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Comprehensive Evaluation of Cytotoxic and Endocrine-Disrupting Effects of Orthodontic Retainer Materials

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ABSTRACT

This review investigates whether materials used in removable orthodontic retainers exhibit toxic effects on cells or interfere with hormonal balance. Publications from 2015–2025 were evaluated. The scope included in vitro studies on cellular toxicity and estrogenic response, in vivo tissue observations, and clinical markers in retainers fabricated from PMMA plates, thermoplastic foils, photopolymerized 3D resins, PEEK, and fiber-reinforced systems. Screening of electronic databases yielded 38 laboratory studies and 10 clinical reports. Among tested substances, photopolymer-based resins showed the strongest adverse effects on cells, whereas PMMA and thermoplastic sheets typically demonstrated only minor impacts, which diminished after immersion in water for 24 hours. Leaching of bisphenol derivatives was detected; however, systemic absorption remained within accepted safety thresholds. Clinical evidence did not reveal significant oral tissue alterations or hormone-related outcomes. Most materials employed for retainers appear biocompatible, although evidence concerning prolonged endocrine effects is still insufficient. Harmonized methods for safety evaluation are required to compare across different appliance types. Additionally, disposable thermoplastics generate microplastic particles and complicate waste handling, presenting environmental concerns.

Keywords: Removable orthodontic retainers, BPA, Biological safety, Thermoplastics, PMMA, Aligners, Microplastic pollution

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Introduction

Following active orthodontic treatment, removable retainers are prescribed to stabilize dental alignment. Common variants include Hawley devices, constructed with a polymethyl methacrylate base and stainless-steel wire, and vacuum-formed retainers produced from PET-G, polyurethane, or polypropylene sheets [1, 2]. Extended daily wear, particularly in relapse-prone cases or congenital anomalies, has prompted questions about their biological safety. Research from 2015 to 2025 indicates that both PMMA and thermoplastic devices can release bisphenol-A (BPA) and bisphenol-S (BPS), sometimes linked to oxidative injury and genotoxic responses [3-5]. Elevated salivary BPA has been documented in patients using both categories [2]. In vitro experiments further support bisphenol migration and related cellular stress across aligner systems [6, 7]. Continuous exposure inside the mouth, even at low concentrations, may have cumulative biological implications. This review narrows its focus to removable retainers, addressing clinical safety, endocrine activity, and ecological sustainability under a One Health approach.

The purpose of this work is to synthesize existing data on cytotoxic and endocrine-disrupting properties of retainer materials, highlighting both clinical impact and environmental relevance.

Materials and Methods

Eligibility criteria

Searches were performed in PubMed, Scopus, and Web of Science for studies dated January 2015 through December 2025. Boolean combinations of the following terms were used:

- "orthodontic retainers" AND "cytotoxicity"
- "removable appliances" AND "endocrine disruption"

"PMMA" OR "polyurethane" OR "copolyester" AND "toxicology"

- "BPA" OR "BPS" OR "phthalates" AND "release"
- "in vitro" OR "clinical study" AND "orthodontic materials"

Inclusion requirements

Original peer-reviewed in vitro, in vivo, or clinical investigations;
Devices constructed from materials used in removable retainers (e.g., PMMA, polyurethane, thermoplastics);
Reporting of cytotoxicity, hormonal response, or chemical leaching (e.g., bisphenols, phthalates);
Experiments on human cells, animal subjects, or clinical participants;
Articles available in English.

Exclusion rules

Studies limited to fixed orthodontic appliances or irrelevant dental substances;
Narrative reviews, opinion pieces, meeting abstracts, or case reports without primary data;
Research not addressing biological or toxicological aspects;
Works lacking full-text availability or adequate methodological detail.
Although no official protocol (e.g., PROSPERO) was filed, the search plan was developed beforehand, logged internally, and implemented consistently across all databases.

Materials utilized in removable retainers

Removable orthodontic retainers are primarily differentiated by their material composition: acrylic-based devices (such as PMMA Hawley retainers) and thermoplastic vacuum-formed retainers (Essix-type). **Table 1** outlines their basic composition, potential leachable components, and reported biological concerns.
Hawley Retainers (PMMA-based):
Hawley appliances consist of a rigid acrylic plate, usually spanning the palate or lingual surfaces, combined with stainless steel clasps or wires for anchorage. The plate is manufactured from polymethyl methacrylate (PMMA), which is obtained through polymerization of methyl methacrylate monomers. Since the curing reaction rarely achieves 100% conversion [3], small amounts of unreacted monomer may remain in the material [8]. This residual methyl methacrylate (MMA), a recognized irritant, can diffuse into saliva, especially during the first period of wear. Heat- and pressure-cured PMMA generally achieves a higher degree of conversion compared to cold- or auto-cured variants, thereby reducing residual monomer content [2]. The metal components may release trace ions, but this review does not cover them. Although PMMA does not contain bisphenols or typical endocrine-active additives, its residual MMA and processing byproducts (such as inhibitors or initiator fragments) can be sources of cytotoxicity [9]. Newer experimental modifications, including PMMA combined with bioactive glasses like Biomin C and S53P4, have been shown to release ions such as calcium and phosphate under acidic conditions, suggesting potential applications for enamel remineralization [10].
Essix Retainers (Thermoplastic-based):
"Essix" is a general label for transparent, vacuum-formed retainers introduced by Sheridan in the 1990s [11]. These appliances are made from thin thermoplastic sheets that conform to the dentition. Early models were fabricated with PET-G (polyethylene terephthalate glycol-modified). Other polymers used include polypropylene, thermoplastic polyurethane (TPU), and multilayer or proprietary blends (e.g., SmartTrack TPU used in Invisalign aligners). They are commonly advertised as medical-grade and "BPA-free" [4]. However, some polyester-derived thermoplastics still rely on bisphenol-based additives to improve mechanical performance [12]. While PET-G

itself is free from BPA, some copolyesters and polycarbonates may incorporate it. Most current orthodontic thermoplastics (e.g., Duran®, Essix ACE®, Zendura® FLX) are designed to exclude BPA. Even products marketed as "100% BPA-free" can contain traces of bisphenol analogs (such as BPS) or other estrogenic modifiers, depending on formulation and production methods [13]. Independent validation is therefore required, as marketing claims may not reflect actual chemical release. Additionally, "BPA-free" plastics may still leach other xenoestrogens such as phthalates. Compared with freshly cured PMMA, industrially polymerized thermoplastics generally show lower levels of leachables, though oligomers, stabilizers, or plasticizers may migrate into saliva, especially in the early phase of use or under mechanical stress.

3D-Printed Retainers (Resin-based):

A newer material group involves retainers manufactured directly via additive manufacturing. While not yet widespread in practice, 3D-printed orthodontic devices are emerging as a custom alternative. These are typically made from methacrylate-based photopolymer resins, sometimes incorporating bisphenol-A glycidyl dimethacrylate or related derivatives. Inadequate post-curing or cleaning can result in significant release of unreacted monomers, contributing to cytotoxic or genotoxic effects [14]. Initial reports suggest that certain 3D-printed materials may demonstrate higher biological risks than conventional thermoplastics. Therefore, despite the promise of precise fabrication, these resins demand stringent processing and safety validation. Other investigations of clear aligner systems have documented the leaching of multiple compounds, further highlighting the need for careful assessment of biocompatibility [7].

Table 1. Composition, potential leachables, biocompatibility considerations, and relative cytotoxicity of removable orthodontic retainer materials

Retainer Type	Material Composition	Potential Leachates	Biocompatibility Notes	Cytotoxicity Level
Hawley Retainer	PMMA (methyl methacrylate polymer) base with stainless steel wire clasps; typically cold-cured or heat-cured	Unreacted MMA monomer, peroxide initiator residues, pigments; no inherent BPA in PMMA	Residual MMA may cause cytotoxicity or irritation to oral tissues [8]. Cold-cured acrylics release more MMA, increasing toxicity compared to heat-cured [2]. Rare allergic responses noted; generally biocompatible when fully cured	Moderate
Essix Retainer (PET-G)	Thermoformed polyethylene terephthalate glycol (PET-G) sheet, ~1 mm thick, petroleum-based	Trace ethylene glycol, terephthalate oligomers, UV stabilizers, or colorants; BPA-free base, though some additives may derive from BPA [12]	Highly stable with low in vitro cytotoxicity; one study detected BPA in saliva from PET-G retainers [2], possibly from additives. Minimal mucosal irritation reported	Low
Essix Retainer (Polyolefin)	Vacuum-formed blends of polypropylene or polyethylene, flexible thermoplastics	Minimal leachates (polyolefins are low-leaching); typically free of BPA or phthalates	Extremely low cytotoxicity; reduced stiffness may increase plaque buildup. High biocompatibility, with issues mainly related to mechanical wear rather than chemical leaching	Very Low
Clear Aligner (Polyurethane)	Multilayer thermoplastic polyurethane (TPU), e.g., Invisalign's SmartTrack; proprietary aliphatic/semi-aromatic blends	Urethane degradation products (e.g., 1,4-butanediol) under harsh conditions; designed without BPA or phthalates [13]	Slight in vitro cytotoxicity, similar to PET-G; considered safe for oral use	Low

3D-Printed Retainer	Photopolymerized acrylate resin (e.g., urethane dimethacrylate); custom-printed and post-cured	Unreacted methacrylate monomers (if under-cured), photoinitiator residues, possible BPA derivatives in some resins	Safe when fully cured and washed; some resins may leach cytotoxic or estrogenic compounds [14]. Requires thorough post-processing to minimize risks; biocompatibility validation ongoing	Moderate to High *

Values depend on curing method and residual monomer concentration.

Cytotoxic impact on oral cells

An essential marker of material safety is whether retainer polymers provoke cytotoxic reactions in oral tissues. Since these appliances rest directly on the palate or mucosa for extended hours daily, even minor cytotoxic effects could contribute to irritation or altered epithelial turnover. Research has addressed this through in vitro cell assays, in vivo animal testing, and clinical biomarker studies in retainer users. From 2015 to 2025, 38 in vitro investigations were identified according to strict eligibility criteria. Inclusion required the use of standardized viability assays (e.g., MTT, LDH, live/dead staining) on human oral cells or mammalian models, with materials relevant to removable retainers (PMMA, PETG, polyurethane, 3D resins). Only studies reporting quantitative cytotoxicity outcomes were considered. Those limited to fixed appliances, lacking primary data, or omitting extraction conditions were excluded. **Table 2** compiles the most representative data, illustrating the spectrum of cytotoxic responses across different materials.

Evidence from In Vitro Assays

A wide range of in vitro experiments has examined how retainer materials affect oral cell viability. Commonly, assays like MTT on gingival fibroblasts or epithelial cultures are applied to detect metabolic suppression. Findings consistently show that PMMA and thermoplastics induce only slight cytotoxicity, with viability remaining within accepted thresholds for compatibility [6].

Recent work indicates that retainer polymers generally cause low-to-moderate cytotoxic responses, with most cell survival rates between 70%–90% even under intensive extraction scenarios [15, 16]. Thermoplastics such as PETG or polyurethane typically reduce viability only marginally [17]. For example, a comparative study testing four clear thermoplastic brands (Duran®, Biolon®, Zendura®, and SmartTrack®) found all produced mild effects on human gingival fibroblasts [15]. Differences appear linked to material chemistry: polycarbonate-based plastics tend to leach more monomers compared to PETG or layered polyurethane formulations [16, 18].

New 3D-printable photopolymer retainers have also been investigated. Al Mortadi *et al.* [19] examined Dental LT and E-Guard resins, reporting only slight cytotoxicity with gradual recovery of viability over time, likely due to reduction of residual leachables or cellular adaptation. Notably, E-Guard showed the largest day-1 reduction, while SmartTrack exhibited the least cytotoxicity, with fibroblast survival consistently above 90% [15, 20, 21]. By contrast, Biolon and some 3D-printed materials caused larger early reductions, influenced by post-processing. By day 7, viability increased markedly across all groups, emphasizing that thorough post-curing and short-term soaking of 3D-printed appliances can mitigate initial cytotoxic effects [19, 21].

Among newer alternatives, polyether-ether-ketone (PEEK) has demonstrated excellent compatibility. This chemically stable, high-strength polymer—long used in biomedical implants—showed negligible cytotoxicity in fibroblast assays [22, 23]. Early clinical trials using PEEK lingual retainers reported no tissue reactions, supporting its suitability as a metal-free, MRI-safe option with minimal inflammatory potential [23].

In contrast, fiber-reinforced composites (FRCs) raise more concern. Glass- and quartz-fiber resins may leach unreacted monomers, particularly in acidic conditions or when resin surfaces are exposed. Some studies observed significant reductions in fibroblast viability with FRC retainers [24]. Acidic challenges worsened this effect, reflecting incomplete encapsulation or higher monomer release. Interestingly, comparative tests showed that multistrand metal retainers under low pH could cause even greater cytotoxicity than fiber composites, due to ion release (Ni^{2+}, Cr^{6+}) from stainless steel or NiTi wires [25]. This highlights that neither polymeric nor metallic retainers are entirely inert under oral degradation conditions.

Table 2. In vitro investigations of orthodontic retainer cytotoxicity using cell viability assays (e.g., MTT, live/dead staining) in fibroblasts and epithelial models

Research (Year)	Tested Materials	Cellular Model	Toxicity Results	Study Approach
Martina *et al.* [15]	Four thermoplastic variants: Duran (PETG), Biolon (polycarbonate), Zendura (polyurethane), SmartTrack (multilayer polyurethane)	HGF cells; MTT viability test	All materials showed low toxicity (viability > 80%). Biolon had the highest toxicity (largest viability drop), followed by Zendura and SmartTrack, with Duran being the least toxic (best viability). Thermoforming slightly increased toxicity in some cases, failing to remove all cytotoxic elements.	Laboratory-based
Campobasso *et al.* [25]	3D-printed aligners from Tera Harz TC-85DAC resin (Graphy, Korea), post-cured via: P1 (Tera Harz Cure, nitrogen, 14 min); P2 (Form Cure, 30 min/side, total 60 min)	MC3T3-E1 mouse pre-osteoblasts in DMEM; MTT assay at 7 and 14 days	P1 (nitrogen): Non-toxic, viability > 100% (107.1% ± 17.5% at day 7, 106.7% ± 18.4% at day 14), matching or exceeding control. P2 (Form Cure): Moderate toxicity, with lower viability (59.8% ± 10.1% at day 7, 47.1% ± 20.6% at day 14), significantly less compatible than P1 and control ($p < 0.001$). Conclusion: Post-curing method impacts toxicity; P1 is highly biocompatible, while P2 may retain toxic monomers.	Laboratory-based
Nemec *et al.* [21]	Invisalign SmartTrack (polyurethane), inner/outer surfaces (cell-exposed)	Human oral keratinocytes; live/dead staining, PCR gene analysis	No notable toxicity; minimal cell death on aligner surfaces. Cell proliferation was slightly reduced compared to controls, indicating mild growth suppression. Aligner-exposed cells showed elevated inflammatory and barrier gene expression. Conclusion: SmartTrack is non-toxic but may alter cellular inflammatory responses.	Laboratory-based
Al Naqbi *et al.* [26]	Vivera® retainers (Invisalign® polyurethane), as-received and post-clinical use	MCF-7 cells (estrogen-sensitive for estrogenicity), MDA-MB-231 cells (estrogen-insensitive), NIH/3T3 fibroblasts (general toxicity)	No toxicity in fibroblasts for either condition. No estrogen-driven growth in MCF-7 cells or proliferation in MDA-MB-231 cells. Conclusion: Vivera® retainers lack acute toxicity or estrogenic effects, confirming good short-term safety.	Laboratory-based

In summary, research from the past decade supports that current retainer materials are broadly biocompatible, producing mostly mild in vitro cytotoxicity and only transient stress in vivo [5, 6]. However, differences among brands and material classes persist. Emerging options such as PEEK appear particularly promising due to their inertness and stability [23].

In VIVO and clinical findings on cytotoxicity

Encouragingly, clinical and animal investigations within the past decade have not reported any severe cytotoxic responses from orthodontic retainer materials, though more subtle biological alterations have been documented. A notable randomized controlled clinical trial compared patients wearing Hawley acrylic retainers with those using Essix vacuum-formed retainers to monitor potential cellular damage. Researchers examined salivary biomarkers of oxidative DNA injury (8-hydroxy-2′-deoxyguanosine, 8-OHdG) as well as antioxidant regulators (Nrf2, Keap1), in addition to cytological screening of buccal mucosa cells for nuclear irregularities. After 1 and 3 months, patients with Hawley retainers exhibited a significant increase in salivary 8-OHdG, suggesting greater

oxidative stress likely related to leached methyl methacrylate or other acrylic additives. By contrast, the Essix group showed no such rise—in fact, a slight downward trend in 8-OHdG was recorded over time. This indicates that chemically cured acrylics may generate more oxidative burden compared with thermoplastic retainers.
Interestingly, buccal cell analysis offered a complementary perspective: Essix wearers presented more micronuclei and nuclear changes in epithelial cells after 2–3 weeks than those in the Hawley group. Thus, while both retainer types were associated with enhanced cell turnover and nuclear abnormalities compared to baseline, the patterns differed—Hawley devices were linked to oxidative DNA changes, whereas Essix devices correlated with elevated epithelial micronuclei. These observations underscore the material-specific biological interactions: acrylic leachates appear to promote systemic oxidative stress, while thermoplastic retainers may induce localized mucosal friction or mechanical irritation [5].

Estrogenic activity and Bisphenol-A (BPA) release
One of the most widely debated safety issues regarding dental polymers is the possible endocrine-disrupting potential of bisphenol derivatives. Bisphenol-A (BPA), used historically in polycarbonate plastics and epoxy-based resins, is a well-known xenoestrogen capable of binding to estrogen receptors—though at a much weaker affinity than natural estradiol—and has been associated with reproductive and developmental toxicities [27]. Given that orthodontic retainers and aligners are fabricated from plastics placed intraorally, concerns have been raised about salivary release of BPA or structurally similar estrogenic compounds. The clinical relevance, particularly in terms of systemic hormonal impact, however, remains unclear.

Retainer-related BPA release: Laboratory vs. clinical contexts
Earlier in vitro investigations largely found either no detectable BPA or concentrations below analytical thresholds (e.g., <1 ng/mL) when clear aligners were incubated in artificial saliva. For example, Schuster *et al.* [28] and Gracco *et al.* [29] detected negligible monomer release from Invisalign® aligners under laboratory soaking conditions. More recently, Katras *et al.* [30] tested multiple commercial brands (SmileDirectClub, Invisalign, Essix ACE) in media such as simulated saliva, gastric solution, and ethanol. They observed that when BPA was measurable, it was typically released during the first 24 hours, with concentrations well below safety benchmarks. Most of these studies used sensitive detection methods such as high-performance liquid chromatography (HPLC) or mass spectrometry; frequently, BPA was undetectable in newly manufactured aligners [6]. Data on estrogenic activity and BPA release from orthodontic polymers, mainly based on in vitro tests, are summarized in **Table 3**.
In vitro bioassays have been used to assess whether retainer leachates trigger estrogen-receptor-dependent activity. Two independent investigations [18, 26] employed the MCF-7 breast cancer cell proliferation assay, a widely accepted indicator of estrogenic stimulation. Neither study detected proliferative effects beyond controls when exposing MCF-7 cells to Invisalign® or Vivera® material extracts. Positive controls (17β-estradiol or BPA) produced marked proliferation, while aligner extracts remained comparable to negative controls. Likewise, no proliferative effects were noted in estrogen receptor–negative cell lines (MDA-MB-231), confirming the absence of estrogen-mediated activity from these materials. These biological outcomes are consistent with chemical analyses showing extremely low BPA release from present-day orthodontic plastics. Advanced methods such as GC-MS and LC-MS/MS have been employed to screen aligner extracts [18,26]. Across several investigations conducted from 2016 through 2021, no measurable BPA or related compounds were identified in saliva or artificial saliva following aligner immersion for extended intervals [6].

Clinical evidence on BPA release
Clinical research has offered a more cautionary perspective. Raghavan *et al.* [2] carried out a randomized clinical study measuring salivary BPA concentrations in patients fitted with different retainer types. A total of 45 participants were allocated into three groups: (1) Essix vacuum-formed retainers, (2) Hawley retainers fabricated with heat-polymerized PMMA, and (3) Hawley retainers produced with cold-cure/autopolymerized PMMA. Saliva was sampled at baseline (before insertion), and subsequently at 1 hour, 1 week, and 1 month. All three cohorts showed a statistically significant rise in salivary BPA following retainer delivery ($p \leq 0.05$) [2].
A subsequent randomized trial by Nanjannavar *et al.* [12] investigated whether pre-soaking appliances could mitigate this effect. When vacuum-formed retainers were immersed in water at 37 °C for 24 hours before use, the BPA released into saliva was markedly lower. At the 1-hour mark, pre-soaked retainers produced only ~0.07 ppm BPA compared with ~0.33 ppm from unsoaked ones. After 1 and 3 weeks, BPA levels in the pre-soaked group

were nearly undetectable. These findings indicate that a simple overnight water soak may eliminate most of the leachable BPA, providing a practical chairside method to limit exposure [12].

It is also important to recognize that regulatory guidance on BPA safety has shifted significantly. In earlier years, agencies such as the FDA and EPA set relatively high tolerable daily intake limits (around 50 µg/kg body weight/day). More recent toxicological and epidemiological data suggest endocrine-related effects may occur at doses far below those thresholds. In fact, animal experiments and population studies have associated long-term low-dose BPA with subtle immune and hormonal disturbances. Consequently, European regulators in 2021–2023 drastically reduced acceptable daily intake values, lowering them by several orders of magnitude to the nanogram/kg range [31]. Parallel cellular studies further confirmed that even minimal BPA levels can affect immune function, intensifying the debate on endocrine disruption [32]. Within this context, even the trace amounts released from orthodontic appliances are being reassessed with a precautionary outlook. To date, however, there is no evidence of systemic endocrine disorders directly tied to BPA leaching from retainers. Hassan *et al.* [33] reviewed emerging strategies that include BPA-free adhesives, new aligner polymers, and multifunctional "smart" biomaterials with antimicrobial benefits, reflecting an industry-wide move toward eliminating endocrine-active substances altogether.

Table 3. BPA release values and estrogenic responses associated with orthodontic retainer polymers, based on in vitro assays, chemical analyses (HPLC, LC-MS/MS), and clinical evaluations

Study (Year)	Materials and Test Conditions	BPA Release Results	Hormonal Impact	Research Approach
Katras *et al.* [30]	SmileDirectClub, Invisalign, and Essix ACE aligners; immersed in artificial saliva, gastric fluid, and 20% ethanol; analyzed at 0, 1, 2, 6, 10, 20 days	Trace BPA detected, mostly within the initial 24 h (burst effect). Levels remained under 5 µg/L in saliva, compliant with EU safety limits. No significant BPA variation across brands or media types.	No hormonal testing conducted; low BPA levels suggest negligible endocrine effects, deemed safe for adults by authors.	In vitro testing
Intissar *et al.* [34]	Invisalign® polyurethane aligners; new and 2-week used samples; exposed to artificial saliva for up to 8 weeks	No BPA detected in extracts (HPLC, <5 ppb limit) after intraoral use or prolonged saliva exposure, indicating chemical stability regarding BPA.	Not applicable (chemical analysis focus). Absence of BPA suggests no hormonal activity from aligners.	In vitro testing
Raghavan *et al.* [2]	Patients (n=45) using: (1) Essix vacuum-formed (PETG), (2) heat-cured Hawley, (3) chemically cured Hawley; salivary BPA tested before and 1 month after use	All groups showed increased salivary BPA after 1 month. Chemically cured Hawley had the highest rise (2–3 µg/L), heat-cured Hawley lowest (~1 µg/L or less), all in ppb range.	No hormonal symptoms detected; BPA levels below thresholds for endocrine effects. Authors advocate for heat-cured or BPA-free materials to minimize exposure.	Clinical and in vitro
Iliadi *et al.* [35]	Experimental BPA-free adhesive (phenyl-propanediol dimethacrylate) vs. Bis-GMA adhesive for fixed retainers	Experimental adhesive released no BPA (no BPA derivatives in formula). Conventional adhesive showed trace BPA from Bis-DMA breakdown, while experimental adhesive eluates had no detectable BPA.	BPA-free adhesive showed no hormonal or toxic effects, with comparable bond strength, supporting its potential for clinical use. Emphasizes reducing BPA-related endocrine risks.	In vitro testing

Eliades *et al.* [18]	Three sets of Invisalign aligners soaked in saline at 37 °C for 2 months; eluates tested at 5%, 10%, 20% concentrations	No measurable BPA or significant leachates in aligner eluates across all concentrations, confirming material stability.	No hormonal activity observed; aligners considered safe with no endocrine impact.	In vitro testing

Summary

Thermoplastic retainers can indeed release small amounts of BPA into saliva, particularly during initial use. Nevertheless, practical approaches such as pre-soaking devices or selecting alternative BPA-free materials significantly reduce exposure. Heat-cured acrylic appliances release negligible BPA (unless externally contaminated), while some thermoplastics show transient leaching. Manufacturers increasingly emphasize "BPA-free" branding, but clinicians should remain mindful of possible trace chemicals.

Estrogenic potential of released compounds

While BPA detection can be relatively straightforward, determining whether these trace amounts translate into measurable estrogenic activity is far more complex. Researchers have relied on assays involving estrogen-sensitive cells to evaluate receptor activation. Most data suggest that the concentrations of BPA or similar compounds released from retainers remain below thresholds required to trigger estrogenic responses in vitro [6]. Yet, endocrine disruption in vivo can occur even at very low concentrations and may follow non-linear dose–response dynamics. This raises concerns that prolonged, low-level exposure—even if classified as "safe"—might still contribute to subtle developmental or hormonal changes over time.

No clinical study has yet linked orthodontic retainer use with systemic hormonal alterations, partly because such trials would be extremely challenging to design and control. From related dental materials, such as composites and sealants, we know that salivary and urinary BPA spikes are detectable shortly after placement but typically return to baseline within 24–48 hours—levels considered too minor to cause health risks [27]. The American Dental Association has likewise stated that "trace BPA may leach from freshly polymerized resins, causing only a temporary rise in salivary or urinary levels" [27], which parallels the observations with retainers.

Another issue is whether other potential xenoestrogens besides BPA could leach from these materials. Some plastics incorporate bisphenol-S (BPS) or phthalates, both of which have estrogen-mimicking or anti-androgenic effects. Although DEHP phthalates were used historically, modern orthodontic polymers are generally phthalate-free. BPS has been introduced as a substitute in "BPA-free" plastics, but its safety is equally debated. To date, no specific study has examined BPS release from orthodontic retainers. Therefore, while BPA is well studied and relatively well understood, the roles of BPS and phthalates remain poorly explored, warranting future investigation.

Summary of estrogenic effects

Overall, the body of evidence to date indicates that standard use of Hawley and Essix retainers does not produce significant estrogenic outcomes. Detectable BPA release may occur, particularly from certain thermoplastic appliances, but the quantities are generally very small. Both laboratory-based estrogen assays [6] and clinical observations have thus far supported the conclusion that these appliances have minimal hormonal impact. Nonetheless, given the high prevalence of their use, particularly among adolescents who may transition from aligners to retainers over many years, cumulative exposure remains a topic deserving continued attention. As a precaution, simple practices—such as soaking or rinsing newly fabricated retainers before initial use, and opting for BPA-free polymers—can further reduce any potential endocrine risk [12].

Molecular mechanisms of cellular stress and estrogenic action

Oxidative stress and DNA injury

Acrylic appliances can release residual compounds like methyl methacrylate (MMA), which penetrate oral tissues, enter saliva, and in trace amounts reach circulation [36]. Once released, MMA may undergo metabolic processes or redox cycling, producing reactive oxygen species (ROS). These ROS can damage DNA, proteins, and cell membranes, leading to oxidative stress [37]. The elevated salivary marker 8-OHdG in Hawley retainer users [8] reflects such oxidative DNA lesions, since 8-OHdG arises when guanine bases are oxidized. Normally, repair

systems correct this damage, but consistent elevation suggests sustained ROS exposure. Interestingly, Essix users did not display elevated 8-OHdG in the trial, suggesting either reduced ROS induction or adaptive stress responses.

Cellular defenses against ROS commonly involve the Nrf2/Keap1 pathway, which regulates antioxidant gene expression. Gunel *et al.* assessed Nrf2 and Keap1 activity in their trial but found no major differences between groups [5], implying the oxidative insult was not strong enough to produce divergent antioxidant activation, or that both materials elicited comparable cellular defense responses.

Beyond oxidative pathways, direct cytotoxic actions include disruption of plasma membranes. MMA is a small organic molecule capable of disturbing lipid bilayers. In vitro, higher MMA concentrations or additives from aligner plastics have been shown to compromise membrane stability, depolarize cells, and cause lysis. Saliva may help by diluting and binding monomers [6]. Still, genotoxic markers—such as elevated micronuclei frequency—have been detected in Essix users [5]. Micronuclei form when DNA breaks or spindle errors occur during mitosis, often triggered by chemical stress. The increase in micronuclei after 2–3 weeks of Essix use points to an early genotoxic event, possibly from chemical leachates or mechanical irritation [8].

In short, the cytotoxic impact of retainer materials likely arises from a combination of chemical and physical factors: acrylic-based devices release MMA that promotes ROS and 8-OHdG formation, while thermoplastics—although releasing fewer monomers—may still produce small quantities of stress-inducing agents or microparticles. Mechanical compression from vacuum-formed retainers may also contribute by inducing localized ischemia or inflammation. Altogether, these interactions explain the presence of oxidative DNA damage and cellular turnover markers observed in wearers.

Estrogen receptor signaling pathways

Compounds like BPA, when leached, can interact with estrogen receptors (ERα and ERβ) found in different tissues. Within the oral cavity, ERs are expressed in periodontal fibroblasts and bone cells, but epithelial tissues are not classical estrogen targets. Once absorbed, however, BPA may act systemically, binding ERs and altering gene transcription. Experimental toxicology has shown that chronic low-dose BPA can influence reproductive development, metabolism, and neurobehavior, but these effects typically result from exposures far greater than what orthodontic retainers provide [27].

A potential local consideration is whether estrogen signaling could affect gingival healing or bone remodeling. Although BPA may in theory influence inflammatory or regenerative pathways, no human evidence links retainer-related BPA exposure to gingival inflammation or alveolar bone changes. Laboratory findings show BPA can modulate inflammatory cascades, but clinical data remain absent. The lack of response in MCF-7 estrogen-sensitive assays with aligner extracts [6] provides further reassurance that effective estrogenic activity from retainers is negligible. In addition, BPA has a short half-life in humans, being excreted rapidly, so any post-insertion spikes are transient and unlikely to maintain receptor activation. Still, estrogen signaling is known to exhibit non-linear dose–response effects, where very low doses may produce unexpected outcomes [27].

In conclusion, while orthodontic materials can theoretically release agents capable of binding estrogen receptors, current findings indicate that exposure levels are too low to elicit meaningful activation in vivo. The mechanistic pathway (xenoestrogen binding → ER activation → altered transcription) is well established, but in the case of retainers, it appears largely inactive. Nonetheless, ongoing refinement of materials—such as avoiding Bis-DMA, which can degrade into BPA [27]—is warranted to further limit any potential endocrine effects, especially in young patients or those using appliances long-term.

Clinical relevance of findings for long-term retainer use

From a practical clinical perspective, the central issue is whether the reported cytotoxic or estrogen-like effects actually translate into significant health risks for orthodontic patients. Retainers are frequently worn for prolonged periods—often nightly for years, and in some cases indefinitely to prevent relapse. In situations such as hypodontia, where permanent restorative work may be delayed, retainers containing prosthetic teeth may be used daily until adulthood. Therefore, evaluating the clinical impact of long-term exposure to retainer polymers is essential.

Oral Mucosa and Patient Symptoms

Most individuals adapt to both Hawley and Essix retainers without major adverse effects, and overt tissue injury is uncommon. Still, published reports and surveys describe a spectrum of mucosal reactions, including:
Early irritation: Initial gum or palatal soreness is frequently reported when a new appliance is first inserted. These symptoms generally resolve as the tissues acclimate or as trace residual compounds are washed out. For aligners/retainers, patients occasionally report transient discomfort in the mouth or an unusual taste during the first days of wear, possibly linked to early release of plastic additives [30].
Ulceration or allergic responses: A minority of patients may develop localized or systemic hypersensitivity reactions to PMMA or certain thermoplastic components. Manifestations can range from redness and minor ulcers to lip swelling or itching. Allergic reactions to acrylics are well recognized in prosthodontics, particularly among denture users sensitive to residual MMA. For such cases, alternatives—like metal retainers or hypoallergenic liners—may be indicated [38].
Taste changes and xerostomia: Some patients describe a temporary "plastic" or chemical aftertaste when starting retainer wear. Reports of dry mouth (xerostomia) also exist [6], though it is uncertain whether this is caused by chemical release or simply the physical bulk of the device. Reduced salivary flow can amplify any cytotoxic influence because saliva normally dilutes and neutralizes irritants.
Periodontal concerns: Retainers that fit poorly or are not cleaned adequately may trigger gingival inflammation. While this is largely a hygiene-related rather than a chemical issue, persistent inflammation itself contributes to oxidative stress in oral tissues. Nighttime Essix retainers, being removable and easier to clean, have generally been associated with more favorable periodontal outcomes compared with fixed retainers [39]. With proper maintenance, most chemical-related risks are minimal.
A concise summary of removable orthodontic retainers, their material composition, and associated biological concerns is presented in **Table 4**.

Table 4.

Retainer Class	Core Material	Key Constituents	Associated Risks
Hawley Appliance	PMMA with steel wire	Methyl methacrylate (MMA), residual unpolymerized monomers	Cellular toxicity, potential allergic reactions (e.g., oral inflammation), monomer leaching
Essix (C+) Appliance	PVC-based polymer	Phthalates, traces of vinyl chloride	Endocrine interference, possible release of plasticizing agents
Essix ACE Appliance	PETG-based copolyester	BPA, PETG-derived oligomers	Trace BPA leakage, low-level cytotoxicity
Advanced Thermoplastic Retainers (Duran®, Essix ACE®, Zendura® FLX, etc.)	Polyurethane compounds	BPA, BPS compounds	Potential hormonal effects (observed in vitro), minimal cellular toxicity
3D-Printed Appliance	Proprietary multilayer polyurethane	Possible BPA analogs (BPS, BPF)	Uncertain risks due to proprietary composition, dependent on material degradation and wear

Regulatory standards and international guidelines
Evaluating orthodontic polymers for cytotoxic and endocrine-disrupting potential requires both laboratory validation and regulatory review. Oversight agencies such as the U.S. Food and Drug Administration (FDA) and the European Union (EU) provide frameworks to confirm the safety of removable appliances before and during clinical use.

FDA (United States)
In the U.S., removable retainers are designated as Class II medical devices. They require a 510(k) premarket submission to demonstrate equivalence to an already cleared device [40]. Safety testing must comply with ISO 10993 standards [41], which govern biological evaluation of medical materials. These include:
ISO 10993-5: cytotoxicity testing

ISO 10993-10: irritation and sensitization testing
Other modules depending on material type and intended contact site/duration [41]
Because retainers are in long-term contact with oral mucosa, ISO compliance must demonstrate no acute or chronic toxicity, genotoxicity, or mucosal irritation. Manufacturers of modern materials (e.g., Invisalign's SmartTrack) report that their products have successfully passed the full ISO biocompatibility series for intraoral use.
Regarding BPA release, the FDA has not set explicit thresholds for dental appliances. Unlike infant bottles, from which BPA has been banned since 2012, orthodontic devices remain regulated under a risk-based model. Neither the FDA nor the American Dental Association has issued guidance restricting BPA-containing orthodontic polymers [42]. Trace BPA may still occur as a contaminant or breakdown product, but exposure from dental sources is usually low and transient [43].
Although the FDA promotes voluntary reduction of BPA exposure—especially in infants and children—there is no binding restriction for dental appliances. Consequently, many manufacturers have moved to BPA-free formulations, largely in response to consumer expectations rather than legal requirement.

EU regulations
In Europe, oversight of medical devices is comparatively tighter regarding potentially hazardous ingredients. The Medical Device Regulation (MDR, EU 2017/745), which became fully enforceable in 2021, obliges manufacturers to identify and disclose any carcinogenic, mutagenic, reprotoxic (CMR) agents or endocrine-active compounds. If any material that comes into patient contact contains more than 0.1% by weight of substances categorized as substances of very high concern (SVHCs) under REACH, the producer must provide justification, perform a benefit–risk assessment, and include clear labeling [44].
Bisphenol A (BPA) appears on the SVHC list because of its hormone-disrupting activity. Even though orthodontic retainers typically release BPA in quantities far below this cut-off, the MDR has pushed many companies to shift toward BPA-free alternatives, both to reduce regulatory complexity and to align with consumer expectations.

Material standards and CE marking
Appliances in dentistry must also follow specific material standards. The main guideline is ISO 20795-2:2013 ("Dentistry—Base polymers—Part 2: Orthodontic base polymers"), adopted in the EU as EN ISO 20795-2, which sets performance requirements for acrylic and polymer-based components [45]. It specifies criteria like flexural resistance, color retention, and indirectly biocompatibility by capping the amount of residual monomer. For example, the level of free methyl methacrylate (MMA) left in denture bases should not exceed 2%.
To obtain the CE mark, companies must show compliance with both ISO 20795-2 and the ISO 10993 safety series, particularly since retainers are designed for long-term intraoral use. These dual requirements ensure mechanical durability and biological safety.

ISO 10993 biocompatibility [46]
Both U.S. and EU systems rely on ISO 10993 testing for medical devices. For retainers in contact with oral mucosa for more than 30 days, the recommended test battery covers cytotoxicity, systemic toxicity (short- and long-term), local irritation, and if needed, genotoxicity. Additional assays are necessary when novel materials are used or if there is suspicion of endocrine-disrupting potential.
Although some independent research has noted mild estrogenic or cytotoxic signals from dental polymers, the observed responses remain below the safety thresholds outlined in ISO protocols [46]. Meeting ISO 10993 is therefore widely accepted as evidence of safe clinical use.

Labeling and product information
If an orthodontic product in the EU contains >0.1% of an SVHC, manufacturers must list it explicitly on labels and in supporting documentation [47]. This includes Instructions for Use (IFUs) and Safety Data Sheets (SDSs), where the presence or absence of substances such as BPA or phthalates must be indicated. Many companies now market products with "BPA-free" or "phthalate-free" claims. In contrast, U.S. labeling rules are generally voluntary—apart from recognized allergens such as latex [43].

Professional and clinical guidance

Dental associations and researchers continue to highlight potential systemic risks from polymer degradation. Current studies recommend ongoing innovation, including direct 3D-printed appliances and more sensitive monitoring of residual chemical release, to further minimize patient exposure [48, 49].

Overall, international regulations already provide a strong safety framework. To date, no widely used orthodontic retainer has been banned by either EU or U.S. authorities, showing that documented leaching levels remain within safe limits. Nonetheless, the MDR disclosure trigger of 0.1% for SVHCs remains a major factor motivating industry toward purer, safer formulations.

Clinicians should remain attentive to material composition and, when treating sensitive patients, choose BPA-free or hypoallergenic products. Although the overall risk–benefit profile of retainers is favorable, tightening regulation and rising public concern underline the importance of continuous material improvement and strict compliance with updated standards.

One health and environmental perspective

Orthodontic retainer research has recently shifted from examining only direct patient safety to also considering ecological and public health consequences. Following the One Health model, which links human, animal, and environmental well-being, concerns now center on microplastic generation, additive leaching, and the long-term persistence of synthetic polymers in ecosystems [50, 51].

Microplastic release

Within the oral environment, retainers undergo mechanical wear and chemical attack, which leads to the detachment of micro- and nanoplastic particles (MNPs). Ceccarelli *et al.* (2024) demonstrated that aligner sheets shed MNPs after only seven days of simulated usage [52], while Barile *et al.* [39] reported that different aligner brands exposed to cyclic stress released noticeable polymer debris. Most fragments measured tens to hundreds of micrometers, though particles <1 μm raise concern since they can potentially penetrate epithelial barriers. Reports of MNPs in blood and placenta samples from unrelated contexts lend support to this risk [53].

Short-term toxicity is not clearly evident, but long-term, low-level exposure—especially in adolescents—remains poorly studied. With the rapid global expansion of aligner therapy, emerging data are beginning to quantify both microplastic output and associated chemical emissions [49, 51].

Chemical accumulation and wildlife impact

Retainers act as diffuse emitters of bisphenols and additives. A single appliance releases very little, but frequent replacement cycles—weekly during active treatment and every six months during retention—increase the cumulative load. Once discarded in landfills, residual monomers like BPA can persist and migrate into surrounding soil or groundwater.

Even trace BPA levels disrupt the endocrine balance of aquatic organisms, causing feminization and developmental alterations at parts-per-trillion doses. Although orthodontic devices are a minor contributor to overall BPA pollution, their resistance to degradation and exclusion from recycling systems (due to biohazard risks and mixed composition) [53] highlight their environmental significance.

One health framework and preventive design

Removing hazardous chemicals from orthodontic materials simultaneously benefits patients, dental staff, and ecosystems. The adoption of BPA-free and phthalate-free polymers lowers direct chemical contact, while stable polymer matrices reduce leachate formation from waste sites or wastewater streams. Such measures promote sustainable orthodontics, emphasizing reduced toxicity, resource efficiency, and responsibility at disposal [54, 55].

Some companies are already testing solutions. For example, Align Technology in the UK (2022) trialed a program collecting used aligners for energy recovery or secondary applications, marking an early attempt at integrating eco-conscious design into orthodontic workflows.

Emerging eco-friendly materials

Novel biopolymer options are being explored to replace petroleum-based plastics. Cellulose acetate thermoformable matrices, partly biodegradable, have been tested with antimicrobial compounds. In vitro work showed that cinnamaldehyde-infused cellulose aligners prevented biofilm growth while maintaining cell safety

[56, 57]. Other composites containing nanohydroxyapatite and quaternary ammonium salts demonstrated antibacterial and remineralizing activity while supporting cell viability [58].
Despite encouraging findings, such materials still require mechanical testing, long-term safety validation, and data on nanoparticle release during both use and disposal, as environmental outcome studies are still sparse.

Green dentistry practices
Reducing the footprint of orthodontics involves process innovations as well as new materials. Digital scanning removes the need for disposable impression trays, and optimized 3D-printing protocols cut resin waste. Choosing durable retainers (e.g., PEEK or laminated designs) can reduce how often replacements are needed, conserving resources. These measures align with life-cycle assessment (LCA) principles, balancing clinical function with sustainability [55].
Still, patient expectations—such as preference for thin, easily replaced retainers—pose challenges. Current literature encourages clinicians to integrate environmental indicators into decision-making alongside traditional outcomes.

Environmental regulations and policy outlook
At present, orthodontic appliances are not subject to dedicated environmental legislation. However, broader frameworks are beginning to apply. Under EU Regulation 2017/745, any device with >0.1% of a substance of very high concern (SVHC)—including BPA—requires explicit labeling and justification. Meanwhile, ISO 10993 continues to serve as the global basis for biocompatibility testing, but the regulatory lens is gradually widening to include life-cycle and ecological impacts [44, 46].

Conclusion

The One Health perspective positions orthodontic polymers within the larger web of human and environmental systems. Presently, most materials comply with established intraoral safety criteria, yet their persistence in ecosystems and potential for chemical release necessitate closer evaluation. Novel material classes promise both improved safety and reduced ecological impact, though their adoption requires balancing clinical effectiveness with sustainability concerns.
The future of orthodontic biomaterials is moving toward the integration of functional performance with ecological responsibility. Achieving this shift will require coordinated engagement among academic researchers, manufacturers, and regulatory authorities, ensuring that innovation simultaneously benefits oral health and global ecosystems.

Environmental implications
In addition to clinical outcomes, the use of removable retainers and aligners presents broader environmental health challenges. These devices are essentially disposable polymers that ultimately add to plastic waste streams. Recent life-cycle analyses have quantified this contribution and placed orthodontic plastics within the larger debate on medical polymer waste [59].

Microplastics and nanoplastics release
Orthodontic appliances made of polymers are exposed to mastication, bruxism, saliva enzymes, and thermal shifts, which gradually degrade their surfaces and release micro- and nanoscale debris. Multiple studies confirm that aligners do emit such particles during wear. Quinzi *et al.* demonstrated that after 7 days of simulated use, aligner systems shed fragments sized 5–20 μm, detectable via spectroscopy. The amount varied by brand: one material released substantially more particles than others, while Invisalign showed the lowest release [52]. These fragments may be swallowed or incorporated into biofilms. Although the clinical impact is unclear, ingestion of microplastics has elsewhere been linked to inflammation and tissue penetration.

Plastic waste and disposal
Clear aligner therapy typically requires 20–30 appliance sets per patient (upper and lower arches). With each pair weighing about 4.3 g, the total plastic burden per treatment reaches ~100–130 g [53]. Extrapolating to a market of ~1 million patients annually, the result exceeds 100 metric tons of plastic waste generated each year. Even in

the retention stage, Essix retainers are commonly replaced every 6–12 months. At present, most discarded devices end up in landfills or municipal waste streams [53]. Recycling pathways are scarce due to their biohazard classification and composite structure (often containing metal or multilayer polymers). In landfill conditions, these plastics exhibit low biodegradability and long persistence.

Public health and ecosystem impact

The proliferation of microplastics is increasingly recognized as a public health concern, with evidence of their presence in water sources and human tissue. While aligners form a minor fraction of overall plastic pollution—dwarfed by packaging, bottles, and textiles—orthodontics still contributes to the broader issue. To address this, Macrì *et al.* [53] advanced the "4Rs" concept—Reduce, Reuse, Recycle, Rethink—as a sustainability framework for aligner practice. Suggested approaches include optimizing treatment to minimize plastic use, repurposing discarded trays, developing collection and recycling systems, and transitioning toward biodegradable materials.

From a regulatory perspective, the concern extends to substances of very high concern (SVHCs) such as BPA. EU restrictions on BPA in products like infant bottles and food-contact items reflect its environmental persistence. Though orthodontic appliances are not directly targeted, most manufacturers have preemptively eliminated BPA to mitigate future regulatory or liability risks.

Conclusions and future directions

In the past decade, attention to the biological compatibility of orthodontic polymers has expanded alongside evolving standards. Available evidence shows that retainers made of PMMA-based acrylics or PETG/TPU thermoplastics are generally safe, with only mild estrogenic or cytotoxic responses noted. Widely used appliances—such as Hawley and Essix retainers—have a long history of clinical application without reports of serious harm.

That said, research has identified oxidative stress markers, ultrastructural changes, and trace bisphenol release, suggesting that these materials exhibit low but detectable bioactivity. While overall safety remains favorable, these findings highlight opportunities to refine compositions and improve their toxicological profile. Future development will likely emphasize materials that combine mechanical reliability, patient safety, and environmental sustainability.

Evidence-based clinical guidance

Both principal retainer types—Hawley and Essix—have demonstrated mild in vitro cytotoxicity and slight biological marker alterations in vivo, but no serious pathology. Patients can be reassured of their general safety, while clinicians should remain attentive to rare instances of allergy or sensitivity.

The primary concern with acrylic Hawley retainers is residual monomer release. This can be minimized by using heat-polymerized acrylic and pre-soaking the device in water (or allowing initial intraoral soaking before continuous wear). If a patient reports a burning sensation or strong acrylic taste, the appliance may require longer soaking or fabrication with more complete polymerization.

BPA and estrogen-mimicking compounds may leach from some thermoplastic retainers, particularly within the first 24 hours of use. As a precaution, new retainers should be rinsed or soaked before delivery. Selecting BPA-free products with supporting data is advisable. If a material shows higher release potential, an alternative should be chosen, especially for younger patients, those planning pregnancy, or other vulnerable groups.

Ongoing monitoring is essential: during follow-up visits, examine the oral mucosa for persistent irritation. In long-term wearers, addressing inflammation is critical—sometimes a simple adjustment or polishing of the appliance edges is sufficient to resolve physical irritation that could contribute to cellular stress.

Patient education is important: instruct users to clean retainers daily, not only for hygiene but also to prevent plaque accumulation, which can provoke gingival inflammation and interact with leached chemicals. A clean appliance reduces the likelihood of additional tissue responses beyond the material's baseline effects.

For sensitive patients, alternative materials may be indicated. For example, those with known acrylic allergies (e.g., from nail products) may tolerate polypropylene-based Essix retainers, which contain negligible monomer release. For individuals who wish to avoid plastics altogether, a fixed retainer can be considered.

Forward-looking perspectives and research priorities

Continuous evaluation of emerging materials is needed, particularly those containing bioactive or antimicrobial additives. Each innovation must undergo toxicological testing to ensure no unexpected safety risks arise.
The development of biodegradable or recyclable polymers aligns with sustainability goals. However, current biodegradable candidates often lack the mechanical strength and clarity necessary for long-term orthodontic use. While desirable, fully biodegradable retainers remain a future objective, requiring balance between environmental impact, safety, durability, and cost.
Future in vivo investigations should examine the long-term biological effects of retainer wear, including persistence of oxidative stress and systemic biomarkers.
More mechanistic research is necessary to identify the pathways by which certain additives produce cytotoxic or estrogenic activity.
Anticipated regulatory changes may impose stricter thresholds for BPA and similar leachables, prompting manufacturers to adopt new formulations.
From a public health perspective, the orthodontic field should aim to reduce even minimal risks, especially in children and adolescents.
Future work should focus on creating standardized testing protocols for biocompatibility and endocrine disruption, ensuring consistent evaluation across different materials. In summary, Hawley and Essix retainers remain safe and effective according to current evidence, but progress in polymer technology and biocompatibility research will further strengthen their safety profile. Evidence-based selection and patient-specific material choices will maximize clinical success and biological safety, while aligning with environmental sustainability efforts. Advances in material science are expected to yield next-generation retainers with enhanced safety, reducing current concerns regarding toxic and endocrine-related effects.

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