044W5)	Ivoclar (Schaan, Liechtenstein)	Self-etching primer	Self-curing	HEMA, MDP, Bis-GMA, D3MA, ethanol, methacrylate-modified polyacrylic acid, silicon dioxide, potassium hydroxide, and campherquinone
Stela Self Cure (LT n. 1241269)	SDI (Victoria, Australia)	Resin-based restorative material	Self-curing	10–25% UDMA, 5–15% GDMA, 1–10% silica amorphous, 3–7% ytterbium fluoride, 1–5% MDP
Fuji IX GP Fast (LT n. 2311271)	GC Corp (Tokyo, Japan)	Glass ionomer	Self-setting	Alumino-silicate glass, 25–<50% Polyacrylic acid, water, 5–<10% Tartaric acid
Riva Light Cure HV (LT n. 1237227)	SDI (Victoria, Australia)	High-viscosity glass ionomer	Light-curing	10–20% HEMA, 10–20% HEMA-phosphate derivative, 1–10% GDMA, 1–7% DMAEMA, 1–5% tartaric acid, 0–1% EDMAB, 0–1% camphorquinone, 0–1% BHT, >90% glass, oxide, 1–10% silica amorphous
Riva Self Cure (LT n. 1230955)	SDI (Victoria, Australia)	Glass ionomer	Self-curing	20–30% acrylic acid homopolymer, 10–15% tartaric acid, 90–95% fluoro aluminosilicate glass
Equia Forte HT Fil (LT n. 2309201)	GC Europe (Leuven, Belgium)	Bulk fill glass hybrid	Self-setting	95% fluoro aluminosilicate glass, 5% polyacrylic acid powder, reinforced with silicate particles, 25–<50% polyacrylic acid, 5–<10% polybasic carboxylic acid, 5–<10% tartaric acid

Bis-GMA: bisphenol-glycidyl methacrylate; UDMA: urethane dimethacrylate; DCP: Dicyclopropylidene; PEG: polyethylene glycol; DMA: dimethylamine; HEMA: 2-Hydroxyethyl Methacrylate; D3MA: 3-Dimethylaminopropyl methacrylamide; GDMA: Glycidyl Methacrylate; DMAEMA: N,N-Dimethylaminoethyl Methacrylate; EDMAB: Ethyl Dimethyl Amino Benzoate; LT n.: lot number; MDP: 10-Methacryloyloxysidecyl dihydrogen phosphate; BHT: butylated hydroxytoluene.

temperature-controlled ovens (Precision Thelco, Thermo Fisher Scientific, Waltham, MA, USA) set at 37 °C and 44 °C. Buffer solutions were prepared to simulate acidic, neutral, and basic environments. Specifically, for the acidic condition, a 1 M acetic acid/sodium acetate buffer ($CH_3COOH/CH_3COONa\cdot 3H_2O$) was prepared at pH 4.8. For the neutral condition, a phosphate-citrate buffer was formulated at pH 6.8 using sodium hydrogen phosphate (Na_2HPO_4) and citric acid monohydrate ($C_6H_8O_7\cdot H_2O$). For the alkaline condition, a 1 M Tris(hydroxymethyl)aminomethane hydrochloride (Tris-HCl) buffer was prepared at pH 8.8 using Tris ($C_4H_{11}NO_3$) in combination with hydrochloric acid (HCl). The materials were immersed in the corresponding solutions for 1 day, 7 days, and 28 days before being transferred to glass vials for further analysis.

Each of the seven tested materials was evaluated under three pH conditions (4.8, 6.8, and 8.8) and two temperature conditions (37 °C and 44 °C), at three different time points (1 day, 7 days, and 28 days). The pH of each buffer solution was recorded immediately before specimen immersion and re-measured at each collection interval (1, 7, and 28 days) to confirm stability of the experimental conditions.

The pH values were selected to simulate clinically relevant oral conditions: pH 6.8 represents the physiological salivary pH; pH 4.8 reproduces acidic challenges associated with bacterial metabolism and dietary acids; and pH 8.8 reflects alkalinizing conditions linked to salivary buffering and urea metabolism [43, 44]. Similarly, 37 °C corresponds to the average intraoral temperature, while 44 °C was included to simulate transient elevations caused by consumption of hot beverages or febrile episodes [45, 46].

2.2.1 pH measurements

For pH determination, 5 mL of the soaking solution was extracted from each sample and transferred to 15 mL Falcon tubes. The pH was measured using a digital pH meter (Mettler Toledo-SevenExcellence pH/Cond meter S470-Std-K, Giessen, HE, Germany), which had been calibrated prior to use with standard buffer solutions at pH values of 4.0, 7.0, and 9.0. This calibration ensured accurate pH readings throughout the analysis.

2.2.2 Evaluation of bisphenol A (BPA)

The BPA release was assessed using the methodology described by Lopes-Rocha *et al.* [33] (2023). In this approach, a 75% ethanol-water solution was used to as extraction solvent for the qualitative and quantitative analysis of BPA by HPLC-MS/MS, as well as for the preparation of the calibration. Specifically, three samples of each material were immersed in 1 mL of the solution and incubated at either 37 °C or 44 °C for varying durations: 1 day, 7 days, and 28 days. Qualitative and quantitative analyses of the released BPA were performed using high-performance liquid chromatography (HPLC) coupled with mass spectrometry (MS) on a Thermo Scientific™ UltiMate™ 3000 UHPLC system (Dionex Softron GmbH, Dornierstrasse 4, 82110 Germering, BY, Germany) connected to a TSQ Fortis Triple Quadrupole MS.

For the separation of analytes, a Kinetex® C18 column was used, maintained at 40 °C. The mobile phase consisted of methanol (Phase A) and water (Phase B), both containing 0.045 mM ammonium hydroxide (NH_4OH). The injection volume was 20 μL, and the chromatographic system was operated under gradient conditions at a flow rate of 0.150 mL/min. The gradient program was as follows: from 0 to 2 minutes, 5% A and 50% B; at 8 minutes, 10% A and 90% B, and this composition was maintained until 15 minutes. After that, the mobile phase was returned to the initial condition (50% A and 50% B) for column stabilization before the next injection. The MS acquisition was performed in Multiple Reaction Monitoring (MRM) mode, where collision-induced dissociation (CID) of the precursor ions in the collision cell generated characteristic product ions of the $[M-H]^-$ molecule. These specific ions, used for MRM detection, are listed in Table 2.

For the quantification of BPA release, a standard calibration curve was constructed using concentrations of 0.10, 0.25, 0.50, 1.0, 2.5, 5.0, and 10.0 μg/L in a 75% ethanol-water solution. The calibration curve was generated through linear regression, establishing a relationship between the peak area obtained from the mass spectrometry analysis and the nominal concentration of BPA. This process involved external calibration using deuterated standard Bisphenol A_{d16}, ensuring that the analysis reflected the true concentration of BPA in the sample.

To evaluate the sensitivity of the method, the limit of detection (LOD) and limit of quantification (LOQ) were calculated based on the signal-to-noise ratio. The LOD was defined as the concentration at which the signal-to-noise ratio (S/N) was 3, while the LOQ corresponded to an S/N ratio of 10. These values are essential for determining the minimum concentration of BPA that can be reliably detected and quantified using this method. The use of these criteria ensures that the analytical procedure is both accurate and capable of detecting low concentrations of BPA in the samples.

2.3 Statistical analysis

A priori power analysis was performed using G*Power (version 3.1.9.7, Heinrich Heine University Düsseldorf, Düsseldorf, NRW, Germany) to determine the adequacy of the sample size for detecting differences in BPA release across materials and experimental conditions. Sample size estimation was based on expected large effect sizes (Cohen's $f \approx 0.55$), a significance level (α) of 0.05, and a power of 80%. The analysis indicated that three replicates per condition were sufficient to detect statistically significant effects.

For the statistical analysis, STATA 14.0 software (StataCorp LLC, College Station, TX, USA) was used. Descriptive statistics were conducted to determine the mean concentrations, standard error, and the minimum and maximum values for each composite material. The Shapiro-Wilk test was used to assess the normality of the BPA concentration data distribution. Mixed-effects models (MEMs) were applied to evaluate the effect of material, pH, temperature, and time on BPA release. These variables were included as fixed factors, while specimen ID was modeled as a random effect to account for repeated measures. Two-way interactions among fixed factors were tested (*e.g.*, material × pH, material × temperature, pH × time). Model assumptions were verified through residual analysis. *Post-hoc* pairwise comparisons were adjusted using the Bonferroni correction. The statistical significance of each factor was assessed using the Wald test, with differences considered significant at $p < 0.05$.

3. Results

3.1 BPA release

The BPA release profiles for all materials were evaluated across three distinct pH levels, two temperature conditions (44 °C and 37 °C), and at three different time points (1 day, 7 days, and 28 days). These results are presented in Table 3 and illustrated in Fig. 1. Additionally, the detailed results for each material are shown in Figs. 2,3,4,5,6,7,8. Fig. 1 clearly illustrates that the highest release of BPA was observed at 44 °C, with the greatest release occurring after just one day of exposure under acidic conditions. Notably, the Cention Primer material (represented by the green blocks in Fig. 1) exhibited the highest BPA release, with a peak concentration of 1.31 ± 0.17 μg/L, observed in an acidic environment after 1 day of exposure at 44 °C. The Stela Self Cure material (orange blocks in Fig. 1) followed in descending order of BPA release, with the highest concentration recorded under the same conditions (0.51 ± 0.10 μg/L). In contrast, under basic conditions, no BPA release was detected at either temperature or across the three exposure durations studied, with the only exception being the Cention Primer material, which exhibited a minimal BPA release (0.11 ± 0.01 μg/L) after 1 day at 44 °C. Similarly,

TABLE 2. Mass spectrometry transition for acquisition in MRM mode (Multiple Reaction Monitoring).

Analyte	Molecular Weight (g/mol)	Precursor ion [m/z] $[M-H]^-$	Production [m/z]
BPA	228.29	227.2	211 133

BPA: Bisphenol A.

TABLE 3. Average concentrations (μg/L) with standard deviations (SD) observed for the different materials under three different acidity conditions, at two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days).

Parameters			Materials						
pH	Time	T (°C)	Cention Forte Filling	Stela Self Cure	Riva Light Cure	Riva Self Cure	Equia Forte Ht Fil	Cention Primer	Gc Fuji IX GP Fast
4.8	1 d	44	0.31 ± 0.07	0.51 ± 0.10	0.21 ± 0.07	0.31 ± 0.08	0.21 ± 0.05	1.31 ± 0.17	0.11 ± 0.02
		37	<0.10	<0.10	<0.10	<0.10	<0.10	0.51 ± 0.10	<0.10
	7 d	44	<0.10	0.11 ± 0.01	<0.10	<0.10	<0.10	0.71 ± 0.09	<0.10
		37	<0.10	<0.10	<0.10	<0.10	<0.10	0.11 ± 0.02	<0.10
	28 d	44	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10
		37	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10
6.8	1 d	44	<0.10	0.11 ± 0.01	<0.10	0.11 ± 0.01	<0.10	0.81 ± 0.13	<0.10
		37	<0.10	<0.10	<0.10	<0.10	<0.10	0.11 ± 0.01	<0.10
	7 d	44	<0.10	<0.10	<0.10	<0.10	<0.10	0.31 ± 0.09	<0.10
		37	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10
	28 d	44	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10
		37	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10
8.8	1 d	44	<0.10	<0.10	<0.10	<0.10	<0.10	0.11 ± 0.01	<0.10
		37	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10
	7 d	44	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10
		37	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10
	28 d	44	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10
		37	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10	<0.10

T: Temperature.

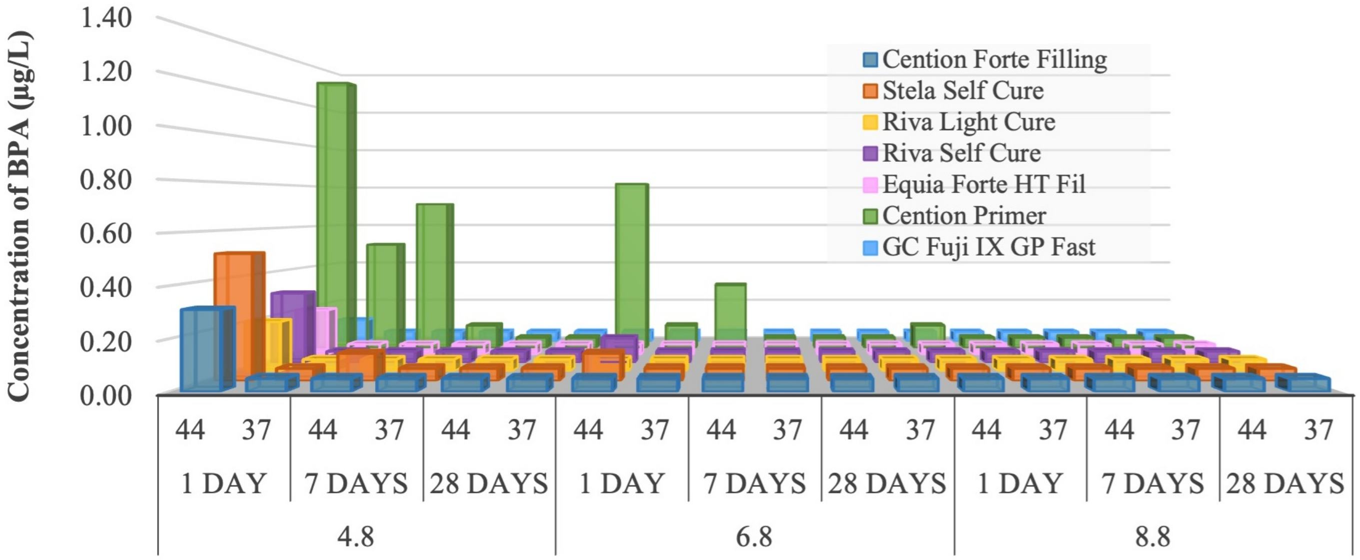

FIGURE 1. Comparison of BPA release (μg/L) in all materials at 3 pH levels (4.8, 6.8, 8.8), two temperatures (44 °C and 37 °C), and at three different observation times (1 day, 7 days, and 28 days). BPA: Bisphenol A.

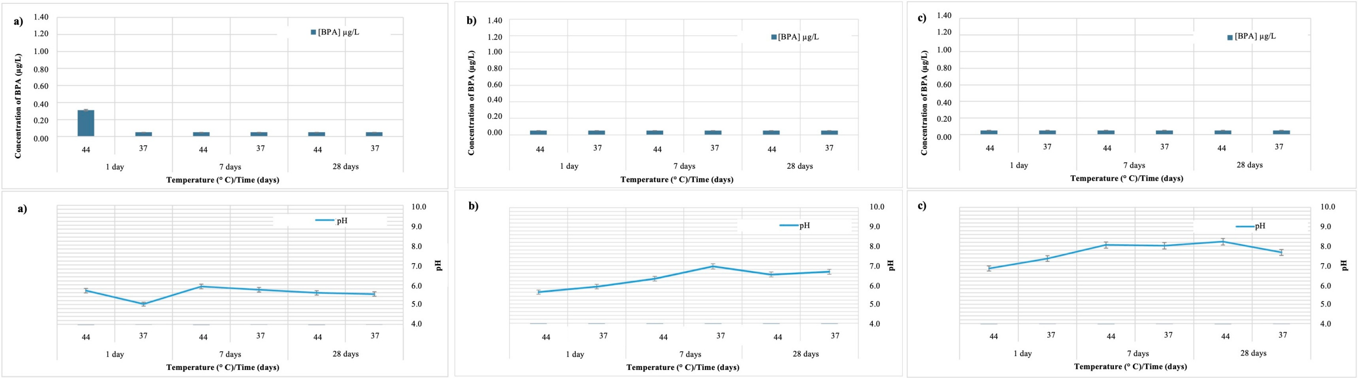

FIGURE 2. Comparison of BPA release (μg/L) and pH variation in Cention Forte Filling material. (a) pH = 4.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (b) pH = 6.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (c) pH = 8.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days). BPA: Bisphenol A.

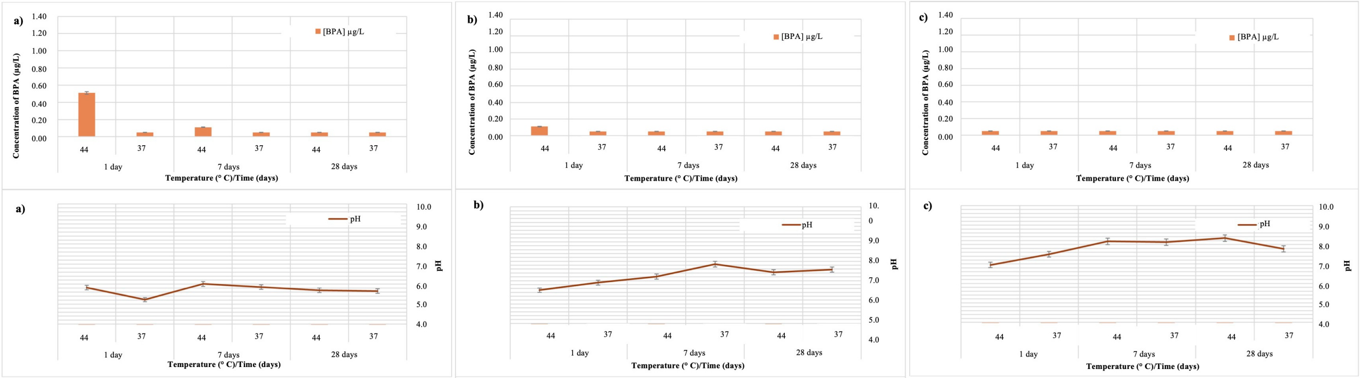

FIGURE 3. Comparison of BPA release (μg/L) and pH variation in Stela Self Cure material. (a) pH = 4.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (b) pH = 6.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (c) pH = 8.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days). BPA: Bisphenol A.

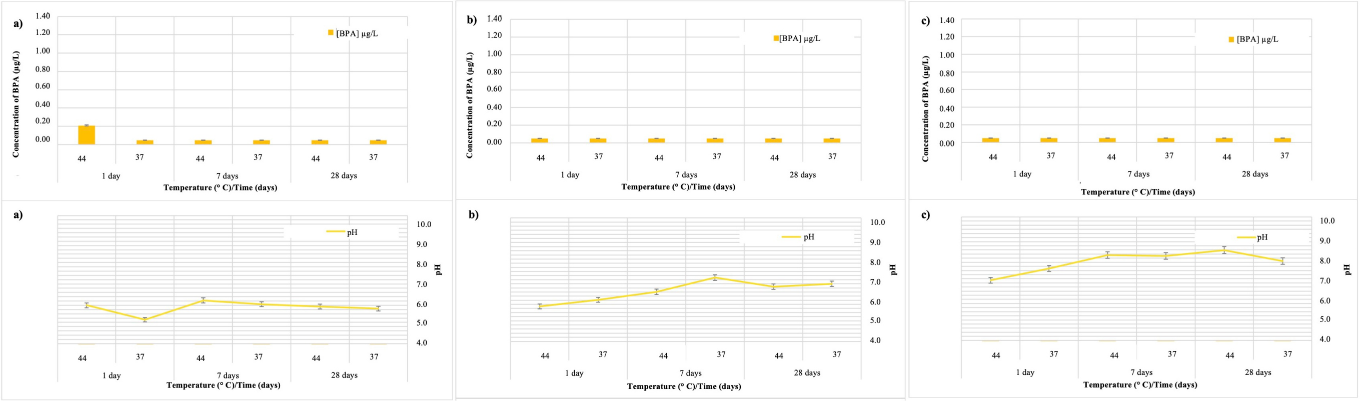

FIGURE 4. Comparison of BPA release (μg/L) and pH variation in Riva Light Cure material. (a) pH = 4.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (b) pH = 6.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (c) pH = 8.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days). BPA: Bisphenol A.

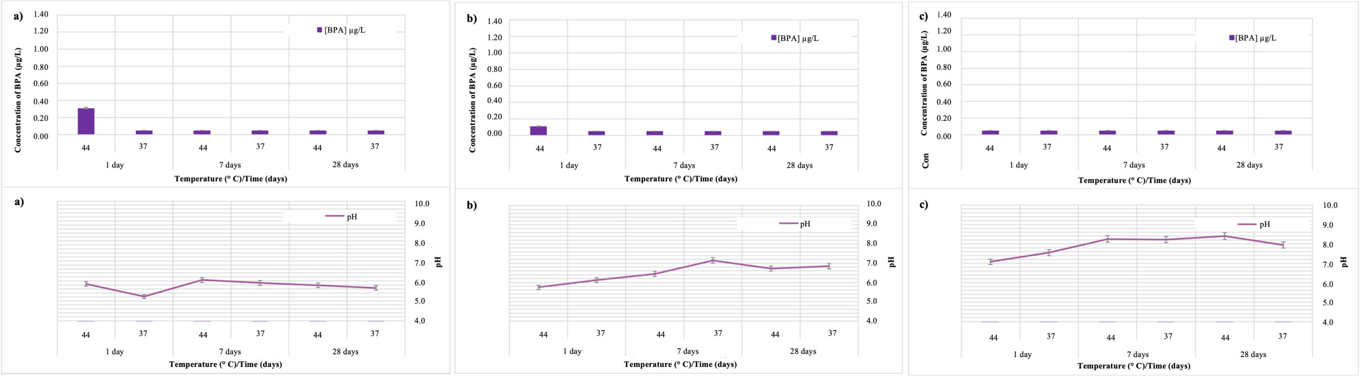

FIGURE 5. Comparison of BPA release (μg/L) and pH variation in Riva Self Cure material. (a) pH = 4.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (b) pH = 6.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (c) pH = 8.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days). BPA: Bisphenol A.

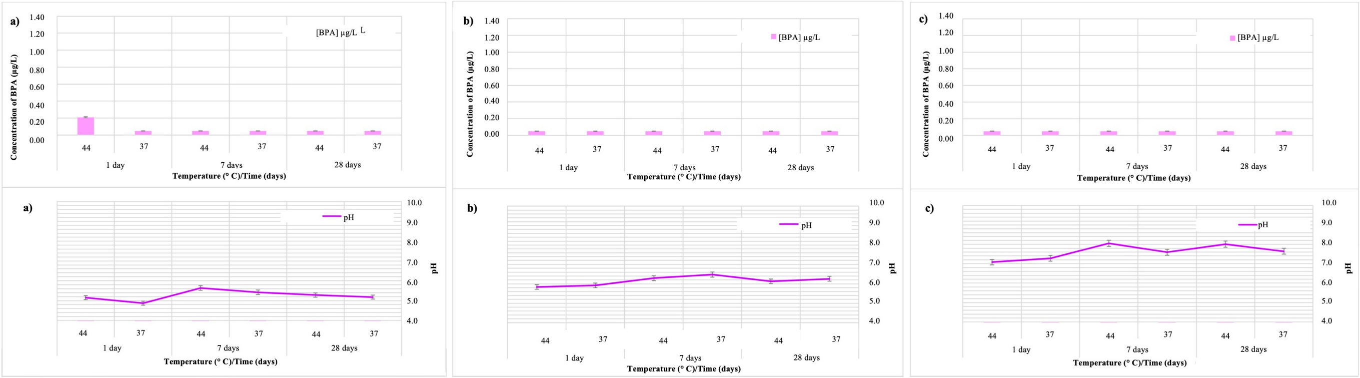

FIGURE 6. Comparison of BPA release (μg/L) and pH variation in Equia Forte HT Fil material. (a) pH = 4.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (b) pH = 6.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (c) pH = 8.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days). BPA: Bisphenol A.

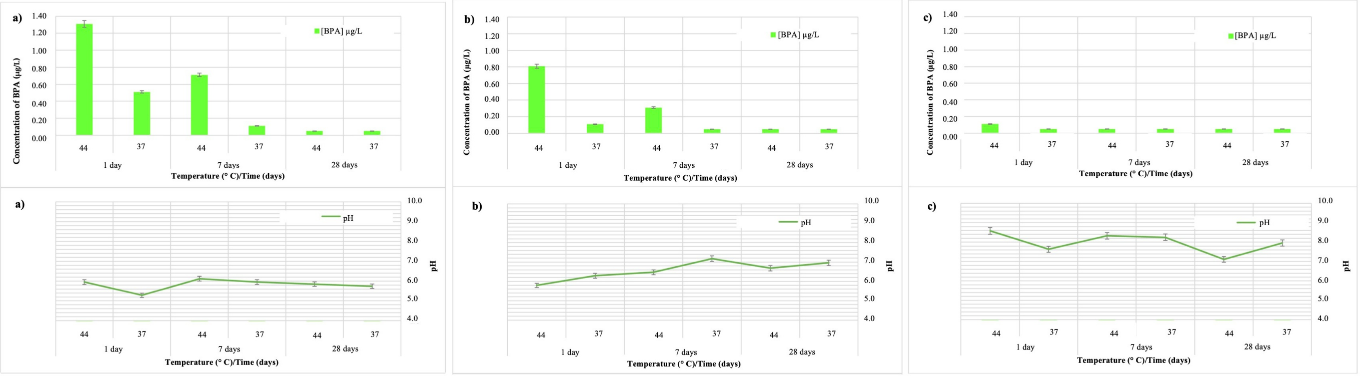

FIGURE 7. Comparison of BPA release (μg/L) and pH variation in Cention Primer material. (a) pH = 4.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (b) pH = 6.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (c) pH = 8.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days). BPA: Bisphenol A.

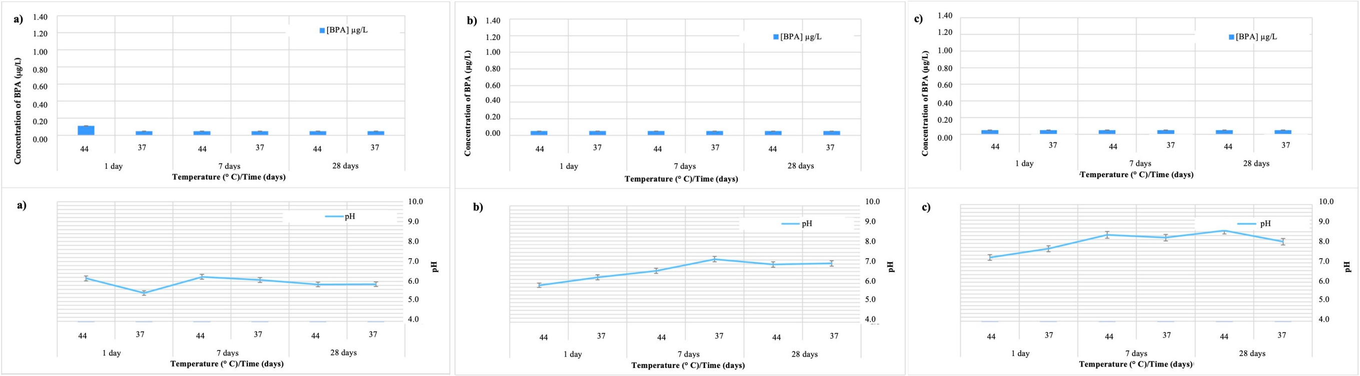

FIGURE 8. Comparison of BPA release (µg/L) and pH variation in GC Fuji IX GP Fast material. (a) pH = 4.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (b) pH = 6.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days); (c) pH = 8.8, two temperatures (44 °C and 37 °C) and at three different observation times (1 day, 7 days and 28 days). BPA: Bisphenol A.

under neutral pH conditions, BPA release was only detectable after 1 day of exposure at the elevated temperature, further reinforcing the influence of both temperature and pH on the release profiles.

To gain a clearer understanding of the factors influencing BPA release, the pH variation of the materials was also evaluated under different conditions. The results revealed that under acidic conditions, all materials showed a slight increase in pH of the buffer solution in which they were immersed, approximately one unit, over time. In neutral pH environments, an initial decrease in pH was observed, followed by stabilization. For basic conditions, a brief decrease in pH was followed by a return to baseline values. These pH fluctuations suggest that while materials demonstrated some sensitivity to environmental conditions, their overall pH stability remained relatively consistent, which could influence BPA release patterns.

Fig. 2 illustrates the BPA concentrations observed for the Cention Forte Filling Material and the monitored pH variations. It is observed that under acidic conditions, the release of BPA was observed only within the first 1 day at 44 °C (0.31 ± 0.07 µg/L), while the pH values varied from 5.02 to 5.91, with a mean value of 5.58 ± 0.31 (Fig. 2a). In neutral and basic conditions, no BPA release was observed, as the concentrations were all below the limit of quantification (Fig. 2b,c). Regarding pH, minimal variations were also noted in both conditions, with pH values ranging from 5.61 to 6.95 (average value of 6.33 ± 0.50) for neutral conditions and ranging from 6.85 to 8.23, with a mean value of 7.70 ± 0.52, in basic environment.

The results obtained for the Stela Self Cure material are presented in Fig. 3, showing the observed BPA concentrations and pH variations. Notably, the highest BPA concentrations were detected under acidic conditions at 44 °C after 1 day (0.51 ± 0.10 µg/L) and after 7 days (0.11 ± 0.01 µg/L). Under these conditions, pH values ranged from 5.22 to 6.01, with an average of 5.71 (Fig. 3a). In a neutral environment, where pH values ranged from 5.71 to 7.05 (average 6.45 ± 0.48), BPA release occurred only after 1 day at 44 °C, while at other exposure times, concentrations remained below the limit of quantification (Fig. 3b). Finally, under basic conditions, with pH values between 6.95 and 8.39 (average 7.82 ± 0.53), no BPA release was detected (Fig. 3c).

The results obtained regarding BPA release and pH variation for the Riva Light Cure material are shown in Fig. 4. In this case as well, pH exhibited minimal variations, and BPA release occurred only during short exposure times. Specifically, under acidic conditions, the pH ranged from 5.12 to 6.03, with an average value of 5.68 ± 0.31. BPA release was observed only at 44 °C after one day of observation, with an average concentration of 0.21 ± 0.07 µg/L (Fig. 4a). Conversely, under neutral and basic conditions, with monitored pH values ranging from 5.70 to 7.10 (average 6.45 ± 0.52) and 6.93 to 8.39 (average 7.82 ± 0.53), respectively, no BPA release was detected. Indeed, under all studied conditions, BPA concentrations remained below the LOQ (Fig. 4b,c).

For the Riva Self Cure material, a release pattern like that of the Stela Self Cure material was observed. The results are illustrated in Fig. 5. Specifically, in addition to the highest release recorded in acidic environment at 44 °C after 1 day (0.31 ± 0.08 µg/L) (Fig. 5a), a slight release was also detected under neutral conditions (pH = 6.8), with an average BPA concentration of 0.11 ± 0.01 µg/L (Fig. 5b). Regarding pH, under acidic conditions, values ranged from 5.22 to 6.05, with an average of 5.74 ± 0.29, while under neutral conditions, pH ranged from 5.75 to 7.15, with an average of 6.51 ± 0.51. In basic conditions, with pH values between 7.08 and 8.40 (average 7.91 ± 0.50), no BPA release was observed (Fig. 5c).

The Equia Forte HT Fil material, similarly to Cention Forte Filling and Riva Light Cure, exhibited BPA release only under acidic conditions at 44 °C after 1 day of exposure (0.21 ± 0.05 µg/L) (Fig. 6a). In neutral or basic conditions, no release was observed (Fig. 6b,c). Regarding pH, under acidic conditions, values ranged from 4.87 to 5.63, with an average of 5.25 ± 0.26. Under neutral conditions, pH was in the range of 5.84–6.48, with an average of 6.15 ± 0.24, while in basic conditions, it ranged from 7.08 to 8.05, with an average of 7.61 ± 0.39.

Unlike all other materials, the Cention Primer material exhibited a higher BPA release (Fig. 7). Specifically, under acidic conditions (pH = 4.8), a decreasing release trend was observed, with the highest concentration recorded at 44 °C after 1 day (1.31 ± 0.17 μg/L) and after 7 days (0.71 ± 0.09 μg/L) (Fig. 7a). Surprisingly, BPA release was also detected at 37 °C, both after 1 day (0.51 ± 0.10 μg/L) and after 7 days (0.11 ± 0.02 μg/L). Under these conditions, pH ranged from 5.28 to 6.12, with an average of 5.82 ± 0.29. Another key difference compared to all other materials was that BPA release was also observed for Cention Primer under neutral conditions (pH ranging from 5.79 to 7.17, with an average of 6.56 ± 0.49). Notably, the highest release occurred at 44 °C after 1 day, with a BPA concentration of 0.81 ± 0.13 μg/L, and after 7 days at the same temperature (0.31 ± 0.09 μg/L) (Fig. 7b). Finally, even under basic conditions (pH ranging from 7.11 to 8.58, with an average of 7.96), a small BPA release was recorded at 44 °C after 1 day (0.11 ± 0.01 μg/L) (Fig. 7c). This behavior contrasts with all other materials, for which no BPA release was ever observed under basic conditions.

Finally, the results obtained for the GC Fuji IX GP Fast material are illustrated in Fig. 8. Regarding pH, under acidic conditions (pH = 4.8), as observed for the other materials, an increase of approximately one unit compared to the initial value was recorded. Specifically, pH ranged from 5.42 to 6.23, with an average of 5.93 ± 0.29. Under these conditions, a minimal BPA release was detected at 44 °C after 1 day (0.11 ± 0.02 μg/L) (Fig. 8a). Under neutral conditions, pH ranged from 5.90 to 7.25, with an average of 6.68 ± 0.51 (Fig. 8b), while under basic conditions, pH values ranged from 7.28 to 8.67, with an average of 8.08 ± 0.51 (Fig. 8c). In these latter two conditions, no BPA release was observed.

The findings reveal that BPA release was highest under acidic conditions at 44 °C, particularly within the first 1 day of exposure. This pattern was observed across all materials, emphasizing the role of elevated temperature and low pH in promoting BPA release. Cention Primer exhibited the highest release, with a peak concentration of 1.31 ± 0.17 μg/L, followed by Stela Self Cure (0.51 ± 0.10 μg/L). Notably, these materials continued to release BPA after seven days, indicating that prolonged exposure to acidic environments may further enhance BPA migration.

In contrast, BPA release was either undetectable or minimal under neutral and basic conditions across all materials. Except for Cention Primer, none of the materials released BPA in basic environments at any time point, highlighting their greater stability in less acidic settings. Under neutral conditions, minor BPA release was observed in a few materials, but only at 44 °C and essentially within the 1 day. Among all tested materials, Cention Primer exhibited a distinct pattern, releasing BPA under all pH conditions, including neutral and basic environments. This behavior contrasts with the other materials, which released BPA exclusively in acidic conditions. These results suggest that the chemical composition and properties of Cention Primer contribute to its higher susceptibility to BPA release. Additionally, materials such as Equia Forte HT Fil, Cention Forte Filling, and Riva Light Cure displayed more controlled BPA release, with no detectable levels under neutral or basic conditions. This suggests that certain formulations provide improved chemical stability, reducing the potential for BPA exposure in clinical applications.

To better understand the factors influencing BPA release, the study also examined pH variations. Across all materials, acidic environments caused a slight pH increase of approximately one unit over time, indicating a buffering effect. In neutral conditions, pH initially decreased before stabilizing, while in basic environments, only minor fluctuations were observed. These findings suggest that while the materials interact with their surroundings, their overall pH stability remains consistent, potentially limiting BPA release in less acidic conditions.

3.2 Results of the statistical analysis

The statistical analysis demonstrated that BPA release from the tested different dental restorative materials was significantly influenced by the pH of the immersion medium and by the duration of exposure. In contrast, temperature variations did not show a statistically significant effect within the tested conditions. More specifically, pH had a highly significant impact on BPA release (p = 0.003), with the highest concentrations observed under acidic conditions, compared to neutral and basic environments. Regarding exposure time, a strong statistical association was found (p = 0.007), with BPA release peaking at 1 day. After 7 days, a substantial reduction was observed, and at 28 days, BPA levels were undetectable in most materials. On the other hand, temperature (37 °C and 44 °C) did not have a statistically significant influence on BPA release (p = 0.38), suggesting that thermal variation within this physiological range does not significantly alter the release behavior. The multivariate analysis confirmed the significant role of pH and exposure time in modulating BPA release (pH p = 0.003; time p = 0.007), with clear differences detected between the various composite materials (p = 0.021). The Shapiro-Wilk test indicated that the distribution of BPA release values did not significantly deviate from normality. These findings highlight the importance of environmental pH and exposure time in determining BPA release from dental composite materials, while temperature appears to exert minimal influence under the experimental conditions tested.

4. Discussion

The present *in-vitro* study demonstrates that BPA release from pediatric restorative materials is influenced mainly by pH and time, with Bis-GMA–containing materials showing the highest values. Beyond these quantitative results, the findings provide important insights into the sources and clinical significance of BPA exposure in children. Although BPA release from resin-based composites has been extensively studied, there is a relative paucity of data on materials specifically marketed for pediatric use, despite the fact that children are more susceptible to endocrine-disrupting compounds. This study therefore addresses an important gap in the literature by providing baseline data on commonly used pediatric restorative materials.

Concerns have grown regarding the biocompatibility and safety of resin-based dental filling materials, which are increasingly used in the restoration of carious teeth in pediatric patients [47]. These materials are exposed to various challenges, including thermal fluctuations, mechanical wear from oral hygiene practices and chewing, chemical degradation due to acidic foods and beverages, and enzymatic activity from oral bacteria [48]. Such factors contribute to the gradual breakdown of these materials, leading to the release of their components into the oral environment. Furthermore, the polymerization process used in resin-based dental materials, primarily triggered by light curing, does not achieve complete monomer-to-polymer conversion [49]. As a result, a portion of residual monomers remains, with conversion rates ranging between 50% and 80% in resin composites, allowing the release of unreacted monomers into the oral cavity. While the levels of released substances are generally too low to cause systemic toxicity, they have been associated with cytotoxic, genotoxic, and allergic responses in certain cases [50]. One compound of particular concern is BPA, an organic chemical classified as an endocrine disruptor by the European Commission. Even at low exposure levels, BPA has the potential to impact patient health, making its presence in dental materials a subject of ongoing scrutiny [51].

BPA release from commercially available pediatric dental filling materials has already been reported in several *in vitro* and *in vivo* studies [52]. BPA release from resin-based dental materials has been described in the literature both *in vitro* studies using organic solvents and artificial saliva and in clinical studies using saliva and urine [53–57]. The data in the literature show a great heterogeneity for this substance's levels, which vary from one study to another [58]. In fact, BPA levels depend on analysis techniques, extraction solutions, fixed detection thresholds, or other experimental conditions, which make studies difficult to compare [59].

Resin based dental materials that are predominantly utilized for the treatment of children and adolescents, including dental filling restorative composites, orthodontic composites, bonding agents, and tooth pit and fissure sealants, are the ones most likely to include BPA-derived monomers, with occurrences of 83.8%, 78.7%, 63.2%, and 66.7%, respectively. Bis-GMA was the most frequently identified BPA derivative at 56.2%, except for resin-modified glass ionomer cements. Bis-EMA follows as the second most common BPA derivative, appearing in 28.1% of dental materials, across nearly all categories except adhesives [59, 60].

In vitro studies are important for analyzing human substances because they allow for controlled conditions that can be either enhanced or worsened while remaining identical in other aspects [61].

The present investigation examined the release of BPA from polymeric and acid-based dental restorative materials used in pediatric dentistry under different pH and temperature conditions. The results indicated that BPA release exists in different percentage for all the investigated materials in the laboratory conditions, but it is essentially concentrated at 1 day evaluation stop and at acidic conditions and at 44 °C temperature. In the other analyzed conditions, 7 days, and 28 days, not significant or no BPA release was detected, except for Cention Primer. The investigation showed that environmental factors influenced the materials differently at day 1. While temperature variations did not reach statistical significance ($p = 0.382$), a numerical trend toward higher BPA release was observed at 44 °C, particularly in day 1. In contrast, acidic pH conditions significantly enhanced release. The inclusion of 44 °C as a testing condition was intended as an exploratory stress condition to reproduce short-term intraoral temperature increases (*e.g.*, following the consumption of hot beverages or during episodes of fever). However, it must be emphasized that in our study temperature did not show a statistically significant effect on BPA release ($p = 0.382$). Therefore, the observed numerical increase at 44 °C should be interpreted cautiously and considered exploratory only, rather than as evidence of a clinically relevant effect. All the materials examined showed, looking at Fig. 1, at this temperature and acidic pH, a marked difference at 1 day. This early peak reflects the diffusion of unreacted monomers and is a common finding in both *in vitro* and *in vivo* investigations. At 37 °C, no significant differences were observed among the same materials except for Cention Primer. At neutral pH, on the contrary, no differences were scored at the different 1 and 7 days, in both the different temperature conditions, except for Cention Primer material again, which released measurable BPA, but at 44 °C. Only at 28 days, at acid, neutral and basic pH, under the two investigated temperature points, Cention Primer similarly behaves as the other materials, with not significant BPA release. So, all the materials at 28 days, independent of pH and temperature conditions had no detectable BPA release. It should be noted that the higher BPA release observed for Cention Primer was not unexpected, as it is the only Bis-GMA–containing material included in this study. Indeed, Cention Primer was considered as a positive control to confirm the sensitivity and reliability of our analytical method. Nevertheless, the added value of this work lies in the precise quantification of release levels under different environmental conditions using LC-MS/MS, and in the comparison with other restorative materials marketed as "BPA-free". Since both polymeric and acid-based pediatric dental restorative materials released BPA under test conditions, the original null hypothesis is rejected. Fig. 1 also shows that, in terms of BPA concentration release (μg/L), the highest score was only observed at 44 °C in an acidic environment (pH 4.8), at 1 day check, with Cention Primer (1.31 μg/L). Stela Self Cure (0.51 μg/L), Cention Forte Filling (0.31 μg/L) and Riva Self Cure (0.31 μg/L) showed lower percentage. The lowest BPA levels were scored in Riva Light cure (0.21 μg/L) and in Equia Forte HT Fil (0.21 μg/L), and finally in Fuji IX GP fast (0.11 μg/L).

In the same pH conditions, but at 37 °C, the tested materials did not show the same scores, but lower values, except for Cention Primer, which still showed a relevant BPA release of 0.50 μg/L. These findings are consistent with previous studies showing that acidic conditions promote BPA release by facilitating hydrolysis and degradation of resin matrices [62, 63]. This highlights the importance of considering the oral environment when selecting dental materials which may differ substantially between children and adults or elderly patients, as factors such as acidic beverages, dietary habits, and fluctuations in salivary, pH may contribute to the release of potentially harmful compounds.

The results suggest that, for Cention Primer, which is not a true dental filling material, but a dentine primer (liquid) used in combination with Cention Forte Filling to apply on dentinal tissue before the second material, its chemical composition, particularly the presence of Bis-GMA and other BPA derivatives, contributes to its susceptibility to BPA release. The persistence of BPA release in this material also after 7 days, in acidic pH and at 44 °C than 37 °C, can be suggested as a point of study for further investigation focusing on long-term stability and clinical implications. A comparison between resin-based materials like Cention Primer and Cention Forte Filling and Stela Self Cure, on one side, and real glass ionomer-based materials like Riva Self Cure and Equia Forte HT Fil and Fuji IX GP fast, on the other side, showed that in acidic pH environment at 44 °C, all the tested materials, also if in a different way, released BPA, but at different level. The first mentioned resin-based dental materials released more BPA. On the other hand, glass ionomer materials are more stable. Looking at Fig. 1, at 7 days and 28 days, all the investigated materials, not under varying temperature conditions, showed no significant differences but residual BPA release under neutral or basic conditions. These findings suggest that glass ionomer materials may serve as a safer dental filling restorative material in pediatric dentistry and as alternatives for young patient's dental therapies. According to the literature [64, 65], while conventional resin based dental filling composites release higher amounts of BPA, resin-modified glass ionomers (RM-GICs) investigated in this study minimal and not significant BPA release. However, it is now important to consider the BPA contamination effect, already shown by De Nys *et al.* [66], in various dental filling materials employed in pediatric dentistry.

Although some of the pediatric dental restorative materials investigated in this study do not contain Bis-GMA, the results showed that small amounts of BPA were still released at several time intervals. Looking at Table 1, which reflects data from the different companies' sheets, it is apparently a contradiction to see no Bis-GMA or derivates in the composition of Equia Forte, Riva Self Cure, Stela Self Cure and GC Fuji IX GP Fast. In fact, in Fig. 1, at day 1, mainly, but also at different timing, it was scored the presence of BPA also for these last materials, relatively lower for GC Fuji IX GP Fast, where theoretically, it was not possible. This could be explained by the fact that the plastic capsule technology that carry these dental filling materials into the oral cavity could be able of contaminating the single filling materials, during the preservation and storage period, even before the capsule itself is activated and mixed. The release of BPA by these plastic capsules would possibly explain the contamination of those materials named by manufacturers as BPA-free such as Stela Self Cure and Riva Self Cure or those materials whose composition does not indicate the presence of Bis-GMA or derivatives such as GC Fuji IX GP Fast and Equia Forte. This consideration might be in line with another literature remark according to which the main components are not always indicated in the material safety data sheet [67]. Indeed, for commercial reasons or to protect trade secrets, manufacturers are sometimes reluctant to disclose all the components of their products. Unlike pharmaceuticals, there is currently no obligation to report the exact composition of a material. The material safety data sheet (MSDS) of a product should give information on all its components with a proportion above 1% (REACH Regulation (EC) 1907:2006 in the European Union, OSHA Hazard Communication Regulations 1910.1200g8 for the United States) [57].

Our findings can also be contextualized in relation to reported *in vivo* data. Clinical studies have documented BPA detection in saliva immediately after resin-based dental procedures, typically ranging from 0.3 to 2.8 μg/L, and in urine samples of pediatric patients at concentrations between 0.5 and 3.0 ng/mL within the first 24 hours post-treatment [56, 57]. In addition, as already mentioned in the introduction, given that the European Food Safety Authority has decided to reduce the permitted tolerable daily intake to 0.2 ng/kg/day, which is lower than the levels of BPA normally detected in saliva after resin placement in the oral cavity, this aspect should be taken into account for the recommendation of materials completely free of BPA-derived monomers placed in the oral cavity for years. Indeed, the chronic and continuous release of monomers capable of being degraded to BPA, even at very low doses, may have long-term side effects on patients' health [68]. When compared to the most recent EFSA tolerable daily intake (0.2 ng/kg body weight/day), the amounts of BPA released in this study appear small in absolute terms. However, given the extremely stringent value of this new threshold, even short-term exposures from restorative materials may contribute to cumulative intake in children. Considering their lower body weight and increased vulnerability to endocrine disruptors, the release levels measured in our study, although limited, may still carry a partial clinical relevance. For example, using the most recent EFSA tolerable daily intake (0.2 ng/kg/day), a 20-kg child would have a daily TDI of ~4 ng/day. Our peak measured concentration for the positive control (Cention Primer) was 1.31 μg/L, *i.e.*, 1.31 ng/mL. As a conservative, worst-case illustration, if ~1 mL of fluid adjacent to a fresh restoration were to instantaneously equilibrate at this peak level, the corresponding dose would be ~1.31 ng, *i.e.*, about 33% of the daily TDI for a 20-kg child; for 0.51 μg/L (1-day peak with another resin-based material) the illustrative dose would be 0.51 ng (~13% of the TDI). In contrast, for conditions yielding <0.10 μg/L (*i.e.*, <0.10 ng/mL), the illustrative dose would be <0.10 ng ($<3\%$ of the TDI). These values are not direct exposure estimates in fact they do not account for saliva turnover, clearance, restoration geometry, or intermittent temperature/pH spikes but they provide a transparent upper-bound frame of reference linking our *in-vitro* results with a regulatory benchmark. This comparison supports the preferential use of materials with lower measured release in children and underscores the importance of exposure-minimizing clinical protocols.

Furthermore, this study demonstrates that temperature showed a trend toward influencing BPA release, at 1 day, with notably higher levels detected at 44 °C compared to 37 °C. Therefore, external factors such as the consumption of hot beverages or increased intraoral temperatures due to pediatric inflammation may enhance BPA release in clinical settings [69].

It is important to note that the precise origin of the detected BPA remains uncertain. Historically, Bis-GMA was synthesized from BPA, but most contemporary formulations no longer use BPA as a direct starting monomer. Therefore, the small but measurable BPA concentrations found in materials labeled as "BPA-free" may not necessarily derive from Bis-GMA degradation [66, 70]. Instead, they could result from alternative degradation pathways involving other aromatic dimethacrylates (*e.g.*, Bis-DMA or Bis-EMA), or from trace environmental or packaging-related contamination during manufacturing and storage. This hypothesis is consistent with reports of BPA traces even in products whose declared formulations exclude Bis-GMA [63, 71]. Consequently, while our findings confirm measurable BPA release under specific conditions, the molecular source of this compound within dental materials remains to be fully elucidated. Future studies including capsule-only controls and expanded analytical targeting of non-Bis-GMA monomer by-products will be essential to distinguish intrinsic resin degradation from extrinsic contamination.

In summary, this study highlights the importance of selecting materials based on environmental stability and pediatric patient-specific considerations. While dental filling materials containing Bis-GMA, Bis-EMA and other derivates monomers provide superior esthetics and mechanical properties, their potential for BPA release under acidic and high-temperature conditions requires careful evaluation in pediatric dentistry. From a clinical perspective, restorative materials that showed no or minimal BPA release under most experimental conditions (notably the glass ionomer-based formulations tested in this study) should be preferred in pediatric patients whenever the indication allows. Given the current uncertainty regarding the molecular source of BPA, exposure-minimizing clinical protocols and the selection of materials demonstrating consistently low release levels under stress conditions are strongly recommended. Conversely, materials containing Bis-GMA (in our study, Cention Primer, deliberately included as a positive control) exhibited the highest release and warrant careful use with exposure-minimizing protocols (*e.g.*, meticulous rubber dam isolation, immediate finishing/polishing, removal of oxygen-inhibited layer, and thorough rinsing). When esthetic and mechanical demands require resin-based options, selecting products with lower BPA release profiles and adopting stringent isolation and post-cure procedures may help reduce exposure.

Despite the significant results obtained from the present study by means of a sensitive and specific analytical methodology based on high-performance liquid chromatography coupled with mass spectrometry (LC-MS/MS) and the simulation of realistic conditions that materials may encounter in the oral cavity, such as pH and temperature variations, the study nevertheless has some limitations. First, this is an *in vitro* analysis, which does not consider the complex interactions that occur in the human mouth, such as the presence of salivary enzymes, saliva flow and pH variation caused by dietary and metabolic factors. Another limitation was the duration of the study, which focused on a maximum period of 28 days. Although this may provide indications on the tendency of BPA release in the short and medium term, it was evident at 28 days a clear decrease of BPA release also for Cention Primer (liquid). So, all the materials at 28 days, not dependent on pH and temperature conditions had no detectable BPA release, in other words, they could be considered safe for the long period. This fact is sufficient to fully predict the long-term behavior of these dental pediatric dental filling materials.

In addition, although an a priori power analysis confirmed that n = 3 specimens per condition was adequate to detect large effects with sufficient statistical power, this design remains underpowered for detecting moderate or small differences. Such smaller effects may nevertheless carry clinical relevance, and therefore future studies with larger sample sizes are required to confirm and expand our findings.

Another limitation concerns the choice of immersion media. The use of buffer solutions (acetate, phosphate-citrate, Tris-HCl) provided standardized and reproducible conditions to specifically test the influence of pH, but this approach does not fully replicate the complexity of artificial or natural saliva, which contains proteins, enzymes, and ions that may affect BPA release. Furthermore, although 44 °C was included as a stress condition to simulate transient intraoral temperature rises caused by hot beverages or fever, such elevated values are not continuously sustained *in vivo*. Future investigations should therefore consider testing in artificial saliva and under a broader range of physiological conditions to improve the translational relevance of the findings.

An additional consideration concerns the potential role of external contamination sources, such as plastic capsules used for material delivery. Although this possibility may partially explain the detection of BPA in materials labeled as "BPA-free", it was not specifically investigated in this study. Specifically, no capsule-only control group was included to isolate and quantify potential BPA release from packaging materials. Implementing such a control should be considered a priority in future studies, as it would help clarify whether the BPA detected in nominally "BPA-free" formulations originates from intrinsic resin degradation or extrinsic contamination during storage and handling.

Furthermore, the immersion medium plays a critical role in BPA release. Several authors have shown that organic solvents (ethanol, methanol) accelerate BPA elution compared with water, saliva, or artificial saliva, by enhancing polymer swelling and degradation of ester bonds [65, 66]. In this study, the use of ethanol-water mixtures provided a standardized and sensitive method to quantify release, but future studies should further explore release profiles in saliva or artificial saliva to improve translational relevance.

Finally, a further limitation is that the present study used static immersion conditions, which do not account for intraoral thermal fluctuations. Future investigations should not only consider but actively incorporate more advanced oral environment simulations, including thermal cycling protocols as recommended by ISO (International Organization for Standardization) 11405 and ISO 10477 (typically 5–55 °C, 500–10,000 cycles), saliva-based immersion media that reproduce the enzymatic and ionic composition of the oral cavity, and standardized mechanical loading to mimic masticatory stresses. These aspects are essential requirements for future research to ensure closer replication of intraoral dynamics and to validate the clinical translation of our findings. Although it is difficult to precisely assess the proportion of overall BPA exposure attributable to oral intake from pediatric dental materials, their contribution to total BPA contamination is not negligible. Future research should focus on long-term *in vivo* assessments, cumulative BPA exposure, and the development of innovative BPA-free pediatric dental restorative materials that ensure clinical efficacy without reducing biocompatibility.

5. Conclusions

In conclusion, this study demonstrated that BPA release from pediatric restorative materials is strongly influenced by environmental conditions, particularly acidic pH, and the early post-placement phase. Among the tested products, resin-based restorative materials, and glass ionomer-based formulations (Equia Forte HT Fil, Riva Self Cure, Fuji IX GP Fast, Stela Self Cure) consistently showed the lowest or negligible BPA release, suggesting that they may represent safer options for pediatric patients whenever clinically indicated. By contrast, Bis-GMA–containing materials such as Cention Primer exhibited the highest release and should be used with caution, adopting strict exposure-minimizing protocols. The results also suggest that potential contamination from plastic carriers may contribute to BPA detection in materials labeled as "BPA-free", highlighting the importance of cautious interpretation.

Looking forward, further research is urgently needed to strengthen the clinical translation of these findings. Specifically, future studies should incorporate thermal cycling according to ISO standards, long-term *in vivo* assessments of salivary and urinary BPA, and evaluations under mechanical loading to better simulate real oral conditions. In parallel, innovation in material science should prioritize the development of restorative options that are completely free of BPA and its derivatives, without compromising esthetic and mechanical performance.

Ultimately, prioritizing materials with minimal BPA release and advancing truly BPA-free technologies represent essential steps to ensure safer restorative care for children.

AVAILABILITY OF DATA AND MATERIALS

All datasets are already provided as part of the submitted article.

AUTHOR CONTRIBUTIONS

AA and PA—conceptualization. FDD and LG—methodology. MP, RG and FG—software. PA—validation. AA, PA and RG—formal analysis; visualization; supervision. AA, FDD, LG and FG—investigation. AA, FDD and MP—resources. AA, FDD, RG, FG and PA—data curation. AA—writing–original draft preparation. AA, FDD and LG—writing–review and editing. PA and FG—project administration. All authors have read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest. Pietro Ausiello is serving as one of the Editorial Board members of this journal. We declare that Pietro Ausiello had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to APPF.

REFERENCES

[1] German MJ. Developments in resin-based composites. British Dental Journal. 2022; 232: 638–643.

[2] Ferracane JL. A historical perspective on dental composite restorative materials. Journal of Functional Biomaterials. 2024; 15: 173.

[3] Eggenhöffner R, Ghisellini P, Rando C, Pechkova E, Terencio T, Mazzolai B, *et al.* Innovative nanostructured fillers for dental resins: nanoporous alumina and Titania nanotubes. Biomedicines. 2023; 11: 1926.

[4] Ausiello P, Ciaramella S, Lanzotti A, Ventre M, Borges AL, Tribst JP, *et al.* Mechanical behavior of Class I cavities restored by different material combinations under loading and polymerization shrinkage stress. A 3D-FEA study. American Journal of Dentistry. 2019; 32: 55–60.

[5] Pires PM, de Almeida Neves A, Lukomska-Szymanska M, Farrar P, Cascales ÁF, Sauro S. Bonding performance and interfacial adaptation of modern bulk-fill restorative composites after aging in artificial saliva: an *in vitro* study. Clinical Oral Investigation. 2024; 28: 132.

[6] Ausiello P, Ciaramella S, De Benedictis A, Lanzotti A, Tribst JPM, Watts DC. The use of different adhesive filling material and mass combinations to restore class II cavities under loading and shrinkage effects: a 3D-FEA. Computer Methods in Biomechanics and Biomedical Engineering. 2021; 24: 485–495.

[7] Obisesan OS, Ajiboye TO, Mhlanga SD, Mufhandu HT. Biomedical applications of biodegradable polycaprolactone-functionalized magnetic iron oxides nanoparticles and their polymer nanocomposites. Colloids and Surfaces B: Biointerfaces. 2023; 227: 113342.

[8] Aminoroaya A, Neisiany RE, Khorasani SN, Panahi P, Das O, Madry H, *et al.* A review of dental composites: challenges, chemistry aspects, filler influences, and future insights. Composites Part B: Engineering. 2021; 216: 108852.

[9] Jafer MA, Qadiri AA, Mtwam NA, Hakami AH, Mowkly AA, Bhandi S, *et al.* Influence of human and bacterial enzymes on resin restorations: a review. Journal of Contemporary Dental Practice. 2022; 23: 371–377.

[10] Vervliet P, De Nys S, Duca RC, Boonen I, Godderis L, Elskens M, *et al.* Degradation products of resin-based materials detected in saliva *in vivo*. Clinical Oral Investigation. 2023; 7: 7189–7198.

[11] Padovani G, Fúcio S, Ambrosano G, Sinhoreti M, Puppin-Rontani R. *In situ* surface biodegradation of restorative materials. Operative Dentistry. 2014; 39: 349–360.

[12] Barros LS, Denucci GC, Amoral FL, Franga FM, Basting RT, Turssi CP. The potential of salivary albumin to degrade composite resin. Acta Odontológica Latinoamericana. 2023; 36: 34–39.

[13] Nedeljkovic I, De Munck J, Ungureanu AA, Slomka V, Bartic C, Vananroye A, *et al*. Biofilm-induced changes to the composite surface. Journal of Dentistry. 2017; 63: 36–43.

[14] Kux BJ, Bacigalupo LM, Scriba A, Emmrich M, Jost-Brinkmann PG. Elution study of acrylic monomers from orthodontic materials using high performance liquid chromatography (HPLC). Journal of Orofacial Orthopedics. 2022; 83: 34–47.

[15] Kielbassa AM, Summer S, Frank W, Lynch E, Batzer JS. Equivalence study of the resin-dentine interface of internal tunnel restorations when using an enamel infiltrant resin with ethanol-wet dentine bonding. Scientific Reports. 2024; 14: 12444.

[16] EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP); Lambré C, Barat Baviera JM, Bolognesi C, Chesson A, Cocconcelli PS, Crebelli R, *et al.* Scientific opinion on the re-evaluation of the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs. EFSA Journal. 2023; 21: 6857392.

[17] Goldberg M. *In vitro* and *in vivo* studies on the toxicity of dental resin

components: a review. Clinical Oral Investigation. 2008; 12: 1–8.

[18] Ohlsson E, Bolay C, Arabulan S, Galler KM, Buchalla W, Schmalz G, *et al*. *In-vitro*-cytotoxicity of self-adhesive dental restorative materials. Dental Materials. 2024; 40: 739–746.

[19] Farahat DS, El-Wassefy NA. Effects of food-simulating solutions on the surface properties of two CAD/CAM resin composites. Journal of Clinical and Experimental Dentistry. 2022; 14: e782–e790.

[20] Wan Ali WNS, Parker S, Patel M. Effect of food-simulating liquids on the leachability of plasticizers from dental tissue conditioners. European Journal of Dentistry. 2024; 18: 883–890.

[21] Gupta SK, Saxena P, Pant VA, Pant AB. Release and toxicity of dental resin composite. Toxicology International. 2012; 19: 225–234.

[22] Treglia AS, Turco S, Ulianich L, Ausiello P, Lofrumento DD, Nicolardi G, *et al.* Cell fate following ER stress: just a matter of "quo ante" recovery or death? Histology and Histopathology. 2012; 27: 1–12.

[23] European Food Safety Authority. Opinion of the scientific panel on food additives, flavourings, processing aids and materials in contact with food (AFC) related to 2,2-bis(4-hydroxyphenyl) propane. EFSA Journal. 2006; 428: 1–75.

[24] Kang YG, Kim JY, Kim J, Won PJ, Nam JH. Release of bisphenol A from resin composite used to bond orthodontic lingual retainers. American Journal of Orthodontics and Dentofacial Orthopedics. 2011; 140: 779–789.

[25] Peters AE, Ford EA, Roman SD, Bromfield EG, Nixon B, Pringle KG, *et al*. Impact of Bisphenol A and its alternatives on oocyte health: a scoping review. Human Reproduction Update. 2024; 30: 653–691.

[26] Kolatorova Sosvorova L, Chlupacova T, Vitku J, Vlk M, Heracek J, Starka L, *et al*. Determination of selected bisphenols, parabens and estrogens in human plasma using LC-MS/MS. Talanta. 2017; 174: 21–28.

[27] Pan J, Liu P, Yu X, Zhang Z, Liu J. The adverse role of endocrine disrupting chemicals in the reproductive system. Frontiers in Endocrinology. 2024; 14: 1324993.

[28] Rochester JR. Bisphenol A and human health: a review of the literature. Reproductive Toxicology. 2013; 42: 132–155.

[29] Kolatorova L, Duskova M, Vitku J, Starka L. Prenatal exposure to bisphenols and parabens and impacts on human physiology. Physiological Research. 2017; 66: S305–S315.

[30] Ma Y, Liu H, Wu J, Yuan L, Wang Y, Du X. The adverse health effects of bisphenol A and related toxicity mechanisms. Environmental Research. 2019; 176: 108575.

[31] Ramírez V, Gálvez-Ontiveros Y, González-Domenech PJ, Baca MÁ, Rodrigo L, Rivas A. Role of endocrine disrupting chemicals in children's neurodevelopment. Environmental Research. 2022; 203: 111890.

[32] Vandenberg LN, Colborn T, Hayes TB, Heindel JJ, Jacobs DR III, Lee DH, *et al*. Hormones and endocrine-disrupting chemicals: low-dose effects and nonmonotonic dose responses. Endocrine Reviews. 2012; 33: 378–455.

[33] Lopes-Rocha L, Gonçalves VMF, Cunha SC, Fernandes JO, Pinho T, Tiritan ME. Evaluation of BPA and Bis-GMA release from recent dental composite materials by LC-MS/MS. Separations. 2023; 10: 455.

[34] Berge TLL, Lygre GB, Jönsson BAG, Lindh CH, Björkman L. Bisphenol A concentration in human saliva related to dental polymer-based fillings. Clinical Oral Investigation. 2017; 21: 2561–2568.

[35] Pulgar R, Olea-Serrano MF, Novillo-Fertrell A, Rivas A, Pazos P, Pedraza V, *et al*. Determination of bisphenol A and related aromatic compounds released from Bis-GMA-based composites and sealants by high performance liquid chromatography. Environmental Health Perspectives. 2000; 108: 21–27.

[36] Yiyan Y, Xinwei G, Jiawen C, Yuanhang Z, Jiazhuo S, Hamed A, *et al.* Biodegradation of Urethane Dimethacrylate-based materials (CAD/CAM resin-ceramic composites) and its effect on the adhesion and proliferation of *Streptococcus mutans*. Journal of the Mechanical Behavior of Biomedical Materials. 2024; 150: 106280.

[37] Ausiello P, Dal Piva AMdO, di Lauro AE, Garcia-Godoy F, Testarelli L, Tribst JPM. Mechanical behavior of Alkasite posterior restorations in comparison to polymeric materials: a 3D-FEA study. Polymers. 2022; 14: 1502.

[38] Aliberti A, Gasparro R, Triassi M, Piscopo M, Ausiello P, Tribst JPM. Fluoride release from pediatric dental restorative materials: a laboratory investigation. Dentistry Journal. 2025; 13: 224.

[39] Aliberti A, Di Duca F, Triassi M, Montuori P, Scippa S, Piscopo M, *et al.* The effect of different pH and temperature values on Ca^{2+}, F^{-}, $PO_4{}^{3-}$, OH^{-}, Si, and Sr^{2+} release from different bioactive restorative dental materials: an *in vitro* study. Polymers. 2025; 17: 640.

[40] Manzoor MF, Tariq T, Fatima B, Sahar A, Tariq F, Munir S, *et al.* An insight into bisphenol A, food exposure and its adverse effects on health: a review. Frontiers in Nutrition. 2022; 9: 1047827.

[41] Francois P, Fouquet V, Attal JP, Dursun E. Commercially available fluoride-releasing restorative materials: a review and a proposal for classification. Materials. 2020; 13: 2313.

[42] Di Lauro A, Di Duca F, Montuori P, Dal Piva AMO, Tribst JPM, Borges ALS, *et al*. Fluoride and calcium release from Alkasite and glass ionomer restorative dental materials: *in vitro* study. Journal of Functional Biomaterials. 2023; 14: 109.

[43] Dawes C. Salivary flow patterns and the health of hard and soft oral tissues. Journal of the American Dental Association. 2008; 139: 18S–24S.

[44] Ten Cate JM, Buzalaf MAR. Fluoride mode of action: once there was an observant dentist. Journal of Dental Research. 2019; 98: 725–730.

[45] Airoldi G, Riva G, Vanelli M, Filippi V, Garattini G. Oral environment temperature changes induced by cold/hot liquid intake. American Journal of Orthodontics and Dentofacial Orthopedics. 1997; 112: 58–63.

[46] Cramer MN, Gagnon D, Laitano O, Crandall CG. Human temperature regulation under heat stress in health, disease, and injury. Physiological Reviews. 2022; 102: 1907–1989.

[47] Alharbi S, Alshabib A, Algamaiah H, Aldosari M, Alayad A. Influence of post-printing polymerization time on the elution of residual monomers and water sorption of 3D-printed resin composite. Materials. 2025; 18: 2905.

[48] Alhotan A, Raszewski Z, Alamoush RA, Chojnacka K, Mikulewicz M, Haider J. Influence of storing composite filling materials in a low-pH artificial saliva on their mechanical properties—an *in vitro* study. Journal of Functional Biomaterials. 2023; 14: 328.

[49] Odabasi D, Guler C, Kucukaslan D. Evaluation of the amount of residual monomer released from different flowable composite resins. BMC Oral Health. 2024; 24: 244.

[50] Romo-Huerta MJ, Cervantes-Urenda ADR, Velasco-Neri J, Torres-Bugarín O. Valdivia ADCM Genotoxicity associated with residual monomers in restorative dentistry: a systematic review. Oral Health and Preventive Dentistry. 2021; 19: 471–480.

[51] Gore AC, Chappell VA, Fenton SE, Flaws JA, Nadal A, Prins GS, *et al.* EDC-2: the endocrine society's second scientific statement on endocrine-disrupting chemicals. Endocrine Reviews. 2015; 36: E1–E150.

[52] Lopes-Rocha L, Hernandez C, Gonçalves V, Pinho T, Tiritan ME. Analytical methods for determination of BPA released from dental resin composites and related materials: a systematic review. Critical Reviews in Analytical Chemistry. 2024; 54: 653–668.

[53] Löfroth M, Ghasemimehr M, Falk A, Vult von Steyern P. Bisphenol A in dental materials—existence, leakage and biological effects. Heliyon. 2019; 5: e01711.

[54] De Angelis F, Sarteur N, Buonvivere M, Vadini M, SÃåteffl M, D'Arcangelo C. Meta-analytical analysis on components released from resin-based dental materials. Clinical Oral Investigation. 2022; 26: 6015–6041.

[55] Jedeon K, De la Dure-Molla M, Brookes SJ, Loiodice S, Marciano C, Kirkham K, *et al.* Enamel defects reflect perinatal exposure to bisphenol A. American Journal of Pathology. 2013; 183: 108–118.

[56] Maserejian NN, Trachtenberg FL, Wheaton OB, Calafat AM, Ranganathan G, Kim HY, *et al.* Changes in urinary bisphenol A concentrations associated with placement of dental composite restorations in children and adolescents. Journal of the American Dental Association. 2016; 147: 620–630.

[57] Marzouk T, Sathyanarayana S, Kim AS, Seminario AL, McKinney CM. A systematic review of exposure to bisphenol a from dental treatment. JDR Clinical and Translational Research. 2019; 4: 106–115.

[58] American Dental Association. Bisphenol A released from resin based dental sealants. ADA Professional Product Review. 2016; 11: 1–6.

[59] Dantagnan CA, Babajko S, Nassif A, Houari S, Jedeon K, François P, *et al*. Analysis of resin-based dental materials' composition depending on their clinical applications. Polymers. 2024; 16: 1022.

[60] Rajkumar DS, Padmanaban R. Impact of bisphenol A and analogues eluted from resin-based dental materials on cellular and molecular processes: an insight on underlying toxicity mechanisms. Journal of Applied Toxicology. 2025; 45: 4–22.

[61] Albelasy EH, Raghip AG, Ismail HS. Internal adaptation and micromorphological analysis of a new self-cure resin composite. Journal of Clinical and Experimental Dentistry. 2025; 17: e912–e919.

[62] Celik MN, Yesildemir O. Endocrine disruptors in child obesity and related disorders: early critical windows of exposure. Current Nutrition Reports. 2025; 14: 14.

[63] Sharma R, Kotyk MW, Wiltshire WA. An investigation into bisphenol A leaching from materials used intraorally. Journal of the American Dental Association. 2016; 147: 545–550.

[64] Tichy A, Simkova M, Vrbova R, Roubickova A, Duskova M, Bradna P. Bisphenol A release from dental composites and resin-modified glass ionomers under two polymerization conditions. Polymers. 2021; 14: 46.

[65] Hampe T, Wiessner A, Frauendorf H, Alhussein M, Karlovsky P, Bürgers R, *et al.* A comparative *in vitro* study on monomer release from bisphenol A-free and conventional temporary crown and bridge materials. European Journal of Oral Sciences. 2021; 129: e12826.

[66] De Nys S, Turkalj M, Duca RC, Covaci A, Elskens M, Godderis L, *et al.* Level of BPA contamination in resin composites determines BPA release. Dental Materials. 2024; 40: 1025–1030.

[67] Vervliet P, de Nys S, Boonen I, Duca RC, Elskens M, van Landuyt KL, *et al.* Qualitative analysis of dental material ingredients, composite resins and sealants using liquid chromatography coupled to quadrupole time of flight mass spectrometry. Journal of Chromatography A. 2018; 1576: 90–100.

[68] Jung YH, Wanga HLV, Ruiza D, Bixlera BJ, Linsenbauma H, Xianga JF, *et al.* Recruitment of CTCF to an *Fto* enhancer is responsible for transgenerational inheritance of BPA-induced obesity. Proceedings of the National Academy of Sciences. 2022; 119: e2214988119.

[69] Hananeh WM, Al Rukibat R, Jaradat S, Borhan Al-Zghoul M. Exposure assessment of bisphenol A by drinking coffee from plastic cups. Roczniki Państwowego Zakładu Higieny. 2021; 72: 49–53.

[70] Alomran WK, Nizami MZI, Xu HHK, Sun J. Evolution of dental resin adhesives—a comprehensive review. Journal of Functional Biomaterials. 2025; 16: 104.

[71] Van Landuyt KL, Nawrot T, Geebelen B, De Munck J, Snauwaert J, Yoshihara K, *et al*. How much do resin-based dental materials release? A meta-analytical approach. Dental Materials. 2011; 27: 723–747.

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