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Biological Effects of Materials Used in Orthodontic Treatment

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Abstract

Orthodontic treatment involves prolonged contact between dental materials and the oral environment, which creates conditions for continuous biological exposure throughout therapy. Orthodontic appliances remain in situ for months or years and are subjected to mechanical stress, thermal fluctuations, changes in oral acidity and microbial activity. These factors may promote corrosion, degradation and the release of metal ions, residual monomers, and other low-molecular-weight compounds with potential biological effects.

The aim of this review is to analyse the biological effects associated with materials used in orthodontic treatment, with an emphasis on allergic reactions, cytotoxicity, genotoxicity, and oxidative stress. Available experimental and clinical evidence indicates that ion release from orthodontic alloys and elution of organic components from polymeric and resin-based materials can occur under clinically relevant conditions. However, exposure levels and biological significance vary considerably depending on material composition, manufacturing features, clinical protocols, local oral conditions, and individual susceptibility.

Overall, current evidence suggests that biological responses are not determined solely by the intrinsic properties of materials but reflect a dynamic interaction between material-related factors and the oral environment. Allergic reactions—particularly to nickel-containing alloys and methacrylate-based polymers—occur mainly in sensitised individuals and may be influenced by local modifiers such as inflammation and changes in oral acidity. Cytotoxic and genotoxic findings reported in experimental models indicate plausible pathways, but clinical extrapolation remains limited due to methodological heterogeneity across studies. Further long-term studies integrating analytical measurements with biological and clinical outcomes are needed to support material- and protocol-specific risk assessment in orthodontic practice.

Keywords: Orthodontic materials; cytotoxicity; oxidative stress; allergic reactions

Introduction

Orthodontics has undergone substantial development over recent decades, not only in terms of diagnostic and therapeutic strategies but also regarding the materials employed in clinical practice. (1-2) A notable trend in contemporary orthodontics is the increasing number of adult patients undergoing treatment. This shift expands the spectrum of biological considerations, as adult

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patients may present with cumulative environmental exposures, pre-existing sensitizations, or systemic conditions that influence biological responses to dental materials. (3-6)

Orthodontic treatment is characterized by prolonged and continuous contact between appliances and the oral tissues. Fixed and removable appliances, including brackets, wires, aligners, retainers, and bonding systems, remain in the oral cavity for extended periods, often exceeding one to two years. (1,7) During this time, materials are exposed to a complex and dynamic environment involving saliva, fluctuating pH, temperature changes, mechanical loading, and microbial biofilms. These conditions can induce physicochemical changes in materials, leading to corrosion, degradation, and elution of biologically active components. (1,2,7,10)

In contrast to many other dental applications, orthodontic materials create a scenario of chronic low-level exposure. Metals may release ions as a result of electrochemical processes, while polymeric and resin-based materials may elute residual monomers, additives, or degradation products. (7-10,12) Such exposure has been associated in the literature with a range of biological effects, including allergic reactions, cytotoxicity, oxidative stress, and, in some experimental settings, genotoxic effects. (3,26,30-33)

The concept of biocompatibility has evolved from a static definition toward a dynamic framework in which biological safety is understood as the outcome of interactions between material properties, environmental conditions, and host-related factors. (1-2) In orthodontics, this perspective is particularly relevant because identical materials may exhibit different biological behaviors depending on clinical protocols, oral hygiene, inflammatory status, and individual susceptibility. (1,2,7,16)

Current evidence indicates that the biological behavior of orthodontic materials should be interpreted in relation to both material composition and the dynamic conditions of the oral environment.

Aim

The aim of this review is to synthesize and critically evaluate current evidence on the biological effects associated with materials used in orthodontic treatment, with emphasis on the mechanisms of component release and the clinical relevance of reported outcomes, including hypersensitivity reactions, cytotoxicity, oxidative stress, and genotoxic effects.

Materials and Methods

A literature search was performed in PubMed, Scopus, and Web of Science using predefined keywords related to orthodontic materials and their biological effects. The search terms included “orthodontic materials”, “biocompatibility”, “cytotoxicity”, “nickel release”, “allergic reactions”, “oxidative stress”, “genotoxicity”, “resin monomers”, and “clear aligners”. Only English-language studies related to orthodontic materials and their biological effects were considered. Experimental studies, clinical studies, systematic reviews, and relevant toxicological reports were included, whereas articles not related to orthodontic materials, non-biological outcomes, or duplicate records were excluded. After screening for relevance, the selected studies were analyzed narratively according to material type and reported biological effects.

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Results

Materials Used in Orthodontic Treatment and Pathways of Biological Exposure

The materials used in orthodontic treatment can be broadly classified into three main categories: metallic materials and alloys, polymer-based materials, and resin-based adhesive systems. Each group exhibits distinct physicochemical behavior in the oral environment and is associated with different mechanisms of biological exposure. (1,2,7) The tested materials are summarized in Table 1.

Table 1. Orthodontic materials included in the review and their classification

Material code	Tested material	Material group	Clinical application
UNT	Untreated control	Control	Reference condition
1	Stainless steel with titanium	Metallic material	Fixed orthodontic appliance component
2	Nickel with titanium	Metallic material	Fixed orthodontic appliance component
3	Nickel–titanium archwire	Metallic material	Orthodontic archwire
4	Stainless steel archwire	Metallic material	Orthodontic archwire
5	Sapphire bracket	Fixed appliance material	Orthodontic bracket
6	Metallic bracket	Fixed appliance material	Orthodontic bracket
7	Acrylic resin from removable orthodontic appliance	Polymeric material	Removable appliance base material
8	Trainer material	Polymeric material	Functional/removable orthodontic appliance material
9	Metal alloy from removable orthodontic appliance	Metallic material	Removable appliance metallic component
10	Aligner material	Polymeric material	Clear aligner material

Metallic Materials and Alloys

Metallic materials are widely used in orthodontics for brackets, archwires, bands, and auxiliary components. Commonly employed alloys include stainless steel, nickel–titanium (NiTi), beta-titanium, and cobalt–chromium alloys. (7-10) These materials provide the mechanical strength and elastic properties required for efficient tooth movement; however, in the oral environment they are subject to electrochemical processes that may lead to corrosion and ion release. (7-10)

Corrosion in orthodontic appliances is a multifactorial phenomenon influenced by alloy composition, surface characteristics, galvanic coupling between different metals, and local oral conditions. (7,10) In vivo and in vitro studies consistently demonstrate that orthodontic alloys

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release measurable amounts of metal ions, particularly nickel and chromium, into saliva and, in some cases, into systemic circulation. (16,17,41,42) Systematic reviews confirm that trace metal release is a reproducible finding in both in vivo and in vitro studies, while emphasizing substantial methodological heterogeneity. (16-17)

Local environmental factors play a critical role in modulating ion release. Acidic pH increases ion release from NiTi wires, and fluoride-containing mouthwashes can enhance galvanic corrosion between wires and brackets. (9-10) Differences in ion release have also been reported depending on the type of mouthwash, the type of archwire, and acidity level. (11,45) In addition, orthodontic appliances promote plaque retention and gingival inflammation, creating microenvironments that may enhance corrosion and increase localized exposure relative to idealized conditions. (7,11)

From a biological perspective, metal ion release represents the primary pathway through which metallic orthodontic materials interact with oral tissues. Nickel is a well-recognized contact allergen, and clinical relevance depends on both release levels and patient sensitization status. (3,6,46,47)

Polymeric Materials: Acrylics, Elastomers, and Thermoplastics

Polymeric materials are extensively used in orthodontics for removable appliances, retainers, elastomeric components, and clear aligners. Unlike metals, polymers do not undergo electrochemical corrosion; instead, their biological relevance is primarily associated with the elution of organic compounds, including residual monomers, additives, plasticizers, and degradation products. (12,18-20,26)

Acrylic resins, commonly used for the bases of removable appliances and retainers, are typically based on methacrylate chemistry. Their biological behavior is strongly influenced by the degree of polymerization and curing protocols. (18,19) Analytical studies demonstrate that acrylic orthodontic base-plate materials release not only methyl methacrylate and ethyl methacrylate but also a broader spectrum of leachable substances, with profiles dependent on material composition and polymerization conditions. (12)

Residual monomer content is linked with tissue sensitivity and has clinical implications. (18) Different curing cycles can produce substantial differences in residual monomer levels, directly influencing exposure. (19) Clinically, allergy to autopolymerized acrylic resin has been documented in orthodontic patients. (20)

Thermoplastic materials used for clear aligners and retainers represent a relatively recent addition to orthodontic practice. These materials undergo prolonged daily intraoral exposure, making aging and property changes clinically relevant. (13-15) Studies under simulated intraoral conditions and retrieval analyses after clinical use demonstrate mechanical and chemical changes over time. (13-15) In vitro investigations demonstrate material-specific differences in cytotoxicity among thermoplastic aligner materials, and targeted studies have examined epithelial cell behavior on specific aligner polymers. (28,29) Cytotoxicity and estrogenicity have also been reported for specific commercial systems (e.g., Invisalign, Vivera retainers). (26,27)

Elastomeric materials are widely used for ligatures and auxiliaries. Contemporary orthodontic practice has seen changes in adverse reactions with increased use of latex-free materials, and professional guidance emphasizes prevention and structured management of latex allergy. (49,50)

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Resin-Based Adhesive Systems for Bonding

Resin-based adhesive systems and composites are essential for bonding brackets and retainers. These materials are multicomponent systems containing methacrylate monomers, photoinitiators, fillers, and additives. (22-24) Their biological significance arises from the potential elution of residual monomers and degradation products, especially when polymerization is incomplete or when chemical interactions occur in the oral environment. (21,23-25)

Experimental evidence indicates that resin-based composites and their leached components can induce cytotoxic effects under specific conditions. (24) Dentine permeability and transport conditions influence observed cytotoxicity in vitro, highlighting that exposure modeling affects outcomes. (22) Interactions between resin monomers/composites and human saliva-derived esterases suggest enzymatically mediated degradation and time-dependent changes in elution profiles. (23)

A specific area of concern is the release of bisphenol A (BPA) or BPA-related compounds. BPA release has been reported from orthodontic bonding materials, including adhesives used for lingual fixed retainers, with findings dependent on product and protocol. (30,36-38) Clinical studies have measured BPA in saliva (and comparative settings) associated with orthodontic retainers, and BPA and other compounds in saliva/urine have been associated with placement of composite restorations. (39,40) Broader toxicological evidence on BPA exists from in vivo laboratory studies. (51)

From a clinical standpoint, the localized application of bonding materials around brackets and retainers means that small amounts of elution may still produce relatively high local tissue exposure, making polymerization quality and removal of excess adhesive relevant preventive steps. (21,25)

BIOLOGICAL EFFECTS OF ORTHODONTIC MATERIALS

Allergic Reactions and Hypersensitivity

Allergic reactions are among the most clinically recognizable biological effects associated with orthodontic materials. In orthodontics, delayed-type (type 4) hypersensitivity reactions are most frequently discussed and are mainly associated with nickel-containing metallic components and certain polymer-based materials. (3,6,46)

Nickel is a prevalent contact allergen in the general population, and many orthodontic patients may be sensitized prior to treatment. (4-6) However, sensitization does not necessarily predict clinical symptoms during orthodontic therapy; clinical studies show variable expression of nickel hypersensitivity before, during, and after orthodontic treatment. (47,48)

Intraoral manifestations may include erythema, edema, burning sensation, lichenoid reactions, and gingival symptoms, whereas extraoral dermatitis has also been reported in association with orthodontic appliances. (3,46) Patch testing is a standard approach for evaluating suspected contact allergy and is widely used in dental screening series. (52) Lymphocyte transformation testing has been explored as an adjunct in nickel sensitivity, but comparative discussions

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emphasize differences between patch testing and LTT and limitations of LTT as a replacement for clinical diagnosis. (53,54)

Polymer-based materials, particularly acrylic resins, can induce hypersensitivity reactions associated with residual monomer and other leachables. (12,18-20) Tissue sensitivity has been linked to residual monomer content, and curing cycles significantly affect residual monomer levels. (18,19) Clinical allergy to autopolymerized acrylic resin has been reported in orthodontic patients. (20)

Latex-containing elastomeric components may provoke hypersensitivity; changes in occupational and patient reactions over time have been reported, and position guidance emphasizes prevention and structured management. (49,50)

Rare but clinically relevant reactions have also been described with clear aligner therapy, including angioedema, stomatitis, and urticaria linked to contact allergy to Invisalign; adverse clinical events have additionally been analyzed in the MAUDE database. (34,35)

Cytotoxic Effects

Cytotoxicity is commonly evaluated using in vitro cell culture models, but interpretation requires caution because outcomes depend heavily on assay choice and experimental design. (21,25,55,56) General principles and limitations of cell-based assays, including the risk of misleading viability findings in certain conditions, support using careful methodology and contextual clinical interpretation. (55,56)

For metallic materials, cytotoxic potential is linked to corrosion and ion release, which is demonstrable in vitro and in vivo. (8-10,16,17) However, systematic reviews highlight methodological heterogeneity and limited direct comparability across studies. (16,17) Local conditions such as acidity and fluoride exposure can increase ion release, potentially affecting local biological exposure. (9-11,45)

For polymeric and resin-based materials, cytotoxicity is associated with elution of residual monomers and degradation products. Composite materials and leached components have demonstrated cytotoxicity in vitro. (24) Dentine permeability affects observed cytotoxicity in bonding systems, emphasizing exposure-model dependence. (22) Saliva-derived esterases interact with resin monomers and composites, supporting time-dependent degradation and altered elution profiles. (23) Conceptual frameworks in biocompatibility testing stress the need for clinically relevant exposure conditions and cautious extrapolation to clinical risk. (21,25)

Thermoplastic aligner materials show material-specific differences in cytotoxicity in vitro, and clinical aging/retrieval studies indicate that properties change after use. (13-15,28,29) Cytotoxicity and estrogenicity have been reported in specific systems (Invisalign, Vivera). (26,27)

Genotoxicity and Oxidative Stress

Oxidative stress and genotoxicity represent subtler biological effects that may be detected at the molecular level. The comet assay is widely used to measure oxidative DNA damage and repair capacity. (31) Toxicological literature describes mechanisms by which nickel exposure can

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contribute to oxidative stress and related molecular effects, including pathways relevant to carcinogenesis and interference with protective enzyme systems. (57-59)
In orthodontic patients, in vivo studies have reported DNA damage in oral mucosal cells during treatment with fixed appliances, together with evidence of metal release (notably nickel and chromium). (32,33) However, interpretation requires caution: orthodontic appliances can promote plaque retention and gingival inflammation, and local inflammatory conditions may independently contribute to oxidative stress and influence biomarker findings. (7,11,32,33)

Clinical Interpretation and Risk Modulation in Orthodontic Practice

Biological effects in orthodontics are best understood as exposure-dependent rather than material-intrinsic. Biocompatibility is dynamic and influenced by material properties, clinical protocols, oral conditions, and patient factors. (1,2,21,25)
Metal ion release varies substantially across studies due to methodological differences and oral-environment modifiers. (16,17,41-44) Lower pH increases NiTi ion release, and fluoride mouthwashes can enhance galvanic corrosion; mouthwash type, arch type, and acidity further influence release. (9-11,45) Because fixed appliances promote plaque accumulation and inflammation, clinicians should consider the oral environment as a key risk modifier. (7,11)
Patient susceptibility is central: nickel sensitization is common but does not consistently translate into clinical symptoms during treatment. (4-6,47,48) When reactions are suspected, structured clinical assessment and patch testing are appropriate. (3,52)

Clinical strategies supported by the reviewed evidence include:
1. Optimizing oral hygiene and controlling inflammation to reduce plaque-associated acidic microenvironments and inflammatory oxidative burden. (7,11)
2. Rational/individualized use of fluoride agents, especially in patients with sensitivities, acknowledging their potential effects on corrosion in certain contexts. (10,45,60,61)
3. Strict adherence to polymerization protocols and removal of excess adhesive, to reduce elution of resin-based components and improve biocompatibility. (21,24,25)
4. Product- and system-specific evaluation for thermoplastics, recognizing aging effects and variable in vitro profiles. (13-15,28,29)
5. Systematic evaluation of suspected adverse reactions, including consideration of clear aligner–related adverse events and differential diagnosis. (34,35)

LIMITATIONS OF CURRENT EVIDENCE AND FUTURE DIRECTIONS

Systematic reviews emphasize that much of the evidence is heterogeneous in methodology, limiting direct comparison and clinical extrapolation. (16,17) In vitro cytotoxicity testing is sensitive to exposure modeling and assay limitations, reinforcing cautious interpretation. (21,25,55,56) Biomarkers such as comet assay detect molecular effects but require contextual interpretation and long-term correlation with clinical outcomes. (31-33)
Future research should prioritize standardized protocols and long-term clinical studies integrating analytical measurements, biomarkers, and clinically meaningful endpoints. (1,16,31)

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Conclusion

Materials used in orthodontic treatment may release metal ions and organic components under both clinical and experimental conditions. Such exposures may be associated with hypersensitivity reactions, cytotoxic effects, and measurable changes in biomarkers related to oxidative stress and genotoxicity. Importantly, the biological impact is not determined by material composition alone; it is strongly influenced by the oral environment, clinical protocols, treatment duration, and individual susceptibility. Therefore, a clinically meaningful approach should prioritize exposure control (oral hygiene and inflammation management), protocol optimization, and patient-specific risk stratification, together with material- and system-specific interpretation rather than generalized “safe/unsafe” judgments.

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