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Silent Curse of Clear Aligners - A Review

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ABSTRACT
Clear aligner therapy is gaining popularity as an orthodontic treatment option due to its convenience in terms of aesthetics and comfort. However, growing evidence is suggestive of its wide range potential biological and health-related issues, namely, from cytotoxicity and chemical release to changes in oral microbiome and hypersensitivity reactions. A literature review was performed to identify key studies acknowledging cytotoxicity, chemical leaching, oral tissue response, microbiome alterations, estrogenic responses, and hypersensitivity related to materials used for aligner fabrication. This review takes under consideration existing research on the biological effects, safety concerns, and potential risks associated with the use of clear aligners. The current evidence implicates that although most clear aligner systems are usually biocompatible, certain materials can exert cytotoxic effects in vitro, affect oral epithelial cells differently based on the testing environment, demonstrate estrogenic activity in select assays, may contribute to hypersensitivity or alterations in oral microflora, and may release chemical agents under specific conditions. Although clear aligners provide significant clinical benefits, being aware of possible biological concerns, especially in susceptible individuals is responsibility of the clinician. Long-term clinical research is highly needed for further standardization.
Keywords: *Clear Aligner therapy, Orthodontics, Thermoformed aligners, 3D printed aligners, Cytotoxicity, Chemical Leaching, Endocrine disruption, Microbial alterations, Estrogenic response*

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INTRODUCTION

Clear aligners are a modern orthodontic treatment modality designed to correct malocclusion using a series of custom made removable transparent trays that offer an aesthetic and comfortable alternative to traditional fixed braces.

Clear aligners have evolved significantly since their introduction in terms of materials, manufacturing process, and their indications in different orthodontic cases. In 1945, Harold D. Kesling pioneered rubber-based tooth positioners made from wax-setups which was later improved in 1964 with vacuum-formed appliances by Nahoum and further advanced in 1993, using a polypropylene thermoplastic co-polyester sheet to create clearer, more adaptable appliances by Sheridan. Over-time, aligners have undergone modifications to enhance their clinical effectiveness, comfort, and aesthetic appeal, increasing their popularity for malocclusion treatment [1].

Conventional thermoformed aligners are made of a single layer of plastic sheets made of different types of polymers, such as polyethylene terephthalate glycol (PETG) or thermoformed polyurethane (TPU) [2].

The 3D printed manufacturing method uses computer-aided design and computer-aided manufacturing technology (CAD/CAM) through additive (adding layers successively) and subtractive methods (grinding or milling of industrially prefabricated materials), or through liquid materials (e.g., stereolithography). Such advanced technologies such as 3D imaging and computer-aided design (CAD) has enhanced the precision and personalization of aligner treatments. First photocurable 3D printed aligners launched in the market were Tera Harz TC-85 by Graphy. Tera Harz TC-85 is bio-compatible photopolymer material and is available in two colours as clear and white. TC-85DAC (clear) is fully transparent, whereas TC-85DAW (white) provides durability and aesthetics [3].

Current materials used for 3D printing include acrylonitrile-butadiene-styrene plastic, stereolithography materials (epoxy resins), glass filled polyamide, silver, steel, titanium, photopolymers, and wax[1].

Current aligners are composed of several thermoplastic polyurethanes, including Essix plastic, medical-grade polyurethane, and proprietary blend of BPA-free plastic polymers.
As an alternative to fixed orthodontic appliance, clear aligner therapy has gained widespread popularity[1]. Clear Aligners are worn for 20-22 hours per day for effective orthodontic movement and would ultimately also influence the flow of saliva and oral health as a whole [4].
Although they have numerous advantages, concerns have been raised about the biological effects of thermoplastic materials and 3D resins used in aligner fabrication [5].
Polyurethane (PU) and Polycarbonate (PC) showed minimal cytotoxicity, meaning they had little to no harmful effect on the cells. Whereas, PETG exhibited slightly higher cytotoxicity, suggestive of a more noticeable negative impact on cell viability [4].
However, these materials, especially plastics, are not without drawbacks, including their tendency of incomplete polymerisation, potentially leading to the release of Microplastics. These issues also include cytotoxic responses, potential of disrupting endocrine functioning, reactions associated with oral tissues, changes in microbiome, and allergic reactions [5].

CYTOTOXICITY OF ALIGNER MATERIALS
Several in vitro studies have examined the cytotoxic potential of aligner plastic material, including thermoplastic polyurethanes and PETG-based materials [4, 6]. Evidence has shown that **leaching of aligners** can reduce cell viability under certain conditions, particularly in saline environments, suggestive of material extractables impacting oral epithelial or fibroblast cells [4, 6]. There have been reports of differences in cytotoxic response among systems, though most materials have shown low or moderate cytotoxicity within standard testing parameters.
Stefano et al assessed the thermoforming effect on the cytotoxicity of plastic materials for clear aligner. More cytotoxic behaviour was seen in thermoformed materials; however, only three materials were examined in a non-thermoformed state because acquiring the non-thermoformed SmartTrack material was not possible. It was previously shown that the release of monomers by dental composite materials induced cytotoxicity, [7] so it was assumed that thermoplastic materials show a similar mechanism of action. Considering that the polyethylene terephthalate released more added substances as the temperature increased, [8] it is possible that the thermoforming process could increase the release of monomers and consequently increase the cytotoxicity.

CELLULAR AND TISSUE RESPONSES
Premraj et al performed a study examining oral epithelial cell reactions which showed clear differences in cell behaviour when exposure to aligner material eluates were in saline than in artificial saliva, illuminating the role of environmental factors in carrying out biological responses. They stated that changes in viability, membrane permeability, and adhesion of epithelial cells in a saline-solution environment were seen on exposure to Invisalign plastic. They concluded microleakage and hapten formation secondary to compromised epithelial integrity might lead to isocyanate allergy, which could be systemic or localized to gingiva. However, these results also suggest that saliva might offer protection [9].

CHEMICAL RELEASE AND ESTROGENIC RESPONSE
Systematic reviews on chemical leaching indicate that clear aligners can release low levels of monomers or additives under laboratory conditions[2], though clinical relevance at intraoral concentrations remains unclear [2]. Some assays show weak estrogenic activity in select materials, raising queries about endocrine effects, although evidence is not sufficiently conclusive [10].
One of the primary concerns is the potential release of Bisphenol-A (BPA) and other monomers. BPA is an endocrine disruptor with known estrogenic activity, has been detected in some thermoplastic dental materials, which raises concerns about its collective exposure over a prolonged time [11]. Studies show that although BPA is released from aligners, however the levels generally fall within regulatory safety limits. The long-term effects of prolonged exposure remain unclear, particularly for susceptible populations such as adolescents and pregnant women [12, 13]. In addition to that, alternative derivatives of bisphenol such as BPS and BPF, that are usually used in BPA-free plastics, may pose similar health risks, which necessitates further investigation into their systemic absorption and biological impact. This leaching is exaggerated by thermal and mechanical stresses encountered during thermoforming and oral wear [4].

ORAL MICROBIOME ALTERATIONS
Comparative clinical research suggests that aligner patients may undergo changes in oral microbial flora, potentially due to higher surface contact and retentive areas on the appliance surface, although patterns differ from those seen with fixed appliances [14].

Asli et al performed a study concluding that prolonged usage of orthodontic appliances may have a negative effect on microbial flora and increase the risk of new carious lesions and periodontal problems. Therefore, within short intervals of time, patients should be recalled for motivation and encouraging the maintenance of oral hygiene during their orthodontic therapy [15].

HYPERSENSITIVITY AND ALLERGIC REACTIONS

Systematic reviews of hypersensitivity in orthodontic contexts include reported cases of oral irritation, dermatitis, and mucosal reactions in association with clear aligner wear. While incidence appears low, clinically significant reactions warrant careful patient history and monitoring [16].

Manifestations potentially related to hypersensitivity reactions were most frequent with fixed appliances, followed by removable appliances and clear aligners. Nickel emerged as the most frequently identified allergen, followed by cobalt, titanium, and chromium [16].

The Amato et al, findings also emphasize the significance of a detailed assessment before the commencement of any treatment, including allergy history and testing, especially in atopic or allergic individuals, to identify potential allergens and using hypoallergenic materials in sensitized patients. During treatment, regular check-ups and prompt intervention is of high importance. Removal of allergenic material is essential to prevent further exposure. Regular follow-up is of essence to spot recurrent reactions early. Clinicians should be flexible to modify materials and treatment strategies to ensure safety and therapeutic continuity [17].

Concern	Evidence Level	Finding
Cytotoxicity	Moderate (in vitro)	Most materials show low-moderate cytotoxicity; affected under eluate medium [4, 6]
Chemical Release	Variable	Detectable in vitro; clinical significance is unsure [2]
Estrogenic Response	Limited	Few weak estrogenic responses in lab assays [10]
Microbiome Change	Moderate	Alterations observed and clinical effects still under evaluation [14]
Hypersensitivity	Low	Occasional oral or extra-oral reactions reported [16]

TABLE 1 : Findings of various studies performed to examine biological risks of Clear Aligners

CLINICAL AND ENVIRONMENTAL IMPLICATIONS

Clinicians should evaluate patients beforehand prior material sensitivities, keep a check on oral tissues during treatment, and emphasize hygiene protocols. Environmentally, the increased production and disposal of thermoplastic aligners contribute to plastic waste, raising sustainability concerns [17].

Recent studies have showed proof of the deposition of microplastics in the digestive system, which has highlighted risks regarding their toxicity and long-term effects on the gut microbiota. Intake of these microplastics directly or indirectly through contaminated food and water sources poses a problem to gut health. Microplastics and Nanoplastics (MNPs) can cause various forms of harmful effects, including cellular deformation, enterocyte decomposition, inflammation, genotoxicity, and oxidative stress responses in the gut. It has been seen that nanoparticles lead to decreased digestive enzyme activity, induce goblet cell enlargement, and increase mucus secretion. They also trigger the secretion of proinflammatory cytokines such as tumor necrosis factor α, interferon γ, and interleukin-6. This inflammatory response leads to leukocyte infiltration, hyperemia, and loss of villi and crypt cells [17].

These microplastics can enter the bloodstream, spread to other tissues, and persist within the body for long duration of time [18].

The environmental consequences associated with plastic aligners are also significant along with its effects on human health [19].

Research shows that microplastics can trigger inflammation, oxidative stress, and impaired lung function. Microplastics, owing to their small size, deeply infiltrate the lungs and reach the alveoli. This flags an issue about prolonged health effects, including the development of respiratory diseases and their potential translocation to other organs [20]. A motivating resolution for managing the deleterious effects of plastic aligners is the development of effective recycling processes. It is essential to explore environmentally friendly alternatives and promote responsible disposal of clear aligners. Recyclable materials should be given priority and patients must be educated about proper recycling methods, thereby preventing clear aligners from contributing to the intensifying issue of plastic pollution [21].

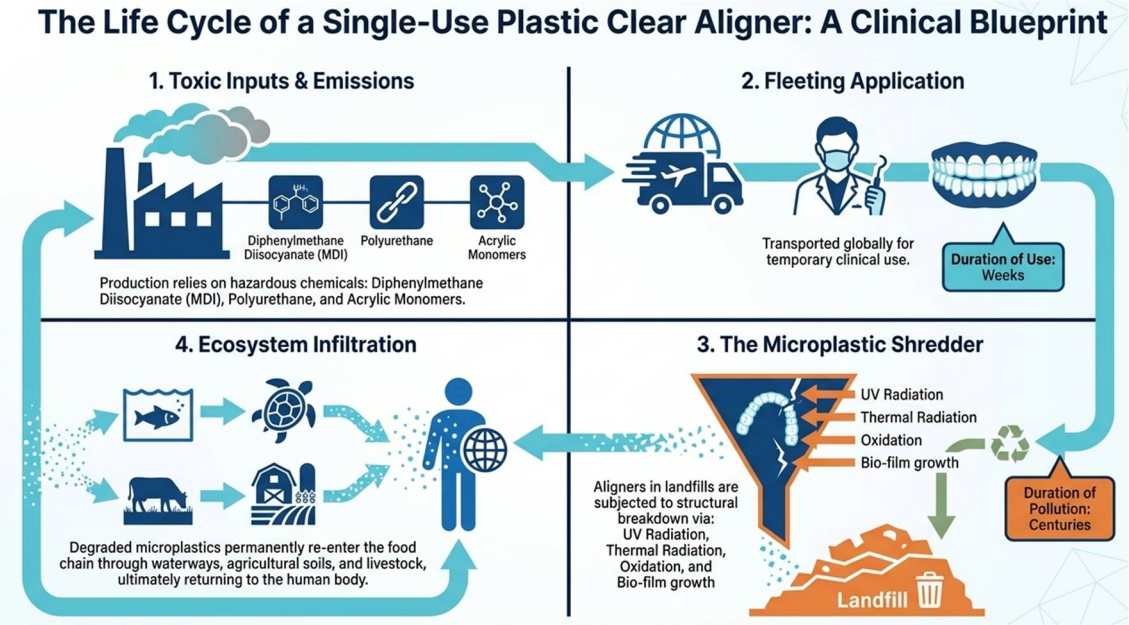

Figure 1: The life cycle of a single use plastic clear aligner [1]

BENEFITS

Despite all of the mentioned worrisome concerns, clear aligners offer:

- Preferable aesthetics over conventional fixed braces.
- Patient compliance and comfort has improved.
- Oral hygiene maintenance practices are more convenient for patients.
- Risk of decalcification has decreased as compared to the traditional appliances.

So, clear aligners provide aesthetic superiority, enhanced comfort, convenience of removability, and potentially lower risk of enamel decalcification compared with conventional fixed appliances.

LIMITATIONS

- The predominance of **in vitro data** limits direct translation to clinical safety[4,6].
- Heterogeneity in aligner materials and testing protocols hinders standardization[2].
- Insufficient long-term human studies have taken place to evaluate systemic effects or chronic biological responses.

CONCLUSION

Clear aligner therapy represents an important milestone in orthodontics, offering many advantages which are clinically significant. Nonetheless, evidence of mild cytotoxicity, potential chemical release, microbiome shifts, and rare hypersensitivity reactions confirms the need for ongoing investigation. Furthermore, the worries expressed about their environmental impact due to single use and improper disposal is a major problem which should be dealt on priority. Future research should emphasize standardized testing methods and long-term clinical studies to ensure optimal patient safety and eco-friendly materials for their manufacturing. Although, clear aligners are not inherently harmful, but awareness of their subtle biological effects is essential for reliable orthodontic care.

REFERENCES

1. Bichu, Yashodhan M et al. (2022). "Advances in orthodontic clear aligner materials." *Bioactive materials* vol. 22 384-403. doi:10.1016/j.bioactmat.2022.10.006
2. Ferreira M, Costa H, Veiga N, Correia MJ, Gomes ATPC, Lopes PC. (2025). Do Clear Aligners Release Toxic Chemicals?-A Systematic Review. *J Funct Biomater*. 16(5):173. doi:10.3390/jfb16050173
3. Available from: http://itgraphy.com/wp/material/dental/, 2022.
4. Martina S, Rongo R, Bucci R, Razionale AV, Valletta R, D'Antò V. (2019). In vitro cytotoxicity of different thermoplastic materials for clear aligners. *Angle Orthod*. 89(6):942-945. doi:10.2319/091718-674.1

5. Francisco I, Paula AB, Ribeiro M, et al. (2022). The Biological Effects of 3D Resins Used in Orthodontics: A Systematic Review. *Bioengineering (Basel)*. 9(1):15.. doi:10.3390/bioengineering9010015
6. Alhendi A, Khounganian R, Almudhi A. (2022). Cytotoxicity assessment of different clear aligner systems: An in vitro study. *Angle Orthod*. 92(5):655-660. doi:10.2319/121621-919.1
7. Stanislawski, L et al. (1999). "Factors responsible for pulp cell cytotoxicity induced by resin-modified glass ionomer cements." *Journal of biomedical materials research* vol. 48,3: 277-88. doi:10.1002/(sici)1097-4636. 48:3<277::aid-jbm11>3.0.co;2-t
8. Bach, Cristina et al. (2013). "Effect of temperature on the release of intentionally and non-intentionally added substances from polyethylene terephthalate (PET) bottles into water: chemical analysis and potential toxicity." *Food chemistry* vol. 139,1-4. 672-80. doi:10.1016/j.foodchem.2013.01.046
9. Premaraj T, Simet S, Beatty M, Premaraj S. (2014). Oral epithelial cell reaction after exposure to Invisalign plastic material. *Am J Orthod Dentofacial Orthop*. 145(1):64-71. doi:10.1016/j.ajodo.2013.09.011
10. Eliades T, Pratsinis H, Athanasiou AE, Eliades G, Kletsas D. (2009). Cytotoxicity and estrogenicity of Invisalign appliances. *Am J Orthod Dentofacial Orthop*. 136(1):100-103. doi:10.1016/j.ajodo.2009.03.006
11. Al Naqbi, Shaima R et al. (2018)."In Vitro Assessment of Cytotoxicity and Estrogenicity of Vivera® Retainers." *The journal of contemporary dental practice* vol. 19,10 1163-1168.
12. Dinu, S.; Daniel, O.N.; Matichescu, A.; Nicoleta, Z.I.; Szuhanek, C.; Geamantan, A.; Buzatu, R.(2024). In Vitro Biocompatibility and in ovo Irritant Potential Screening of Two Clear Aligners with Orthodontic Applications. *Farmacia* , 72, 513–520.
13. Behnke, Richard et al. (2022). "Influence of Test Specimen Geometry and Water Soaking on the In Vitro Cytotoxicity of Orthocryl®, Orthocryl® LC, Loctite® EA 9483 and Polypropylene." *Molecules (Basel, Switzerland)* vol. 27,12 3949. doi:10.3390/molecules27123949
14. Wang Q, Ma JB, Wang B, Zhang X, Yin YL, Bai H. (2019). Alterations of the oral microbiome in patients treated with the Invisalign system or with fixed appliances. *Am J Orthod Dentofacial Orthop*. 156(5):633-640. doi:10.1016 /j.ajodo.2018.11.017
15. Topaloglu-Ak, Asli et al. (2011). "Effect of orthodontic appliances on oral microbiota--6 month follow-up." *The Journal of clinical pediatric dentistry* vol. 35,4. 433-6. doi:10.17796/jcpd.35.4.61114412637mt661
16. Amato A, Martina S, De Benedetto G, Michelotti A, Amato M, Di Spirito F. (2025). Hypersensitivity in Orthodontics: A Systematic Review of Oral and Extra-Oral Reactions. *J Clin Med*. 14(13):4766. Published 2025 Jul 5. doi:10.3390/jcm14134766
17. Veseli E, Afrashtehfar KI, Khan MK, Veseli K, Behluli E. (2024). The potential health hazards associated with clear aligners. *APOS Trends Orthod*. 14:201-2. doi: 10.25259/APOS_125_2024
18. Covello, Carlo et al. (2024). "Micro(nano)plastics and Their Potential Impact on Human Gut Health: A Narrative Review." *Current issues in molecular biology* vol. 46,3 2658-2677. 2 doi:10.3390/cimb46030168
19. Veseli E, Veseli K, Behluli EI. (2024). The carbon emissions of clear aligner therapy: A critical review. *APOS Trends Orthod*. 14:70-1. doi: 10.25259/APOS_34_2024
20. Saha, Suvash C, and Goutam Saha. (2024). "Effect of microplastics deposition on human lung airways: A review with computational benefits and challenges." *Heliyon* vol. 10,2 e24355. 11, doi:10.1016/j.heliyon.2024.e24355
21. Veseli, E et al. (2024). "Recyclable aligners." *British dental journal* vol. 236,5: 360. doi:10.1038/s41415-024-7194-1

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