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Cytotoxic and Endocrine Disrupting Effects of Removable Orthodontic Retainer Materials: A Comprehensive Review

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ABSTRACT

To investigate the potential cytotoxic and hormone-disrupting effects of materials commonly employed in removable orthodontic retainers. Studies published between 2015 and 2025 were reviewed, including in vitro assessments of cell toxicity, estrogenic activity, in vivo tissue responses, and clinical biomarker evaluations of PMMA plates, thermoplastic foils, 3D-printed resins, PEEK, and fiber-reinforced composites. A total of 38 laboratory studies and 10 clinical studies satisfied the inclusion criteria. Photopolymer-based resins showed the greatest cytotoxicity, whereas PMMA and thermoplastics induced mostly mild effects that further decreased after 24 hours of water immersion. Release of bisphenol-related compounds was observed, but systemic levels remained below safety limits. Clinical observations did not reveal significant mucosal changes or endocrine-related outcomes. Overall, removable retainer materials exhibit satisfactory biocompatibility, though evidence regarding long-term endocrine effects is scarce. Standardized testing protocols are needed to enable reliable comparisons across material types. Furthermore, the use of disposable thermoplastics raises microplastic pollution concerns and complicates waste management, highlighting sustainability issues.

Keywords: Microplastic release, Bisphenol a (bpa), Orthodontic retainers, Biocompatibility, Clear aligners, Polymethyl methacrylate (pmma), Thermoplastics

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Introduction

Removable retainers are routinely used to preserve tooth positions after orthodontic treatment. Common designs include the PMMA-based Hawley retainer, which combines a resin base with a metal wire framework, and vacuum-formed thermoplastic devices made from materials such as PET-G, polypropylene, or polyurethane [1, 2]. Prolonged oral exposure, particularly in patients at high risk of relapse or with missing teeth, has raised safety concerns regarding these materials. Studies from 2015 to 2025 indicate that compounds such as BPA and BPS can leach from these devices, potentially causing cellular damage including oxidative stress and DNA alterations [3–5]. Saliva from users of both PMMA and thermoplastic retainers has shown detectable bisphenol levels [2], and in vitro experiments confirm that released bisphenols may provoke cytotoxic effects across different aligner types [6, 7]. Although exposure levels are generally low, chronic contact could have cumulative biological effects. This review specifically examines removable retainers, integrating evidence on cellular toxicity, hormonal disruption, and environmental impact within a One Health perspective. The goal is to synthesize current knowledge on the biocompatibility and ecological footprint of retainer materials.

Materials and Methods

Search strategy and study selection

A literature search was conducted across PubMed, Scopus, and Web of Science to identify relevant research published from January 2015 to December 2025. The search combined terms related to retainers, cytotoxicity, endocrine disruption, and material composition using Boolean operators:

- "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"

Eligibility criteria

Studies were considered eligible if they:

- Were original peer-reviewed laboratory, animal, or human investigations
- Investigated materials commonly used in removable retainers (e.g., PMMA, thermoplastics, polyurethane)
- Assessed cytotoxicity, hormonal activity, or chemical release (including bisphenols or plasticizers)
- Involved human-derived cells, animal models, or clinical participants
- Were published in English

Studies were excluded if they:

- Focused exclusively on fixed orthodontic devices or unrelated dental materials
- Were reviews, editorials, abstracts, or case reports without original data
- Did not assess biological or toxicological outcomes
- Were inaccessible in full text or lacked methodological clarity
- No formal review protocol was registered, but the search strategy was predetermined, consistently applied across databases, and documented internally for reproducibility.

Materials used in removable retainers

Removable orthodontic retainers can be grouped according to their material composition into acrylic-based devices, such as Hawley retainers, and thermoplastic appliances, including Essix-type clear retainers. **Table 1** provides an overview of these materials along with their reported biocompatibility concerns.

Hawley retainers (Acrylic-Based, PMMA)

Hawley retainers consist of a rigid acrylic plate, typically covering the palate or lingual surfaces, combined with embedded metal wires or clasps to secure the appliance to the teeth. The acrylic component is made from polymethyl methacrylate (PMMA), which is produced through the polymerization of methyl methacrylate monomers. Complete polymerization is rarely achieved [3], leaving a small fraction of residual monomer in the cured material [8]. This leftover methyl methacrylate (MMA) can leach into saliva, especially during the initial days of wear, and is a known irritant. Heat-pressured polymerization generally reduces residual monomer compared with cold- or chemically-cured acrylic [2]. While metal parts (stainless steel wires) can release trace ions, this review focuses on the polymer component. PMMA does not contain BPA or estrogenic additives, but residual monomers and minor components such as hydroquinone or peroxide byproducts may contribute to cytotoxic effects [9]. Modifications of acrylic with bioactive glasses like Biomin C or S53P4 can release calcium and phosphate ions under acidic conditions, potentially aiding remineralization [10].

Essix retainers (Thermoplastics)

Essix retainers, introduced by Sheridan in the 1990s, are clear, vacuum-formed appliances made by molding thin thermoplastic sheets to the patient's dentition [11]. Commonly used polymers include PET-G (polyethylene terephthalate glycol-modified), polypropylene, and thermoplastic polyurethanes (TPU), along with proprietary blends such as Invisalign's SmartTrack. These materials are typically marketed as medical-grade and BPA-free [4]. However, some polyester-based sheets may contain additives for clarity or durability that are bisphenol derivatives [12]. PET-G itself is BPA-free, but certain polycarbonate or co-polyester formulations may still contain trace BPA. Modern thermoplastic retainers, such as Duran®, Essix ACE®, and Zendura® FLX, have largely eliminated BPA, yet trace amounts of other bisphenol analogs (e.g., BPS) or estrogen-mimicking

compounds may persist depending on manufacturing processes [13]. Even BPA-free plastics can release other xenoestrogens, including phthalates or degradation byproducts. Compared with freshly cured PMMA, thermoplastics generally contain fewer leachable substances due to industrial polymerization, but residual oligomers, plasticizers, or stabilizers may still diffuse into saliva, particularly in new appliances or under mechanical stress.

3D-Printed retainers

A newer category involves directly 3D-printed retainers made from photopolymer resins. Though less widely used clinically than Hawley or Essix retainers, they offer potential for customized fabrication. Many 3D-printed dental resins contain methacrylate-based oligomers, sometimes derived from bisphenol-A glycidyl dimethacrylate. Insufficient post-curing or cleaning can result in significant monomer leaching. Initial studies suggest that certain 3D-printed retainer materials may have higher cytotoxicity and genotoxicity than thermoplastic sheets [14]. Additionally, investigations into chemical leaching from clear aligner systems have revealed multiple released compounds, further highlighting biocompatibility concerns [7].

Table 1. Material Composition, Leachable Substances, Biocompatibility, and Cytotoxicity of Removable Orthodontic Retainer Materials

Retainer Material	Material Composition	Potential Leachable Components	Key Biocompatibility Factors	Relative Cytotoxicity
Hawley Retainer (PMMA + Wire)	Acrylic base of polymerized methyl methacrylate (PMMA) with stainless steel wire clasps; typically cold-cured or heat-cured.	Unreacted methyl methacrylate (MMA) monomers, initiator residues (e.g., peroxides), or pigments. PMMA is free of BPA.	Residual monomers may irritate or harm oral tissues [8]. Cold-cured acrylics release more MMA, increasing toxicity compared to heat-cured [2]. Rare allergic responses noted; generally safe when fully cured.	Moderate
Essix Retainer (PET-G)	Thermoformed polyethylene terephthalate glycol (PET-G), a transparent petroleum-based polymer, ~1 mm thick.	Small amounts of ethylene glycol, terephthalate oligomers, UV stabilizers, or colorants. Typically BPA-free, but some additives may derive from BPA [12].	Highly stable with minimal cytotoxicity in lab tests. One study detected BPA in saliva from PET-G retainers, possibly from additives [2]. Low risk of mucosal irritation.	Low
Essix Retainer (Polypropylene/Polyethylene)	Vacuum-formed retainers made from polypropylene or polyethylene blends, which are flexible thermoplastics.	Very few leachables, as polyolefins are stable. No BPA or phthalates typically present.	Extremely low cytotoxicity. Lower rigidity may promote bacterial plaque buildup. Biocompatibility is excellent; issues are mainly mechanical (e.g., wear).	Very Low
Clear Aligner-Type (Polyurethane, e.g., Invisalign)	Multilayer thermoplastic polyurethane (TPU), often proprietary (e.g., Invisalign's SmartTrack).	Urethane degradation products (e.g., 1,4-butanediol) under harsh conditions. Designed without	Shows mild cytotoxicity in vitro, similar to PET-G [13]. Generally safe with low irritation risk.	Low

		BPA or phthalates [13].		
3D-Printed Retainer (Acrylate Resin)	Photopolymerized resins, such as urethane dimethacrylate, custom-printed and post-cured.	Unpolymerized monomers or photoinitiator residues if curing is incomplete; possible BPA derivatives in some resins.	Safe if thoroughly cured and cleaned, but variability exists. Some resins may release compounds causing higher cytotoxicity or estrogenic effects compared to thermoplastics [14]. Proper post-processing is essential.	Moderate to High*

*Varies based on curing thoroughness and residual monomer content.

Cytotoxicity of retainer materials on oral cells

The safety of removable retainers is closely linked to their potential to harm oral cells, as these devices remain in contact with the palate and mucosa for prolonged periods. Even subtle cytotoxic effects could lead to mucosal irritation or influence cellular turnover. Researchers have explored this using laboratory cell cultures, animal models, and clinical biomarker assessments in retainer users. For this review, 38 in vitro studies from 2015 to 2025 were screened. Eligible studies measured cell viability using established assays (such as MTT, LDH, or live/dead staining) on human oral or mammalian cells, tested materials relevant to removable retainers (PMMA, PETG, polyurethane, or 3D-printed resins), and reported quantitative outcomes. Studies focusing only on fixed appliances, lacking original data, or not describing extraction methods were excluded. **Table 2** highlights the most transparent studies, showcasing the range of cytotoxic responses across different retainer materials.

In Vitro evidence

In vitro investigations consistently show that most retainer materials exert limited cytotoxicity. Metabolic assays on gingival fibroblasts or oral epithelial cells often reveal only minor reductions in viability, generally remaining above biocompatibility thresholds [6]. Across multiple studies, cell survival typically stays between 70% and 90%, even under maximal extraction conditions [15, 16]. Thermoplastic retainers, including PETG- or polyurethane-based sheets, tend to be less cytotoxic than freshly cured PMMA [17]. For instance, a comparative analysis of four popular thermoplastics—Duran®, Biolon®, Zendura®, and SmartTrack—found only slight decreases in gingival fibroblast viability [15]. Material composition appears to play a role: polycarbonate-based thermoplastics often release more monomer and show higher cytotoxicity than PETG or multilayer polyurethane under laboratory conditions [16, 18].

3D-printed retainers, an emerging category, have been scrutinized for potential cytotoxicity. Al Mortadi *et al.* [19] tested a photopolymer resin (Dental LT) and an ethanol-based resin (E-Guard) on human gingival fibroblasts. Both materials exhibited mild cytotoxic effects initially, with cell viability improving over time, suggesting that residual leachables diminish or cells adapt. Early observations indicate that some 3D-printed resins may reduce cell viability slightly more than thermoplastics such as SmartTrack. For example, E-Guard showed the largest initial reduction on day one, while SmartTrack consistently maintained over 90% cell viability [15, 20, 21]. Differences in post-processing and soaking of 3D-printed resins also influenced cytotoxicity, with cell survival improving by day seven across all materials. These results underscore the importance of thorough post-curing and short-term rinsing to limit initial leachable release from 3D-printed retainers [19, 21].

Newer retainer materials such as polyether-ether-ketone (PEEK) have emerged as alternatives to traditional metal wires and plates, offering excellent compatibility with oral tissues and very low cytotoxicity. As a strong, inert polymer, PEEK has a long history of safe use in medical devices [22]. Clinical applications in fixed lingual retainers report no adverse reactions, while in vitro studies show minimal effects on fibroblast viability, reflecting its chemical stability [23]. PEEK provides an appealing metal-free option that is both aesthetic and MRI-safe, producing negligible inflammatory or cytotoxic responses compared with conventional stainless-steel wires [23]. Fiber-reinforced composite (FRC) retainers, another tooth-colored alternative, present some biocompatibility concerns. Composites reinforced with glass or quartz fibers can release resin components, and certain FRC devices have been shown to reduce fibroblast survival, particularly when the resin is exposed or under acidic conditions

[24]. Experimental data suggest that incomplete encapsulation or low pH environments increase monomer leaching from these composites. Interestingly, under acidic conditions mimicking cariogenic challenges, traditional multistrand metal retainers sometimes exhibit higher cytotoxicity than FRCs, likely due to release of metal ions such as nickel or chromium [25]. Corrosion of stainless steel or NiTi wires in acidic saliva can generate cytotoxic ions, highlighting that even metallic retainers are not completely inert. Overall, both polymeric and metallic retainers may release substances that affect oral cells, although the extent of cytotoxicity is generally low.

Table 2. In vitro studies assessing the cytotoxic effects of orthodontic retainer materials using cell viability assays (e.g., MTT, live/dead staining) in oral fibroblasts and epithelial cells

Study (Year)	Retainer Material(s) Evaluated	Model/Cells	Key Findings on Cytotoxicity	Study Design
Martina *et al.* [15]	Four thermoplastic materials: Duran (PETG), Biolon (polycarbonate), Zendura (polyurethane), SmartTrack (polyurethane multilayer)	HGF cells; MTT assay	All materials exhibited minimal cytotoxicity (cell viability > 80%). Biolon was the most cytotoxic, followed by Zendura and SmartTrack, while Duran showed the least impact. Thermoforming did not remove cytotoxic components and, in some instances, slightly increased toxicity.	In vitro
Campobasso *et al.* [25]	3D-printed aligners (Tera Harz TC-85DAC resin, Graphy, Korea), post-cured via two methods: P1: Tera Harz Cure system with nitrogen (14 min) P2: Form Cure machine (30 min per side, total 60 min)	MC3T3-E1 mouse pre-osteoblasts; MTT assay in DMEM, measured at days 7 and 14	P1 (nitrogen curing): Non-cytotoxic, with cell viability >100% (107.1% ± 17.5% on day 7, 106.7% ± 18.4% on day 14), comparable or superior to controls. P2 (Form Cure): Moderately cytotoxic, with reduced viability (59.8% ± 10.1% on day 7, 47.1% ± 20.6% on day 14), significantly less biocompatible than P1 and controls ($p < 0.001$). Conclusion: Post-curing method affects cytotoxicity; nitrogen curing (P1) is highly biocompatible, while P2 may leave residual monomers causing toxicity.	In vitro
Nemec *et al.* [21]	Invisalign SmartTrack (polyurethane)—inner vs. outer surfaces	Human oral keratinocytes; live/dead staining, PCR	No significant cytotoxicity observed; minimal dead cells on aligner surfaces. Cell proliferation was slightly reduced compared to plastic controls, suggesting a mild inhibitory effect. Aligner-contact cells showed increased expression of inflammatory and barrier-function genes. Conclusion: SmartTrack is non-cytotoxic but may influence cell behavior, promoting a pro-inflammatory gene profile.	In vitro
Al Naqbi *et al.* [26]	Vivera® retainers (polyurethane thermoplastic, Invisalign®-related), tested as-received and after clinical use	MCF-7 cells (estrogen receptor-positive breast adenocarcinoma for estrogenicity), MDA-MB-231 cells (estrogen receptor-negative control), NIH/3T3 mouse fibroblasts (general cytotoxicity)	No cytotoxicity observed in fibroblasts for eluates from either as-received or used retainers. No estrogen receptor-mediated proliferation in MCF-7 cells or proliferative effects in MDA-MB-231 cells for either condition. Conclusion: Vivera® retainers show no acute cytotoxicity or estrogenicity, indicating good short-term biocompatibility.	In vitro

Overall, research from the past ten years indicates that contemporary orthodontic retainer materials are generally well-tolerated, showing only minor cytotoxic effects in vitro and transient cellular stress in vivo [5, 6]. Nevertheless, variations exist between different material types and brands. Novel materials such as PEEK appear particularly promising, demonstrating minimal cytotoxicity due to their chemical inertness and stability [23].

In Vivo and clinical evidence

Human studies conducted over the last decade have not reported severe cytotoxic reactions to retainer materials, although subtle biological effects have been observed. One notable randomized controlled trial compared patients wearing either a Hawley acrylic retainer or a vacuum-formed Essix retainer, assessing salivary biomarkers of DNA damage (8-hydroxy-2′-deoxyguanosine, 8-OHdG) and antioxidant response (Nrf2, Keap1), alongside cytological analysis of buccal mucosa for nuclear abnormalities. The Hawley group exhibited elevated 8-OHdG levels after one and three months, suggesting oxidative DNA stress likely linked to leached monomers or additives from the acrylic. In contrast, the Essix group showed no increase in 8-OHdG, with slight decreases over time.

Cytological evaluation, however, revealed that Essix users had a higher frequency of micronuclei and other nuclear irregularities in cheek epithelial cells after two to three weeks than the Hawley group. Both types of retainers increased cellular turnover and induced minor nuclear alterations relative to baseline. These findings suggest that acrylic retainers may contribute more to systemic oxidative stress via leachables, whereas thermoplastic retainers may exert localized mechanical or frictional stress, leading to epithelial nuclear changes [5].

Estrogenic potential and BPA release

A major public concern regarding dental plastics is their potential to act as endocrine disruptors by releasing estrogen-mimicking compounds, most notably Bisphenol-A (BPA). BPA, a xenoestrogen present in polycarbonate plastics and epoxy resins, can bind estrogen receptors—albeit with lower affinity than estradiol—and has been linked to developmental and reproductive toxicity [27]. Given that retainers and aligners are continuously worn in the oral cavity, there is potential for BPA or related compounds to leach into saliva. The clinical significance of this exposure, particularly regarding systemic endocrine effects, remains uncertain.

BPA Release: Laboratory vs. clinical findings

Early laboratory studies often detected little to no BPA release from clear aligners, with concentrations typically below detection limits (<1 ng/mL). For example, Schuster *et al.* [28] and Gracco *et al.* [29] reported negligible BPA or monomer release from Invisalign aligners soaked in artificial saliva. More recent work by Katras *et al.* [30] evaluated multiple brands, including SmileDirectClub, Invisalign, and Essix ACE, in various media (saliva, gastric fluid, ethanol) and found that any BPA release occurred mainly within the first 24 hours, with levels well below regulatory safety thresholds. Most studies employed high-performance liquid chromatography or mass spectrometry, confirming that new aligners release minimal detectable BPA [6]. **Table 3** summarizes in vitro findings on BPA release and the associated estrogenic potential of orthodontic retainer materials.

Laboratory studies have examined whether compounds leached from orthodontic retainers can activate estrogen-sensitive cells. Two independent investigations [18, 26] employed the MCF-7 breast cancer cell proliferation assay, which serves as a proxy for estrogen receptor activity, to test various aligner and retainer materials. Both studies reported no estrogenic effects: exposure to Invisalign® or Vivera® retainers did not stimulate MCF-7 cell proliferation above baseline levels. Positive controls, such as 17β-estradiol or BPA, triggered robust cell growth, while the retainer samples behaved similarly to negative controls. Estrogen-insensitive cell lines (MDA-MB-231) also showed no response, confirming that the materials themselves lacked estrogen receptor-mediated activity. These findings correspond with chemical analyses demonstrating minimal BPA release from contemporary orthodontic polymers. Advanced detection methods, including GC-MS and LC-MS/MS, failed to identify measurable BPA or related monomers in new aligner extractions or artificial saliva over extended testing periods from 2016 to 2021 [6,18, 26].

Clinical evidence presents a slightly more cautious picture. Raghavan *et al.* [2] conducted a randomized trial measuring salivary BPA in 45 patients assigned to three groups: (1) Essix vacuum-formed retainers, (2) heat-cured Hawley retainers, and (3) cold-cure Hawley retainers. Saliva samples were collected pre-insertion and at 1

hour, 1 week, and 1 month post-insertion. All groups exhibited a significant rise in salivary BPA following appliance placement ($p \leq 0.05$) [2].

A subsequent trial by Nanjannavar *et al.* [12] evaluated a practical mitigation strategy: pre-soaking retainers in water at 37 °C for 24 hours before use. This simple step dramatically reduced salivary BPA levels: at 1 hour, pre-soaked retainers released ~0.07 ppm BPA versus 0.33 ppm from unsoaked devices, with levels approaching zero at 1 and 3 weeks. These results suggest that overnight water immersion can effectively minimize patient exposure to leachable BPA [12].

Regulatory perspectives on BPA exposure have evolved substantially. While earlier guidelines from the U.S. FDA and EPA allowed tolerable daily intakes of ~50 µg/kg body weight/day, newer evidence indicates that even very low doses may produce subtle endocrine effects. Animal and epidemiological studies link chronic low-level BPA exposure to hormonal and immune alterations, prompting authorities such as the European Food Safety Authority to drastically lower safe intake limits to nanogram/kg levels between 2021 and 2023 [31, 32]. Although the trace amounts of BPA from orthodontic appliances remain far below these thresholds, precautionary assessment is increasingly emphasized. To date, no direct hormonal disorders or systemic endocrine effects have been associated with retainer-derived BPA. Industry trends, highlighted in a review by Hassan *et al.* [33], show growing adoption of BPA-free adhesives, aligner materials, and smart polymers that combine mechanical performance, antimicrobial properties, and endocrine safety.

Table 3. BPA release levels and estrogenic effects of orthodontic retainer materials, based on in vitro studies, chemical analyses (e.g., HPLC, LC-MS/MS), and clinical trials

Study (Year)	Materials and Conditions	BPA Release Findings	Estrogenic Effect	Study Design
Katras *et al.*, 2021 [30]	SmileDirectClub, Invisalign, and Essix ACE aligners were immersed in artificial saliva, simulated gastric fluid, and 20% ethanol, with samples collected at 0, 1, 2, 6, 10, and 20 days.	All aligners exhibited minimal BPA release, primarily occurring during the first 24 hours as an initial "burst." Throughout the testing period, BPA concentrations stayed under 5 µg/L in saliva and consistently below the EU safety limits. No notable differences in BPA release were observed among the three brands or between saliva and gastric fluids.	Although no direct tests for estrogenic activity were conducted, the BPA concentrations were well below levels of toxicological concern, making endocrine effects unlikely; the authors emphasize that these amounts remain "under established safety limits for adult patients."	In vitro
Intissar *et al.*, 2020 [34]	Invisalign® aligners made of polyurethane, comparing new versus 2-week-old aligners, were stored in artificial saliva for up to 8 weeks.	HPLC analysis showed no detectable BPA in any aligner extract, with a detection limit of <5 ppb, even after 2 weeks of intraoral use and extended storage in saliva, indicating that the aligners remained chemically stable regarding BPA over the 8-week period.	Not applicable, as only chemical analysis was performed; results indicate that properly cured aligner polymers do not release detectable BPA, and therefore no estrogenic effect is anticipated.	In vitro
Raghavan *et al.*, 2017 [2]	Forty-five patients wore one of the following retainers: (1) vacuum-formed Essix (PETG), (2) heat-cured acrylic Hawley, or (3) chemically cured acrylic Hawley, with salivary BPA levels assessed prior to and	After one month of retainer use, salivary BPA rose in all groups, with variations by retainer type: chemically cured Hawley showed the highest increase (~6–8 µg/L on average), vacuum-formed Essix had a moderate rise (~2–3 µg/L), and heat-cured Hawley exhibited	No signs of endocrine disruption were observed in any group; although BPA was detectable, concentrations remained below levels associated with hormonal effects in humans, and the authors recommend using heat-cured acrylic or BPA-	In vitro

	one month after retainer insertion.	the smallest change (~1 µg/L or less), with all levels remaining in the parts-per-billion range.	free materials to reduce exposure.	
Iliadi *et al.*, 2017 [35]	An experimental BPA-free orthodontic adhesive was compared with a conventional Bis-GMA adhesive; it contains no BPA and employs an alternative monomer, phenyl-propanediol dimethacrylate, for bonding fixed retainers.	By design, the experimental adhesive does not release BPA, as it contains no BPA or bisphenol derivatives; unlike conventional adhesives that may release trace BPA from Bis-DMA degradation, BPA was undetectable in its eluates.	The BPA-free adhesive contained no estrogenic compounds and demonstrated no estrogenic or cytotoxic effects in vitro, while providing bond strength comparable to conventional adhesives, indicating its suitability for clinical application and reflecting ongoing efforts to remove BPA from orthodontic materials to minimize endocrine risks.	In vitro
Eliades *et al.*, 2009 [18]	Three sets of Invisalign aligners were submerged in normal saline at 37 °C for two months, and the resulting eluates were tested at concentrations of 5%, 10%, and 20%.	Three sets of Invisalign aligners were incubated in normal saline at 37 °C for two months, with the resulting eluates evaluated at 5%, 10%, and 20% concentrations.	Three sets of Invisalign aligners were soaked in normal saline at 37 °C for two months, and the eluates were analyzed at concentrations of 5%, 10%, and 20%.	In vitro

Thermoplastic retainers can release small amounts of BPA into saliva, particularly during the initial period of wear, though simple interventions—such as pre-soaking appliances or selecting BPA-free materials—can markedly reduce this exposure. Heat-cured acrylic retainers generally release minimal to no BPA, aside from potential external contamination, whereas some thermoplastic devices exhibit short-term BPA leaching. In response, many manufacturers now offer BPA-free aligners, yet clinicians should remain cautious about possible trace chemical release.

Estrogenic potential of leached chemicals

Detecting BPA in retainer materials is straightforward, but demonstrating a clear estrogenic effect is more complex. Laboratory assays using estrogen-sensitive cells have suggested that leached BPA or related compounds are present at levels too low to activate estrogen receptors in vitro [6]. Nevertheless, very low-dose endocrine effects in vivo remain a theoretical concern due to potential non-linear dose–response relationships. Chronic exposure—even at low BPA levels—might subtly affect development or hormone regulation. To date, no clinical studies have conclusively linked retainer use to systemic endocrine changes, largely due to the challenges of controlling such studies. Data from other dental materials, such as sealants and composites, indicate that transient BPA spikes occur after placement but normalize within 24–48 hours, with levels considered insufficient to cause harm [27]. The American Dental Association similarly notes that trace BPA released from newly polymerized resins produces only a temporary, minor increase in saliva or urine [27], consistent with retainer observations.

Other compounds, including bisphenol S (BPS) or phthalate plasticizers, may also pose estrogenic or anti-androgenic risks. Most modern orthodontic appliances are now free of phthalates like DEHP, though BPS has sometimes replaced BPA in “BPA-free” plastics, and its safety is still debated. No studies have yet examined BPS leaching specifically from retainers. While BPA has been widely studied, references to BPS and phthalates are limited, serving only to note potential, insufficiently researched alternatives.

Overall, current evidence indicates that typical use of Hawley or Essix retainers does not produce noticeable estrogenic effects. Detectable BPA release can occur, particularly with some thermoplastic materials, but levels are generally low. Both laboratory assays (Yazdi *et al.* [6]) and clinical observations suggest minimal impact on hormonal activity. Given the frequent and long-term use of these appliances—especially in adolescents—ongoing

monitoring of cumulative exposure is advisable. Simple measures, such as pre-rinsing or soaking new plastic retainers and choosing BPA-free options, remain sensible strategies to further minimize endocrine risks [12].

Cellular mechanisms of damage and estrogen action

Oxidative stress and DNA injury

Acrylic retainers may release residual monomers, such as MMA, into saliva and, to a minor extent, the systemic circulation [36]. These monomers can undergo metabolic or redox reactions that generate reactive oxygen species (ROS). ROS can damage DNA, lipids, and proteins within oral tissues [37]. For example, elevated salivary 8-OHdG in Hawley retainer users [8] indicates oxidative DNA damage, as 8-OHdG forms when guanine bases are oxidized. While cellular repair mechanisms typically address such damage, sustained elevations suggest chronic ROS exposure. In contrast, Essix users in the same study did not show increased 8-OHdG, possibly due to reduced ROS generation or more effective protective cellular responses.

The body counters oxidative stress largely through the Nrf2/Keap1 signaling system. Under oxidative conditions, Nrf2 is released from Keap1, moves into the nucleus, and triggers transcription of antioxidant genes. In the study by Gunel *et al.*, measurements of Nrf2 and Keap1 showed no significant differences between Hawley and Essix retainer users [5], suggesting either that the oxidative challenge from these appliances was mild or transient, or that both groups mounted similar antioxidant defenses.

Beyond oxidative mechanisms, direct cell damage can result from chemical leachates. Acrylic monomers like MMA are small, reactive molecules that can compromise cellular membranes. In vitro, high concentrations of MMA or certain additives from aligners have been shown to depolarize membranes and cause cell lysis. Saliva partially counteracts this by diluting and binding monomers [6]. Despite this, genotoxic effects have been reported in patients, such as an increased number of micronuclei [5]. These structures form when chromosomal fragments or entire chromosomes fail to integrate into daughter nuclei during cell division, often due to DNA breaks or spindle disruption caused by chemical exposure. Notably, elevated micronuclei counts observed after 2–3 weeks of Essix retainer use indicate an acute genotoxic response, potentially linked to early chemical release or mechanical stress from retainer pressure on the mucosa [8].

In summary, cytotoxic effects from retainers appear to arise from both chemical and mechanical stressors. MMA released from PMMA is likely a major contributor to ROS formation and DNA oxidation (evidenced by increased 8-OHdG). Thermoplastic appliances, though releasing fewer monomers, may still shed other compounds or microscopic particles capable of stressing cells. Additionally, mechanical pressure from retainers could produce mild ischemia or tissue turnover, indirectly promoting oxidative stress. Collectively, these observations demonstrate a measurable, albeit limited, cellular response to retainer use.

Estrogen receptor activation

Chemicals like BPA can interact with estrogen receptors (ERα and ERβ) in various tissues. Within the oral cavity, ERs are present in periodontal ligament fibroblasts and alveolar bone cells, though the epithelium is not a primary target. If absorbed systemically, BPA could reach distant endocrine organs. Binding to ERs allows BPA to mimic estrogen and influence gene transcription. Toxicology studies of chronic low-dose BPA exposure have shown effects on reproductive organ development, metabolism, and behavior [27], but these involve far higher and longer exposures than those associated with retainers.

Locally, estrogenic signaling may theoretically affect tissue repair or inflammation. While BPA from a retainer could be absorbed through oral mucosa, there is currently no direct evidence that it alters gingival health or alveolar bone. In vitro data suggest BPA can modulate inflammatory pathways, yet clinical studies have not demonstrated such effects in humans. The absence of a response in MCF-7 cells exposed to aligner extracts [6] indicates minimal estrogenic potential. Moreover, BPA is rapidly cleared from the human body, so any transient systemic increase following retainer insertion is unlikely to sustain receptor activation. Estrogenic effects can follow non-linear dose–response patterns, where very low doses sometimes produce disproportionate effects [27].

Taken together, while orthodontic retainers can release compounds capable of engaging estrogen receptors, the concentrations observed are too low to cause meaningful estrogenic responses in vivo. The mechanistic pathway—xenoestrogen binding ER → gene regulation—is understood, but modern appliance materials appear to only minimally trigger it. Continued attention to material composition, such as avoiding Bis-DMA that can degrade into BPA [27], remains important, particularly for long-term appliance use in younger patients.

Clinical relevance of prolonged retainer use

A primary clinical concern is whether the potential cytotoxic or estrogenic effects of orthodontic retainers translate into actual health impacts over time. Many patients wear retainers nightly for years, and in some cases—such as individuals with hypodontia—removable appliances with prosthetic teeth may be used daily well into adulthood. Therefore, evaluating the long-term biological implications of continuous exposure to retainer materials is important.

- Oral Tissue Responses: Most users tolerate both Hawley and Essix retainers without significant adverse effects. Nevertheless, sporadic mucosal reactions have been reported, including:
- Early discomfort: Patients frequently report gum or palate soreness when first using a retainer. These symptoms usually resolve as tissues acclimate or residual monomers dissipate. Some users of aligners or retainers describe transient changes in taste or mild oral discomfort during the initial days of wear, likely reflecting the early release of trace chemicals [30].
- Allergic reactions or ulceration: A small number of individuals may develop hypersensitivity to PMMA or other plastic components, manifesting as localized redness, ulcers, or generalized symptoms such as lip swelling and itching. Acrylic sensitivity is well-known in dentistry, particularly among denture wearers exposed to residual MMA. In such cases, switching to alternative materials, such as metal-based retainers or hypoallergenic linings, may be necessary [38].
- Taste changes and xerostomia: Some patients notice a plastic or chemical taste upon initial use. Reports of dry mouth have also been documented [6], though it is unclear whether this results from the chemical composition of the appliance or simply its physical presence in the oral cavity. Reduced saliva flow may exacerbate cytotoxic effects because saliva normally helps neutralize irritants.
- Gingival and periodontal effects: Retainers that fit poorly or are inadequately cleaned can contribute to gingival inflammation. While this is not a direct chemical toxicity issue, sustained inflammation can increase oxidative stress in oral tissues. Removable Essix retainers, typically worn only at night after the initial period, are generally associated with better periodontal outcomes than fixed appliances, owing to easier removal and cleaning [39]. Adherence to proper hygiene practices largely mitigates material-related risks.

A comprehensive summary of removable orthodontic retainers and their associated biological considerations is presented in **Table 4**.

Table 4. Summary of removable orthodontic retainers, their material composition, and associated biological concerns (cytotoxic or endocrine effects) based on in vitro and clinical data

Retainer Type	Material Composition	Key Monomers / Additives	Potential Biological Concerns
Hawley Retainer	PMMA with embedded stainless steel wire	Residual methyl methacrylate (MMA)	Cytotoxic effects, allergic reactions (e.g., contact stomatitis), leaching of MMA
Essix (C+) Retainer	PVC-based thermoplastic	Phthalates, residual vinyl chloride	Possible endocrine disruption, release of plasticizers
Essix ACE Retainer	Copolyester (PETG-based)	BPA, PETG oligomers	Low-level BPA leaching, minor cytotoxicity
Modern thermoplastic retainers (e.g., Duran®, Essix ACE®, Zendura® FLX)	Polyurethane	BPA, BPS	Potential estrogenic effects in vitro, generally low cytotoxicity
3D-printed retainers (acrylate resin)	Proprietary multilayer polyurethane	BPA analogs (e.g., BPS, BPF?)	Uncertain risk; depends on material aging and wear due to proprietary formulation

Regulatory frameworks and international guidelines

Evaluating the biological safety of dental materials, including cytotoxic and endocrine-disrupting potential, involves both rigorous scientific testing and adherence to regulatory requirements. In both the United States and the European Union, specific frameworks guide the approval and monitoring of removable orthodontic appliances, such as retainers.

United States (FDA)

In the U.S., removable retainers are considered Class II medical devices, requiring a 510(k) submission to show that they are substantially equivalent to legally marketed devices [40]. As part of safety assessment, manufacturers must follow ISO 10993 standards for biocompatibility testing [41]. This includes ISO 10993-5 for cytotoxicity, ISO 10993-10 for irritation and sensitization, and other tests dictated by the material's intended intraoral contact duration and anatomical site [41].

For retainers intended for extended contact with oral tissues, adherence to ISO 10993 ensures that acute or chronic toxicity, genotoxicity, and tissue irritation are adequately evaluated. For example, materials like Invisalign's SmartTrack have reportedly fulfilled the full ISO testing requirements for mucosal applications.

Regarding chemical leachates such as bisphenol A (BPA), the FDA has not imposed specific limits for dental devices. Unlike baby bottles, which have banned BPA since 2012, dental appliances are regulated using a risk-based approach. Current guidance from the FDA and the American Dental Association does not discourage the use of BPA-containing dental materials [42]. Trace amounts of BPA or degradation products may be present, but exposure from orthodontic appliances is usually low and transient [43]. Manufacturers have often chosen BPA-free materials voluntarily, driven by consumer preference rather than regulatory mandates, though minimizing exposure is still recommended, particularly for sensitive populations.

European Union (EU)

The EU enforces stricter rules regarding potentially hazardous substances in medical devices. Regulation (EU) 2017/745 (MDR), fully applied since 2021, requires manufacturers to assess and report the presence of carcinogenic, mutagenic, reprotoxic (CMR), or endocrine-disrupting compounds. Any component exceeding 0.1% by weight of a substance classified as of very high concern (SVHC) under REACH must undergo risk justification, labeling, and a benefit-risk analysis [44].

BPA is designated as an SVHC because of its endocrine-disrupting properties. Although the levels in orthodontic retainers are typically well below the regulatory threshold, MDR compliance has motivated manufacturers to eliminate BPA from materials to reduce both regulatory complexity and potential consumer resistance.

Material Specifications and CE Marking

Retainer materials must also satisfy material-specific standards. ISO 20795-2:2013 ("Dentistry—Base polymers—Part 2: Orthodontic base polymers"), implemented in the EU as EN ISO 20795-2, defines essential physical properties such as flexural strength and color stability for acrylics and other polymeric components [45]. Limiting residual monomer content indirectly contributes to biocompatibility; for example, unreacted MMA in denture base polymers is generally restricted to ≤2%.

CE marking requires demonstration of conformity with ISO 20795-2 as well as ISO 10993, particularly for appliances intended for prolonged intraoral use. Together, these standards ensure that retainers meet mechanical durability and biological safety criteria, providing confidence for both clinicians and patients.

ISO 10993 Biocompatibility [46]

Both FDA and EU regulations rely heavily on ISO 10993 standards to evaluate the biocompatibility of dental appliances. For retainers intended to remain in contact with oral tissues for extended periods (more than 30 days), testing typically covers cytotoxicity, short- and long-term systemic effects, mucosal irritation, and, if indicated, genotoxic potential. Additional evaluations are recommended when new chemical formulations are introduced or if there is suspicion of endocrine-disrupting activity.

Although isolated studies have observed minor cytotoxic or estrogen-like responses from some dental polymers, these effects fall below the safety limits defined in ISO 10993 [46]. Consequently, meeting these standards is generally taken as evidence that the materials are safe for clinical use under current regulatory expectations.

Labeling and product information

In the EU, devices containing substances of very high concern (SVHCs) above 0.1% by weight must clearly disclose this on product labels and technical files [47]. Information provided in Instructions for Use (IFUs) and Safety Data Sheets (SDSs) should indicate the presence—or confirm the absence—of compounds such as BPA or phthalates. Manufacturers increasingly highlight "BPA-free" or "phthalate-free" claims in labeling and marketing materials. In contrast, in the U.S., such declarations are typically voluntary unless concerning recognized allergens like latex [43].

Professional and clinical guidance

Dental associations and professional guidelines have begun acknowledging the potential systemic effects of polymer degradation products. Recent literature emphasizes ongoing improvements in appliance materials—such as direct 3D printing of aligners and enhanced monitoring of monomer release—to further reduce patient exposure to chemical residues [48, 49].

Current international standards provide a robust framework for ensuring the safety of orthodontic retainers. No commercially used appliances have been prohibited by U.S. or EU authorities, indicating that chemical leaching and cytotoxicity observed in practice are within acceptable limits. The EU MDR requirement to disclose SVHCs above 0.1% continues to incentivize manufacturers to adopt cleaner formulations.

Clinicians should remain informed regarding the composition of orthodontic materials and consider BPA-free or hypoallergenic alternatives for sensitive patients. While retainers generally have a favorable risk-benefit profile, evolving regulations and public awareness make ongoing material refinement and compliance with updated standards essential.

One health and environmental perspective

The assessment of orthodontic retainer materials has recently shifted from solely evaluating patient safety to examining their broader ecological and public health consequences. Under the One Health lens, human, animal, and environmental well-being are interconnected, making the environmental footprint of polymer-based devices an emerging concern [50, 51].

Microplastics and nanoparticles

Mechanical wear and chemical exposure cause polymeric retainers to fragment, releasing micro- and nanoplastics (MNPs). Ceccarelli *et al.* observed MNPs detaching from aligners after a simulated one-week use [52], while Barile *et al.* [39] reported shedding of polymer particles from different aligner brands subjected to repeated mechanical loading. Most fragments are tens to hundreds of micrometers in size, but nanoscale particles (<1 μm) could potentially cross epithelial barriers, as evidenced by their detection in human placenta and bloodstream in unrelated studies [53]. Though acute effects appear minor, the long-term impact of continuous low-level exposure, particularly in young patients, remains uncertain. Research is increasingly quantifying both chemical leaching and microplastic release from orthodontic polymers as clear-aligner use grows worldwide [49, 51].

Chemical leachates and ecological effects

Retainers can also release bisphenols and other additives into the environment. While emissions from individual devices are small, frequent replacement during treatment and retention cumulatively increases environmental loading. Persistent monomers like BPA can leach from landfills into soil and water, and even extremely low concentrations can interfere with endocrine systems in aquatic species, causing feminization and developmental changes. Orthodontic appliances contribute modestly to total BPA output, but their chemical resilience and disposal frequency make them notable sources. As noted by [53], their mixed material composition and biohazard classification exclude them from recycling programs, limiting circular economy integration.

Preventive material design within one health

Replacing hazardous chemicals in orthodontic polymers improves safety for patients, clinicians, and ecosystems simultaneously. BPA- and phthalate-free materials reduce chemical exposure, while stable polymers minimize environmental contamination through leachate or wastewater. Such strategies align with sustainable orthodontic practices emphasizing material efficiency, toxicity reduction, and responsible disposal [54, 55]. Industry initiatives, such as the 2022 UK pilot by Align Technology, are testing post-use collection of aligners for energy recovery or downcycling, marking early steps toward embedding sustainability into clinical workflows.

Eco-Friendly material innovations

Biopolymers are being developed as alternatives to conventional plastics. Thermoformable cellulose acetate aligners show partial biodegradability and compatibility with antimicrobial additives. Cinnamaldehyde-loaded cellulose aligners inhibited biofilm formation without cytotoxicity in vitro [56, 57]. Other composites incorporating nanohydroxyapatite and quaternary ammonium compounds demonstrated antibacterial and remineralizing properties while preserving cell viability [58]. However, their mechanical performance, long-term

biocompatibility, and potential nanoparticle release during wear or disposal require further investigation, and data on their environmental fate are still limited.

Sustainable clinical practices

Reducing orthodontics' environmental footprint involves optimizing both materials and procedures. Digital impressions eliminate the need for disposable trays, and precise 3D printing reduces resin waste. Durable materials such as PEEK or laminated polymers may extend retainer lifespan, lowering consumption and resource use. Life-cycle assessment principles support balancing clinical effectiveness with environmental responsibility [55]. Achieving this balance also requires reconciling sustainability with patient preferences, such as frequent replacement of thin retainers.

Regulatory and policy considerations

Although orthodontic devices are not directly regulated for environmental impact, broader legislation may influence material choices. EU Regulation 2017/745 requires justification and labeling for devices containing >0.1% substances of very high concern (SVHCs), including BPA. ISO 10993 standards remain central for biocompatibility testing, but there is a growing regulatory emphasis on incorporating environmental and life-cycle considerations [44, 46].

Conclusion

Applying the One Health perspective places orthodontic materials within the broader context of interconnected human and environmental health. Although current polymers are generally safe for intraoral use, their prolonged environmental persistence and chemical leaching raise important concerns. Newer materials show promise for improved safety and sustainability, yet achieving an optimal balance between clinical effectiveness and ecological responsibility remains essential.

The evolution of orthodontic biomaterials is increasingly focused on combining functional performance with environmental stewardship. Successfully advancing this goal will require coordinated collaboration among scientists, manufacturers, and regulatory bodies to ensure that innovations support both oral health and the health of the planet.

Environmental implications

Removable retainers and clear aligners raise considerations beyond patient safety, extending to environmental health due to their polymeric composition and eventual contribution to plastic waste. Recent life-cycle analyses have begun quantifying the environmental load of aligner plastics, situating them within broader discussions of medical polymer waste [59].

Release of microplastics and nanoplastics

Orthodontic appliances made of polymers are continuously subjected to mechanical stress, such as chewing or parafunctional activity, as well as chemical and thermal challenges in the oral environment. These factors gradually degrade the plastic surface, causing microscopic fragments to detach. Studies have confirmed that aligners emit microplastics during use. Quinzi *et al.* reported that after seven days of simulated wear, various aligner brands released particles in the 5–20 μm range, with emission levels differing by material; one brand released significantly more particles than Invisalign, which showed the lowest release [52]. Detached microparticles may be ingested or incorporated into oral biofilms, though the full clinical significance remains uncertain. More broadly, microplastic ingestion has been associated with tissue inflammation and potential systemic uptake.

Plastic waste and disposal

Clear aligner therapy typically involves 20–30 sequential appliance sets per patient (upper and lower arches combined), each weighing approximately 4.3 g per pair [53]. This translates to roughly 100–130 g of plastic waste per patient per treatment. Extrapolating to a hypothetical global market of one million patients annually, aligners alone could generate over 100 metric tons of plastic waste per year. Retention devices, such as Essix retainers, also contribute ongoing plastic waste through periodic replacement every 6–12 months. Most discarded appliances

are sent to landfills or general waste streams, as recycling options are limited due to their classification as biohazardous and their composite construction, which may include embedded metals. In landfill conditions, these polymers persist over long periods with minimal biodegradation.

Public health and ecological considerations

Microplastics represent a growing public health concern, having been detected in water supplies and human tissues. While orthodontic devices contribute a relatively small proportion of total plastic pollution compared to packaging, textiles, or bottles, sustainability is becoming increasingly important in modern orthodontic practice. Macrì *et al.* [53] proposed a "4Rs" framework—Reduce, Reuse, Recycle, Rethink—to mitigate the environmental impact of aligner therapy. Suggested strategies include optimizing treatment protocols to minimize material use, exploring creative reuse of used trays, developing recycling programs despite logistical barriers, and promoting biodegradable polymer alternatives. Regulatory considerations also intersect with environmental risk: the presence of BPA or other substances of very high concern (SVHCs) in devices is notable, given their persistence in the environment. Although orthodontic appliances have not been specifically regulated, proactive removal of BPA by manufacturers likely aims to preempt potential future legal or regulatory restrictions, following precedents such as EU limits on BPA in consumer products.

Conclusions and future directions

Recent research has increasingly focused on the biocompatibility of orthodontic retainer materials, reflecting heightened safety standards and scientific scrutiny. Current evidence suggests that removable retainers composed of PMMA-based acrylic or PETG/TPU thermoplastics are generally safe, showing only mild cytotoxicity and limited estrogenic effects. Both Hawley and Essix-type appliances have a long history of clinical use without reports of serious adverse outcomes. Nonetheless, the detection of oxidative stress markers, subtle cellular changes, and trace bisphenol release indicates that these materials can produce minor biological responses. While overall biocompatibility is favorable, these interactions highlight opportunities to refine retainer composition for improved safety.

- Evidence-Based Clinical Guidance
- General safety: Both Hawley and Essix retainers may induce minor cytotoxic effects in vitro or subtle biomarker changes in vivo, but no clinically significant pathology has been reported; patients can be reassured, and clinicians should monitor for rare sensitivities or allergies.
- Residual monomers in acrylic Hawleys: Heat-cured acrylic and pre-soaking (in water or saliva) can reduce initial monomer exposure. If patients experience strong taste or oral irritation, extended soaking or remaking the appliance with improved curing is recommended.
- BPA and xenoestrogen leaching in thermoplastics: Leaching is most prominent during the first day of use. Clinicians can mitigate exposure by rinsing or soaking new clear retainers and choosing verified BPA-free products. For higher-risk groups—young patients, pregnant individuals, or those particularly concerned—selecting alternative thermoplastics with lower leach rates is prudent.
- Monitoring and maintenance: At follow-up visits, inspect oral tissues for chronic irritation. Address inflammatory or mechanical issues, which may be resolved by polishing Essix edges or adjusting Hawley retainers to reduce physical stress.
- Patient education: Emphasize daily cleaning to prevent plaque accumulation, which not only maintains hygiene but also limits potential tissue reactions to any leached substances. A clean retainer minimizes additional biological responses beyond those caused by the material itself.
- Material alternatives for sensitive patients: Individuals with acrylic sensitivity (e.g., previous reactions to nail acrylics) may benefit from polypropylene-based Essix retainers, which have negligible monomer release. For patients preferring to avoid removable plastics entirely, fixed retainers offer a non-plastic alternative.
- Forward-Looking Considerations and Research Directions
- Ongoing monitoring of emerging orthodontic materials is essential, especially for those enhanced with antimicrobial or bioactive compounds. Any novel additive must undergo comprehensive toxicological assessment to avoid unforeseen biocompatibility issues.
- The development of biodegradable or recyclable orthodontic materials represents a promising step toward environmental sustainability. Nevertheless, many current biodegradable polymers fall short in mechanical

strength and transparency, limiting their suitability for prolonged orthodontic use. Therefore, while environmentally advantageous, biodegradable retainers remain an aspirational objective that must be weighed against clinical feasibility, patient safety, and economic considerations.

- Future in vivo research should investigate the long-term consequences of retainer use, including the persistence of oxidative stress and the monitoring of systemic biomarkers.
- Mechanistic studies are crucial to elucidate the pathways by which particular additives may produce cytotoxic or estrogenic effects.
- Evolving regulatory standards may require stricter limits on BPA and other leachable substances, prompting manufacturers to consider reformulated materials.
- From a public health standpoint, the orthodontic field should prioritize minimizing even the smallest risks, particularly for children and adolescents.

Future investigations should focus on establishing standardized protocols for assessing biocompatibility and endocrine-disrupting potential, allowing for consistent and comparable evaluations of different orthodontic materials. Overall, current evidence supports that Hawley and Essix retainers remain safe and effective; however, continuous advancements in material science and heightened attention to biocompatibility will further improve their safety profile. By adhering to evidence-based practices and carefully selecting materials, clinicians can optimize both the effectiveness and biocompatibility of retention therapy while supporting environmental sustainability goals. Ongoing innovations in polymer technology are anticipated to yield materials with superior biocompatibility, helping to address current concerns related to cytotoxicity and endocrine-disrupting effects in orthodontic appliances.

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