International Journal of Dental Research and Allied Sciences
2025, Volume 5, Issue 2, Page No: 125-139

Available online at: www.tsdp.net
ISSN: 3062-3502

Review Article

A Narrative Review of Nickel Ion Release from NiTi and Stainless Steel Orthodontic Archwires: In Vitro and In Vivo Perspectives

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Received: 03 August 2025; **Revised:** 03 November 2025; **Accepted:** 06 November 2025

ABSTRACT

Nickel-titanium (NiTi) and stainless steel (SS) archwires are fundamental components of fixed orthodontic therapy due to their unique mechanical properties. Despite their widespread use, there is ongoing concern regarding nickel-related adverse effects, including hypersensitivity reactions, cytotoxicity, and the release of metal ions into the oral environment. This narrative review synthesizes recent research on nickel ion liberation from orthodontic archwires, incorporating both in vitro and in vivo studies under varying environmental conditions, building on insights from prior systematic reviews. Searches of Web of Science, Scopus, and PubMed were conducted to identify studies examining how factors such as pH, corrosion, duration of use, and other environmental variables influence nickel release. Evidence indicates that while nickel ions are detectable during short-term exposure, the concentrations generally remain below thresholds associated with toxicity. Long-term data, however, are sparse and often limited to either laboratory or clinical settings rather than both. Comprehensive in vivo monitoring is essential to clarify the clinical relevance of nickel release and its potential systemic impact over time. Coordinated efforts among clinicians, researchers, and regulatory agencies are necessary to inform material selection, minimize patient risk, and establish evidence-based guidelines for the safe use of nickel-containing orthodontic appliances.

Keywords: Artificial saliva, Nickel-containing archwires, In vitro, In vivo, Nickel release, Orthodontic appliances

How to Cite This Article: Özcan Z, Yıldız A. A Narrative Review of Nickel Ion Release from NiTi and Stainless Steel Orthodontic Archwires: In Vitro and In Vivo Perspectives. Int J Dent Res Allied Sci. 2025;5(2):125-39. https://doi.org/10.51847/a1w5WPfNz1

Introduction

Exposure to elevated levels of nickel has been associated with a range of adverse health effects [1]. Historical reports include fatal cases following inhalation of nickel carbonyl, and by the early 20th century, nickel was identified as a common cause of contact dermatitis. Occupational exposure in nickel-processing industries was linked to increased incidences of lung and nasal cancers [2, 3]. In 2008, nickel was designated "Allergen of the Year" by Gillette [4], reflecting dermatologists' concerns about the rising prevalence of nickel hypersensitivity. These observations have fueled ongoing research into the broader impact of nickel on human health [5]. Nickel is also classified as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC), although there is currently no definitive evidence implicating nickel released from orthodontic appliances in cancer development among patients [6].
Most industrial nickel is used in the production of stainless steel and nickel alloys [7], which are widely applied in medical devices, including orthodontic archwires. Archwires are central to fixed orthodontic treatment, serving as the primary means of achieving controlled tooth movement [8]. Despite advances in materials and orthodontic techniques, no single

archwire is universally ideal for all stages of treatment [9]. Among commonly used materials are nickel-titanium (NiTi) alloys—with or without additional elements such as copper—and stainless steel (SS).

NiTi and SS wires are frequently employed due to their favorable mechanical properties. NiTi wires may contain over 50% nickel, whereas copper-nickel-titanium alloys typically contain slightly less than 50%, and SS wires contain approximately 8% nickel [10–12]. SS wires are generally easier to manipulate and present a lower risk of eliciting allergic reactions compared to NiTi wires. The 12–13% chromium content in SS alloys facilitates the formation of a thin, passivating chromium oxide layer that inhibits corrosion by limiting oxygen penetration into the underlying metal [13]. However, SS wires are relatively rigid and less flexible, often requiring more frequent adjustments during treatment [14, 15].

NiTi archwires, in contrast, exhibit high elasticity, shape memory, and resistance to permanent deformation. While exposure to elevated temperatures can induce irreversible changes, temporary deformations at lower temperatures can typically be reversed upon reheating [16]. Despite these advantages, concerns remain regarding the cytotoxic, allergenic, and potentially mutagenic effects of nickel, raising questions about NiTi biocompatibility [17].

Prolonged orthodontic therapy may influence the integrity of both NiTi and SS wires due to variations in pH, fluoride concentration, and oral environment conditions. Although corrosion of orthodontic appliances is well documented, its clinical and health implications remain poorly understood. Research shows that metal ions are released during treatment, but typically at concentrations far below those encountered in the daily diet. Further studies in clinically relevant settings are needed to fully assess these effects [18, 19].

Nickel hypersensitivity and allergic reactions in orthodontic patients can arise from multiple factors, including inherent nickel sensitivity, with some studies indicating higher sensitization rates in females [11, 20, 21].

The introduction of NiTi alloys into orthodontics prompted investigations into their biocompatibility. Wever *et al*. [22] conducted a combined in vitro and in vivo evaluation of NiTi alloys, demonstrating low ion release and strong corrosion resistance, supporting their short-term biological safety. Recent studies over the past decade corroborate these findings, indicating that nickel ion concentrations in patients' saliva remain below toxic thresholds during orthodontic treatment and often decrease after an initial release peak [23].

Allergic reactions induced by nickel from orthodontic alloys

While nickel-titanium (NiTi) alloys are generally considered safe for clinical use, the release of nickel ions can still provoke adverse effects in susceptible individuals. Similar to a type IV (delayed-type) hypersensitivity reaction, nickel-induced allergic responses in orthodontics involve a two-phase process: sensitization, during which immune cells recognize nickel ions and generate memory T-cells, and elicitation, where repeated exposure triggers the release of pro-inflammatory cytokines. This immunological cascade typically results in localized inflammation, often presenting extra-orally as contact dermatitis, characterized by erythema, swelling, or, in severe cases, oral ulceration [24, 25]. Other metals present in orthodontic appliances, including chromium, cobalt, copper, titanium, and silver, can also elicit allergic responses [11]. Beyond type IV reactions, nickel released from fixed appliances may cause additional systemic or extra-oral manifestations, as highlighted in reviews by Di Spirito *et al*. [26].

Although recent studies indicate that the concentration of metal ions released during orthodontic treatment is substantially lower than that encountered in daily dietary intake, the complex interactions between material properties, oral environment, and patient-specific factors continue to pose challenges for fully understanding the clinical implications [27–29]. Nickel remains the most common cause of metal-induced allergic contact dermatitis, responsible for more allergic reactions than all other metals combined [30].

Influence of saliva and environmental factors on nickel release

The oral environment plays a pivotal role in determining the rate and extent of nickel ion release from orthodontic appliances. Brackets, bands, and archwires are continuously exposed to variable conditions such as fluctuating pH levels—often influenced by diet—temperature changes, mechanical stress, and the corrosion susceptibility of the alloy [31]. Multiple studies have simulated oral conditions by immersing nickel-containing archwires in artificial saliva for periods corresponding to typical treatment durations [29, 32, 33]. These investigations demonstrate that nickel concentrations in saliva and serum can increase after the placement of fixed appliances [34]. Nevertheless, the detected levels remain well below toxic thresholds, with permissible limits in drinking water far exceeding the amounts observed from orthodontic exposure [35].

Surface passivation layers, primarily composed of chromium and titanium oxides, serve to inhibit corrosion and slow ion release. However, these protective layers can degrade due to mechanical wear, polishing, or low pH conditions [13]. Additional strategies to further reduce nickel release include applying protective coatings to orthodontic appliances [36, 37].

Interestingly, some studies have linked exposure to electromagnetic radiation from mobile phones to elevated nickel release from Ni-containing archwires [38, 39]. Mitigation strategies, such as using earphones to increase the distance from the phone, appear to reduce this effect [39].

Systematic reviews by Mikulewicz and Chojnacka (2009, 2010) [31, 35] concluded that short-term use of orthodontic appliances does not result in toxic nickel or metal ion levels. However, data on long-term exposure remain limited. A 2019 meta-analysis by Imani *et al.* [40] supported the notion that small amounts of nickel are released, potentially inducing oral tolerance in early treatment stages, but emphasized the need for larger, more diverse studies controlling for variables such as saliva composition.

The aim of this review is to summarize the evolution of knowledge regarding nickel ion release, highlight recent findings, and identify directions for future research. Studies are categorized into in vitro and in vivo investigations, with an emphasis on how environmental and material-specific factors influence nickel release from orthodontic archwires.

Scope and sources of reviewed literature

This narrative review provides a detailed examination of current evidence regarding nickel ion release from the most commonly used orthodontic archwire alloys: stainless steel (SS) and nickel-titanium (NiTi). The review encompasses various types of archwires, including CrNi stainless steel wires, thermodynamic heat-activated (martensitic) NiTi and CuNiTi wires, as well as superelastic (austenitic) NiTi wires.

To capture relevant and high-quality studies, a focused literature search was conducted using the Web of Science, Scopus, and PubMed databases. Keywords included combinations of terms such as “nickel ion release,” “nickel content dynamics,” “stainless steel orthodontic archwires,” “nickel-titanium archwires,” “in vivo,” and “in vitro.” Studies were selected based on the following inclusion criteria: (a) the research evaluated nickel-containing archwires composed of SS or NiTi alloys; (b) nickel ion release was assessed under either in vitro or in vivo conditions; and (c) environmental factors potentially influencing nickel release, such as pH, temperature, or other oral conditions, were examined.

It should be noted that this review employed a narrative rather than a systematic approach. While the literature search and study selection were conducted with care to ensure relevance and breadth, the methodology did not follow the strict protocols typical of systematic reviews. Instead, the aim was to provide a critical synthesis of the available evidence, highlighting key factors that modulate nickel release from orthodontic materials and offering contextual interpretation.

Studies that did not meet the above criteria were excluded from this review **(Figure 1)**. This strategy allowed the review to remain focused on the most pertinent research while still offering a comprehensive overview of nickel ion release from contemporary orthodontic archwires.

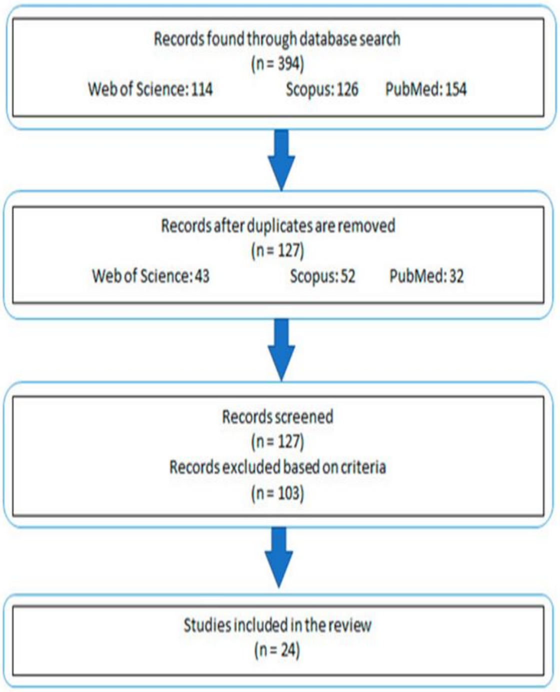

Figure 1. Schematic representation of the study selection and exclusion process.

Key findings from the literature

Analytical methods such as atomic absorption spectrometry (AAS) and atomic emission spectroscopy (AES) are most commonly employed to quantify metal ion release due to their sensitivity with low-volume samples. Additionally, scanning electron microscopy coupled with energy-dispersive spectroscopy (SEM/EDS) is frequently used to assess surface composition and examine localized morphological changes in orthodontic materials.

In vitro studies of nickel-containing archwires

The majority of in vitro investigations simulate the oral environment using artificial saliva. **Table 1** summarizes the compositions of the artificial saliva used across the studies included in this review.

Several studies have explored the influence of artificial saliva and other factors on nickel ion release over varying time periods. For instance, Cioffi *et al*. [41] examined pseudoelastic NiTi archwires under simulated physiological conditions and fluoridated media. Their results indicated that tensile stress-induced phase transformations did not trigger nickel release, whereas prolonged fluoride exposure significantly increased ion leaching, highlighting the need for further evaluation of fluoride's short-term effects.

Similarly, researchers [42] investigated common archwires immersed in various commercial mouthwashes. Their findings revealed that fluoride-containing mouthwashes can enhance nickel release, potentially increasing hypersensitivity risk, warranting caution during clinical use.

Mirjalili *et al*. [18] assessed localized corrosion and the effect of pre-passivation treatments on archwires using potentiodynamic and potentiostatic techniques. NiTi wires showed no pitting corrosion in artificial saliva, while SS wires exhibited minimal protective effects. Artificial crevices did not significantly influence corrosion behavior, whereas pre-passivation improved resistance to pitting in both alloy types in the presence of fluoride ions.

Other researchers [43] analyzed NiTi wires alongside SS brackets, bands, and ligatures. They reported varying surface morphologies due to manufacturing differences. As-received SS bands and brackets displayed signs of pitting corrosion. Upon immersion, adhesive coatings formed on SS components, but protective oxide layers were absent. Salt precipitates, primarily KCl, were observed, and SS bands released higher amounts of ions compared to other components, attributed to welding processes rather than surface roughness.

Gianidis *et al*. [44] studied SS, NiTi, and CuNiTi archwires immersed in artificial saliva. Analysis revealed that chromium and nickel were the predominant ions released over 30 days, with ion release increasing at lower pH (maximum at pH 3.5). Nonetheless, levels remained below typical dietary intake.

Laird *et al*. [45] evaluated nickel release from five archwires in buffer solutions with varying pH. Results indicated that ion release increased over time but decreased at higher pH, and coated wires consistently released fewer ions than uncoated ones.

Osmani *et al*. [46] examined six archwire types (NiTi, coated NiTi, SS, nickel-free SS, CoCr, and TMA) at different pH levels. NiTi released more nickel and titanium than coated NiTi, while SS released more iron, chromium, and nickel compared to nickel-free SS. CoCr alloys emitted high cobalt concentrations with lower levels of other metals, and overall, ion release was lower at near-neutral pH and in hypoallergenic alloys. Al-Jammal *et al*. [47] corroborated these findings using NiCr alloys, showing that ion release was highest at acidic pH (2.5), with nickel being released more than chromium.

Chikhale *et al*. [48] compared TMA and NiTi wires, demonstrating higher nickel release from NiTi, whereas TMA released more titanium. Despite this, all release levels remained within safety limits.

Aiswareya *et al*. [29] combined bracket and archwire analyses, measuring nickel and chromium release from NiTi and SS wires attached to SS and ceramic brackets in artificial saliva. Wires attached to SS brackets released more ions, though the wire material alone did not significantly affect release. Cytotoxicity testing on HeLa cells indicated no harmful effects at measured concentrations.

Kao *et al*. [49] studied the cytotoxicity of fluoride-corroded SS and heat-activated NiTi wires on U2OS cells at varying pH, concluding that fluoride-containing agents can pose cytotoxic risks, emphasizing clinical caution. Senkutvan *et al*. [33] confirmed that while ion release occurs in acidic conditions, levels from NiTi, SS, CuNiTi, and ion-implanted NiTi wires remain below thresholds likely to trigger allergic reactions, supporting their clinical safety.

Table 1. Artificial Saliva Compositions and Their References

Composition	pH	References
Phosphate Buffered Saline (PBS)	4.6	[41]
PBS with 0.001% Sodium Fluoride (NaF)	4.8	[41]
PBS with 0.01% Sodium Fluoride (NaF)	5.0	[41]
PBS with 0.1% Sodium Fluoride (NaF)	5.6	[41]

Sodium Chloride (0.844 mg), Potassium Chloride (1.2 mg), Calcium Chloride Anhydrous (0.146 mg), Magnesium Chloride Hexahydrate (0.052 mg), Potassium Phosphate Dibasic (0.34 mg), 70% Sorbitol Solution (60 mg), Methyl Paraben (2 mg), Hydroxyethyl Cellulose (3.5 mg)	-	[17, 30, 48]
Sodium Chloride (0.4 g), Potassium Chloride (1.21 g), Sodium Hypophosphate (0.78 g), Sodium Sulfide (0.005 g), Urea (1 g), Distilled and Deionized Water (1000 mL)	-	[29, 33]
Neutral Solution: Calcium (1.5 mM), Phosphorus (0.9 mM), Tris Buffer (20 mM), Potassium Chloride (150 mM)	7.0	[32]
Acidic Solution: Calcium (2 mM), Phosphorus (2 mM), Acetate Buffer (74 mM)	4.3	[32]
Potassium Chloride (0.4 g), Sodium Chloride (0.4 g), Calcium Chloride Dihydrate (0.906 g), Sodium Dihydrogen Phosphate Dihydrate (0.69 g), Sodium Sulfide Nonahydrate (0.005 g), Urea (1 g)	-	[18]
Sodium Chloride (0.84 mg/100 mL), Potassium Chloride (1.2 mg/100 mL), Magnesium Chloride (0.052 mg/100 mL), Calcium Chloride (0.146 mg/100 mL), Potassium Dihydrogen Phosphate (0.34 mg/100 mL), 70% Sorbitol Solution (60 mL), Hydroxyethyl Cellulose (3.5 mg/100 mL)	-	[49]
Potassium Chloride (1.5 g/L), Sodium Bicarbonate (1.5 g/L), Potassium Thiocyanate (0.5 g/L), Lactic Acid (0.9 g/L)	-	[37, 42, 46]
Dipotassium Hydrogen Phosphate (7.69 g), Potassium Dihydrogen Phosphate (2.46 g), Sodium Chloride (5.3 g), Potassium Chloride (9.3 g), Distilled Water (1000 mL)	-	[47]

Sodium chloride (NaCl); potassium chloride (KCl); monosodium phosphate (NaH_2PO_4); water (H_2O); sodium sulfide (Na_2S); urea ($CO(NH_2)_2$); calcium chloride ($CaCl_2$); sodium bicarbonate ($NaHCO_3$); potassium thiocyanate (KSCN).

In vivo and environmental factors affecting nickel ion release

Unlike in vitro conditions, saliva in the oral cavity is dynamic, which significantly impacts metal ion release. To simulate this, Mikulewicz *et al*. [50] designed a thermostatic glass reactor with a continuous flow of artificial saliva to mimic oral conditions. Their results indicated that nickel release from stainless steel (SS) archwires remained well below toxic thresholds, supporting their clinical safety.

Patient use of oral hygiene products is another important factor influencing ion release. Jamilian *et al*. [30] examined nickel and chromium leaching from SS and round NiTi archwires immersed in three solutions—Oral B®, OrthoKin®, and artificial saliva. Ion release increased over time, with artificial saliva producing the lowest concentrations, and SS wires releasing ions at a slower rate than NiTi wires.

Similarly, Mirhashemi *et al*. [51] evaluated the impact of various mouthwashes on ion release from orthodontic wires. Listerine caused the highest levels of metal release, whereas Oral B® had the lowest. Zubaidy and Hamdany [52] investigated the effect of magnetically treated water (MTW) on SS archwires and found significantly reduced nickel release compared to conventional mouthwashes, suggesting MTW as a potentially safer alternative during treatment.

Beyond hygiene products, natural extracts may also modulate ion release. Erwansyah *et al*. [53] demonstrated that Salacca zalacca (snake fruit) extract at 300 ppm could inhibit nickel release from SS wires, indicating a possible protective effect.

Wire geometry also plays a role in ion leaching. Azizi *et al*. [17] compared round and rectangular NiTi wires, finding that rectangular wires released more ions, particularly during the initial hour of immersion in artificial saliva, highlighting that archwire shape affects ion release under simulated oral conditions.

Even though measured ion release generally remains below harmful thresholds, evaluating direct cellular toxicity is important. Dugo *et al*. [54] assessed the cytotoxic effects of NiTi and SS archwire components (wires, brackets, bands, and ligatures) on four human cell lines (CAL 27—epithelial, HepG2—hepatic, CaCo-2—colon, and AGS—gastric). Most eluates demonstrated cytotoxicity in CAL 27 cells, while CaCo-2 cells were more resistant. All samples generated reactive oxygen species (ROS) in AGS and HepG2 cells, with higher concentrations sometimes reducing ROS compared to lower concentrations. Trace metals such as Cr, Mn, and Al contributed to mild genotoxicity and pro-oxidative DNA effects, though these effects were not considered clinically significant. Statistical analysis linked Fe and Ni to ROS production, while Mn and Cr influenced hydroxyl radical generation, collectively contributing to cytotoxicity.

Thiyagarajan *et al*. [55] used electrochemical methods to study nickel release from NiTi, SS, and CuNiTi archwires immersed in artificial saliva for three days. NiTi and CuNiTi wires displayed superior corrosion resistance compared to SS, and nickel release was minimal, further supporting the relative safety of these materials in orthodontic treatment.

In vivo investigations of nickel release from orthodontic archwires

Clinical studies on nickel-containing archwires have explored their behavior during orthodontic treatment periods ranging from one week up to 18 months. This section summarizes these investigations according to treatment duration and concludes with analyses examining trends in nickel release over time. **Table 3** presents a concise overview of each study, including wire type, brand, ions analyzed, duration of use, and evaluation methods.

Nickel-containing orthodontic appliances have attracted attention due to their potential to elicit allergic responses and release metal ions into the oral cavity. Ghazal *et al*. [56] compared superelastic and heat-activated NiTi wires, focusing on surface morphology and nickel release over 30 days of clinical use. Both wire types released similar quantities of nickel ions, though superelastic wires demonstrated greater surface roughness. Interestingly, nickel release decreased when the retrieved wires were re-immersed in artificial saliva, suggesting that ion release may reduce with time despite ongoing surface alterations.

Ibañez *et al*. [57] investigated changes in metal ion release over time in heat-activated NiTi and stainless steel (SS) archwires, correlating release with salivary pH. Although a peak in ion release was observed, the levels remained within safety thresholds. Salivary pH initially dropped to acidic levels after three months but returned to near-neutral values by six months, indicating potential adaptation of the oral environment during treatment.

Almasry *et al*. [58] monitored nickel release from round thermoactive NiTi wires during the first two months of use. A minor increase in nickel levels was noted; however, concentrations stayed below recognized safety limits, confirming that clinically relevant nickel release remains low during short-term therapy.

Bass *et al*. [59] focused on patients with known nickel hypersensitivity treated with SS and NiTi archwires. Among 29 participants, five females were initially sensitive to nickel, and two additional cases developed sensitivity during treatment. The study concluded that nickel hypersensitivity occurs predominantly in female patients, and orthodontic appliances may provoke reactions in susceptible individuals without significantly affecting overall oral health.

Lages *et al*. [60] evaluated salivary metal ion concentrations in patients using metal and esthetic appliances, including SS brackets and heat-activated NiTi wires. No significant differences in nickel levels were detected between the control group and patients with either metal or esthetic devices. However, the type of appliance influenced nickel concentration, highlighting the importance of material selection in minimizing ion exposure.

Amini *et al*. [61] compared salivary metal content between patients with fixed orthodontic appliances and untreated same-gender siblings. The treated group, using NiTi and SS archwires along with SS brackets and bands, exhibited higher salivary nickel levels, whereas chromium concentrations were comparable between groups. These findings indicate that fixed orthodontic appliances contribute to increased nickel exposure in the oral environment.

Table 2. General overview of the nickel-containing archwires and methods used in the reviewed in vitro studies.

Material	Brand and Manufacturer	Ions Studied	Study Media	Exposure Time	Method of Analysis	Reference
NiTi	Nitinol N (0.5 × 0.5 mm), Nitinol S (0.05 and 1 mm foil) (Memory-Metalle GmbH, Weil am Rhein, Germany); Sentalloy Standard (0.46 × 0.46 mm), Neo Sentalloy Standard (0.46 × 0.63 mm) (GAC International Inc., Bohemia, NY, USA)	Ni	Artificial saliva (fluoridated and non-fluoridated)	7 days	Thin Layer Activation, X-ray Photoelectron Spectroscopy	[41]
NiTi	Round (0.020 in) and Rectangular (0.016 × 0.016 in) NiTi Archwires (Ortho Technology, Tampa, FL, USA)	Ni, Ti	Artificial saliva	1 h, 24 h, 7 days, 21 days	Inductively Coupled Plasma Atomic Emission Spectrometry	[17]

NiTi, TiMo	NiTi Archwire (17 × 25 in), TMA Archwire (17 × 25 in) (Modern Orthodontics, Ludhiana, India)	Ni, Ti	Artificial saliva	90 days	Atomic Absorption Spectrometry	[48]
SS, NiTi, TiMo	SS (American Orthodontics, Sheboygan, WI, USA); NiTi (Neo Sentalloy, GAC, West Columbia, USA); TiMo (Beta Blue, Highland Metals, Bangkok, Thailand)	Ni, Ti	Mouthwashes (brands not specified)	1 day, 4 days, 7 days, 14 days	Inductively Coupled Plasma Mass Spectrometry, Scanning Electron Microscopy	[43]
NiTi, CuNiTi	NiTi Memory Wire (0.016 in), Damon Optimal-Force Cu Ni-Ti (0.016 in), Tanzo Cu NiTi (0.016 in) (American Orthodontics); Flexy NiTi Cu (0.016 in) (Orthometric)	Ni, Cu	Neutral and acidic solutions	7 days	Graphite Furnace Atomic Absorption Spectrometry, Inductively Coupled Plasma Atomic Emission Spectrometry	[32]
NiTi, Coated NiTi, SS, Ni-free SS, CoCr, TMA	BioForce Sentalloy, High Aesthetic (Dentsply GAC, New York, NY, USA); Remanium, Noninium, Elgiloy, Rematitan Special (Dentaurum, Ispringen, Germany)	Ni, Ti	Artificial saliva	3 days, 7 days, 14 days, 28 days	Inductively Coupled Plasma Mass Spectrometry	[46]
NiTi, CuNiTi, SS	Not specified	Ni	Artificial saliva	3 days	Cyclic Voltammetry, Electrochemical Impedance Spectroscopy, Polarization (Tafel) Plot	[55]
NiTi, Esthetic Wires, SS	NiTi (0.019 × 0.025 in, Ormco, Glendora, CA, USA); FLI Wire (0.019 × 0.025 in, Rocky Mountain Orthodontics, Denver, CO, USA); Iconix (0.019 × 0.025 in, American Orthodontics, Sheboygan, WI, USA); Bio-Active RC (0.019 × 0.025 in, GC Orthodontics, TOMY Inc., Fuchu City, Tokyo); SS (0.019 × 0.025 in, 3M Unitek, St. Paul, MN, USA)	Ni, Cr	Buffer solutions (pH 4, 5.5, 7)	4 weeks, 13 weeks	Inductively Coupled Plasma Mass Spectrometry	[45]
NiTi, SS	Rematitan® LITE Ideal Arches (0.43 × 0.64 mm, Dentaurum, PA, USA)	Fe, Ni, Cr, Mn, Al, Ti, Cu	Artificial saliva	3 days, 7 days, 14 days	Scanning Electron Microscopy with Energy Dispersive Spectroscopy, Inductively Coupled Plasma Mass Spectrometry	[42]
NiTi, SS, CuNiTi	SS Upper 016 Form III (0.016 × 0.016), NiTi Form I Upper 016 (0.016 × 0.016), Tanzo® CuNiTi (0.016 × 0.016), Tru-Arch® UM (0.016 × 0.016), Tru-Arch® CuNiTi 35°C UL (0.016 × 0.022) (Ormco)	Ni, Mn, Cr, Mo, Ti	Artificial saliva	7 days, 30 days	Inductively Coupled Plasma Optical Emission Spectrometer	[44]

NiTi, SS	SS (Fe-18Cr-8Ni, 0.010/0.014/0.016 × 0.022 in), Heat-Activated Nitinol (0.016/0.016 × 0.022 in) (3M Unitek, Monrovia, CA, USA)	Ni, Ti, Cr	Artificial saliva	1 h, 24 h	Atomic Absorption Method	[49]
NiTi, SS, CuNiTi, Ion-implanted NiTi	NiTi (0.016 × 0.022 in), SS (0.016 × 0.022 in) (American Orthodontics, Sheboygan, WI, USA); Ion-implanted NiTi (0.016 × 0.022 in, GAC International, Bohemia, NY, USA); CuNiTi (0.016 × 0.022 in, Ormco)	Ni	Artificial saliva	7 days, 14 days, 21 days	Atomic Absorption Method	[33]
NiTi, SS	SS Rectangular Archwires (0.017 × 0.025 in), NiTi Rectangular Archwires (0.017 × 0.025 in) (Ormco)	Ni, Cr	Artificial saliva	7 days, 14 days, 1 month	Flame Atomic Absorption Spectrometry	[29]
NiTi, SS	Nitinol (0.4 mm, Dentaurum, Germany); SS304 (0.4 mm, Tiger Ortho, Boston, MA, USA)	Ni, Ti, Cr, Mo, Mn	Fusayama–Meyer solution	Not specified	Potentiodynamic and Potentiostatic Polarizations, Energy Dispersive X-ray, Atomic Absorption Spectroscopy	[18]
NiTi, SS	SS (0.018 in diameter), NiTi (0.018 in diameter) (American Orthodontics, Sheboygan, WI, USA)	Ni, Cr	Oral B®, Orthokin®, Artificial Saliva (SaliLube®, Sinphar Pharmaceutical Co., Ltd., Taipei, Taiwan)	1 h, 6 h, 24 h, 7 days	Atomic Absorption Method	[30]
NiTi, SS	Not specified	Ni, Cr	Oral B®, Oral B® 3D White Luxe, Listerine, Listerine Advanced White	1 h, 6 h, 24 h, 168 h	Atomic Absorption Spectroscopy	[51]
SS	Not specified	Ni, Cr	Snakefruit Extract (Salacca zalacca)	24 h	Atomic Absorption Spectrophotometry	[50]
SS	SS Archwires (0.016 × 0.022 in, Dentaurum, Germany)	Ni	Magnetically Treated Water, OrthoKin®	24 h, 2 weeks, 4 weeks	Scanning Electron Microscopy, Atomic Absorption Spectrometry	[52]
NiCr (Alloy)	Not specified	Ni, Cr	Artificial saliva	12 days, 24 days, 36 days	Atomic Absorption Spectroscopy	[47]

Nickel-Titanium (NiTi); nickel-titanium with coating (coated NiTi); copper nickel-titanium (CuNiTi); stainless steel (SS); nickel-chromium (NiCr); nickel-free stainless steel (Ni-free SS); titan-molybdenum (TiMo); cobalt-chromium (CoCr); titanium-molybdenum alloy (TMA); days (d); inches (in).

Table 3. General overview of the nickel-containing archwires and analytical methods used in the reviewed in vivo studies.

Material	Brand and Manufacturer	Ions Studied	Study Media	Exposure Time	Method of Analysis	References
NiTi	NiTi Force I® (0.019 × 0.025 in), Therma-Ti Lite® (0.019 × 0.025 in) (American Orthodontics, Sheboygan, WI, USA)	Ni	Oral environment	1 month	Scanning Electron Microscopy, Atomic Force Microscopy, Atomic Absorption Spectrophotometry	[56]
NiTi, CuNiTi	Superelastic (Austenitic) NiTi (0.016 × 0.022 in), Heat-Activated NiTi (0.016 × 0.022 in), Heat-Activated CuNiTi (0.016 × 0.022 in) (Manufacturer not specified)	Ni	Oral environment	6 weeks, 8 weeks	Energy Dispersive X-ray, Dynamic Modeling	[62]
NiTi, Rh-coated NiTi, SS	Heat-Activated Nitinol Archwire, Rhodium Polymer-Coated Heat-Activated Nitinol Archwire (0.014 in) (Abzil, São José do Rio Preto, SP, Brazil; BioActive, Crystal 3D, São Carlos, SP, Brazil)	Ni, Cr, Fe, Cu	Oral environment	1–6 months	Total Reflection X-Ray Fluorescence Technique	[60]
NiTi, SS	Not specified	Not specified	Oral environment	3 months	Nickel Patch, Gingival Index, Plaque Index, Intraoral Photographs	[59]
NiTi, SS	Ni-Ti Heat-Activated Wires (0.016 in), Stainless Steel Wires (0.016 × 0.022 in) (3M™ Unitek™)	Ni, Ti	Oral environment	1 month	Coupled Plasma Optical Emission Spectroscopy, Scanning Electron Microscopy	[57]
NiTi, SS	Round Thermoactive Archwires (0.016 in) (Equire Thermo-Aktive, Dentaurum, Germany)	Ni	Oral environment	7 days, 1 month, 2 months	Atomic Absorption Spectrophotometry	[58]
NiTi, SS, CuNiTi	Stainless Steel CrNi, Superelastic (Austenitic) NiTi, Thermodynamic Heat-Activated NiTi, Thermodynamic Heat-Activated CuNiTi, TriTanium™, Bio-Active™ (Manufacturer not specified)	Ni	Oral environment	6 weeks, 8 weeks	Scanning Electron Microscopy with Energy Dispersive Spectroscopy, Dynamic Modeling	[63]
NiTi, SS	Pre-adjusted Roth Stainless Steel Brackets (0.018 in), Stainless Steel Orthodontic Bands (Discovery, Dentaurum, Pforzheim, Germany; Unitek/3M, Monrovia, CA, USA); Nitinol, Stainless Steel Archwires (Ormco Corporation, Orange, CA, USA; Remantium, Dentaurum)	Ni, Cr	Oral environment	12–18 months	Atomic Absorption Spectrophotometry	[61]

Nickel-Titanium (NiTi); nickel-titanium with coating (coated NiTi); copper nickel-titanium (CuNiTi); stainless steel (SS); nickel-chromium (NiCr).

Dynamics of nickel release from orthodontic archwires

Several studies have investigated how nickel content in orthodontic archwires changes during clinical use, aiming to inform recommendations regarding safe usage durations and minimize potential risks associated with nickel exposure [62, 63].

A 2019 study [62] examined austenitic NiTi, heat-activated NiTi, and CuNiTi archwires. Wires were divided into four groups: autoclaved as-received (S0), non-autoclaved as-received (S1), used intraorally for up to six weeks (S2), and used for over eight weeks (S3). Nickel levels were measured across multiple areas along each wire, with both overall averages (global) and specific localized spots (local) analyzed. While global averages showed minimal differences between groups, local assessments revealed significant changes in nickel content among S1, S2, and S3. Based on these data, the authors proposed a general model of nickel release over time, noting that patient-specific factors should guide clinical decisions.

Building on this, a 2025 study [63] included the same NiTi and CuNiTi wires, as well as stainless steel (SS) and multi-force archwires. Wires were grouped into as-received, used for up to six weeks, and used for more than eight weeks. The results highlighted that nickel release patterns differ across alloys and are influenced by both material composition and intraoral conditions. Stable alloys such as SS-CrNi, HA-NiTi-Cu, and TriTanium™ were deemed suitable for longer-term use. In contrast, superelastic NiTi, HA-NiTi without copper, and Bio-Active™ released more nickel and were recommended primarily for short- to medium-term application. The study emphasized that these findings serve as general guidance and that clinicians should tailor wire selection to individual patient needs.

These findings reinforce that nickel-containing orthodontic devices can release metal ions and, in some cases, cause sensitization—particularly in female patients. However, the quantities of nickel released are generally within clinically safe limits. The extent of release is affected by several factors, including wire surface texture, type of alloy, and duration of use. Appropriate material choice and periodic monitoring can reduce the risk of hypersensitivity reactions during treatment.

Additional variables, such as fluoride exposure, saliva pH, oral hygiene products, dietary habits, immersion time, saliva flow dynamics, and wire geometry, also influence nickel release. Understanding these factors is critical for ensuring patient safety and optimizing the selection of orthodontic materials.

Literature overview

Across the 24 studies reviewed, which focus primarily on NiTi (with and without copper) and stainless steel archwires, a clearer picture of nickel release in both laboratory and clinical settings emerges. Research has evolved from broad concerns about NiTi biocompatibility to a nuanced understanding of the factors controlling nickel ion release. These insights are essential for clinicians aiming to balance mechanical performance with patient safety in fixed orthodontic treatments.

Biocompatibility and short-term safety of NiTi alloys

Wever *et al*. [22] provided foundational evidence on the short-term biocompatibility of nickel-titanium (NiTi) alloys, which are widely used in orthodontic archwires. Through combined in vitro and in vivo evaluations, their research demonstrated that NiTi exhibits minimal cytotoxicity, low potential for sensitization, and strong resistance to corrosion, supporting its suitability for clinical application. These findings are reinforced by Kovac *et al*. [64], who reported that ion release from NiTi wires and stainless steel (SS) brackets remains below the recommended daily intake limits even after extended periods of exposure. Notably, higher concentrations of ions were observed in accumulated debris compared to artificial saliva, highlighting the relevance of localized nickel accumulation—such as in food particles or plaque—which could contribute to hypersensitivity in susceptible patients. Matusiewicz [65] also emphasizes that metallic debris released through corrosion can accumulate over time, particularly in individuals with suboptimal oral hygiene.

In vitro studies consistently indicate that nickel and other metal ions released by orthodontic appliances do not reach harmful levels. However, the controlled nature of these studies cannot fully replicate the complexity of individual oral environments, making in vivo research essential. Clinical studies confirm that nickel release from orthodontic archwires is generally within safe thresholds but can occasionally trigger sensitization, with a higher prevalence among female patients. Careful material selection and periodic monitoring can effectively minimize such risks, ensuring orthodontic treatment remains safe for the majority of patients.

Effects of fluoride, salivary pH, and oral environment

Exposure to fluoride has been identified as a critical factor influencing nickel release. Cioffi *et al*. [41] and Mirjalili *et al*. [18] found that while NiTi wires maintain their phase stability under tensile stress, prolonged contact with fluoridated media significantly enhances nickel ion release. Given the widespread use of fluoride-containing oral care products among orthodontic patients, this finding carries important clinical implications. Similarly, Kao *et al*. [49]

highlighted potential cytotoxic effects from fluoride corrosion extracts in acidic conditions, underscoring the need for careful management of low-pH fluoride agents in patients with NiTi archwires. Alternative interventions, such as magnetically treated water, have been shown to reduce ion release compared to conventional mouthwashes, as demonstrated by Zubaidy and Hamdany [52].

The dynamic properties of saliva further influence nickel release. Mikulewicz *et al*. [50] developed a thermostatic reactor to simulate continuous salivary flow, confirming that nickel release from SS wires remains well below toxic thresholds. This approach emphasizes the importance of mimicking physiological conditions in laboratory experiments for clinically relevant results. Additionally, studies by Senkutvan *et al*. [33] and Ibañez *et al*. [57] show that while nickel release is initially higher in acidic conditions, it decreases over time and generally stays within safe limits, suggesting an adaptive response of the oral environment to the presence of orthodontic appliances. Osmani *et al*. [46] further corroborate this, demonstrating that metal ion release is minimized at neutral or slightly alkaline pH, while acidic environments promote greater ion leaching **(Figure 2)**.

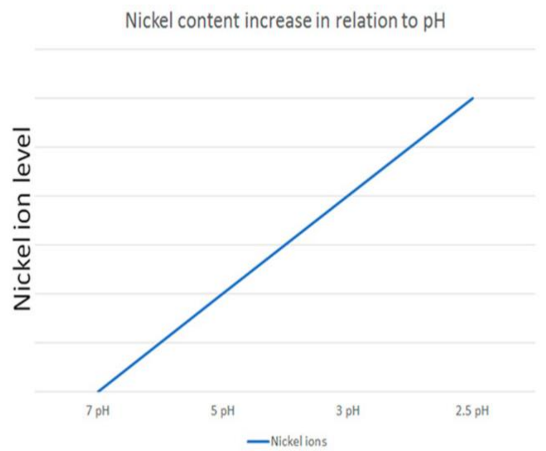

Figure 2. An illustrative example of how nickel ion release varies in relation to pH levels, based on the reviewed studies.

Influence of surface features, wire geometry, and material choice

Surface characteristics and wire shape have been shown to significantly affect nickel ion release. Studies by Didovic *et al*. [42] and Aiswareya *et al*. [29] demonstrated that variations in surface roughness and manufacturing methods can alter the amount of ions released, with stainless steel (SS) bands generally exhibiting higher release compared to nickel-titanium (NiTi) wires—likely due to the welding processes used in SS production. Additionally, Azizi *et al*. [17] reported that rectangular NiTi wires release more nickel ions than round wires, highlighting that wire geometry should be considered when treating patients at risk for nickel hypersensitivity.

Material selection also plays a key role in minimizing nickel exposure. Lages *et al*. [60] found no significant differences in nickel levels between patients with metal versus esthetic orthodontic appliances, suggesting that esthetic options may be suitable for nickel-sensitive individuals. Conversely, Bass *et al*. [59] noted a higher prevalence of nickel sensitivity among female patients, which may be exacerbated during orthodontic treatment, underscoring the importance of tailored material selection and careful monitoring.

Clinical implications and recommendations

Predictive models developed in recent studies [62, 63] offer orthodontists guidance on nickel release dynamics, allowing for treatment plans that consider patient-specific sensitivity. Based on the reviewed evidence, the following recommendations can be made for different archwire types:

- *SS CrNi (stainless steel chromium–nickel):* Stable nickel release over time makes it suitable for long-term applications spanning several months.
- *NiTi Superelastic:* Ideal for short-term use (approximately 4–6 weeks), as early peak nickel release aligns with optimal force delivery, but prolonged use may pose sensitization risks.
- *Heat-Activated NiTi (without copper):* Best for 6–8 weeks of application due to higher initial nickel release; replacement may be necessary for longer treatments.
- *Heat-Activated NiTi (with copper):* Demonstrates a stable release profile, supporting safe use in long-term treatments.
- *TriTanium™:* Recommended for extended treatment periods, as nickel release stabilizes over time.
- *Bio-Active™:* Suitable for short- to medium-term use (up to 4–6 weeks), with initial high release aiding early tooth movement; replacement may be warranted for prolonged stability.

Overall, nickel ion release is influenced by multiple factors, including fluoride exposure, oral pH, immersion duration, saliva dynamics, hygiene products, diet, and wire design. These variables are critical for both patient safety and material selection in clinical practice.

Directions for future research

Future investigations should prioritize long-term in vivo studies to better understand cumulative nickel exposure during orthodontic treatment. Research into new alloys with improved corrosion resistance and lower ion release potential could enhance safety. Additionally, exploring protective strategies—such as natural compounds like snake fruit extract [53] and optimized surface treatments, including pre-passivation [18]—may further reduce nickel release and its associated risks.

Conclusion

This narrative review highlights the current understanding of nickel release from orthodontic archwires, yet its findings are bounded by the limitations of the reviewed studies and the non-systematic nature of the analysis.

Evidence indicates that nickel-containing wires, including stainless steel (SS) and nickel-titanium (NiTi) alloys, do release nickel ions in both laboratory and clinical settings. The concentrations observed generally remain below thresholds considered harmful, suggesting minimal immediate risk. Nonetheless, the potential for inducing nickel hypersensitivity or allergic reactions in susceptible patients remains, emphasizing the need for individualized material selection. Factors such as saliva composition, pH fluctuations, wire geometry, oral hygiene practices, dietary habits, and pre-existing allergies should inform clinical decisions. Short-term use of these archwires appears safe, but continuous monitoring is recommended to detect early signs of sensitization.

Long-term studies, particularly those that combine in vitro simulations with in vivo observations, are still limited. Comprehensive investigations are necessary to better understand cumulative ion release and its implications over the entire course of orthodontic treatment. Future research should also focus on the chemical form, oxidation state, and bioavailability of released ions, as these factors may influence their biological impact. Advancements in ultra-sensitive trace element detection will be critical for these assessments.

Ultimately, developing evidence-based guidelines for material selection requires collaboration among clinicians, researchers, and regulatory bodies. Prioritizing patient safety while addressing potential risks associated with metal ion release will improve clinical outcomes and guide the future design of biocompatible orthodontic materials.

Acknowledgments: None

Conflict of Interest: None

Financial Support: None

Ethics Statement: None

References

1. Kasprzak K. Nickel carcinogenesis. Mutat Res Fundam Mol Mech Mutagen. 2003;533(1):67–97.
2. Seilkop SK, Oller AR. Respiratory cancer risks associated with low-level nickel exposure: An integrated assessment based on animal, epidemiological, and mechanistic data. Regul Toxicol Pharmacol. 2003;37(2):173–90.
3. Sunderman FW, Dingle B, Hopfer SM, Swift T. Acute nickel toxicity in electroplating workers who accidently ingested a solution of nickel sulfate and nickel chloride. Am J Ind Med. 1988;14(3):257–66.
4. Gillete B. Nickel named 'allergen of the year': ACDS adds to list of allergies warranting attention. Dermatol Times. 2008;4(1):15–6.
5. Sivulka DJ. Assessment of respiratory carcinogenicity associated with exposure to metallic nickel: A review. Regul Toxicol Pharmacol. 2005;43(2):117–33.
6. Suryawanshi H, Hande A, Dasari AK, Aileni KR, AlZoubi I, Patil SR. Metal ion release from orthodontic appliances: Concerns regarding potential carcinogenic effects. Oral Oncol Rep. 2024;10(1):100309.
7. Duda A, Błaszczyk U. The impact of nickel on human health. J Elem. 2008;13(4):685–96.
8. Chainani P, Paul P, Shivlani V. Recent advances in orthodontic archwires: A review. Cureus. 2023;15(8):e47633.
9. Sankar H, Ammayappan P, Ashok T, Varma AJ. Orthodontic archwires: An update. J Sci Dent. 2023;13(2):19–24.
10. Mattick CR. Religious, cultural, and ethical dilemmas in orthodontics. J Orthod. 2003;30(1):88–92.
11. Chakravarthi S, Padmanabhan S, Chitharanjan A. Allergy and orthodontics. J Orthod Sci. 2012;1(2):83–7.
12. Schiff N, Grosgogeat B, Lissac M, Dalard F. Influence of fluoridated mouthwashes on corrosion resistance of orthodontic wires. Biomaterials. 2004;25(19):4535–42.
13. Brantley WA, Eliades T. Orthodontic Materials: Scientific and Clinical Aspects. Stuttgart: Thieme; 2001. ISBN: 978-3-13-125281-4.

14. Kapila S, Sachdeva R. Mechanical properties and clinical applications of orthodontic wires. Am J Orthod Dentofacial Orthop. 1989;96(2):100–9.
15. Biedziak BD. Materiały i Techniki Ortodontyczne. Lublin: Polskie Towarzystwo Ortodontyczne; 2009. ISBN: 978-83-928880-0-0.
16. Lombardo L, Toni G, Stefanoni F, Mollica F, Guarneri MP, Siciliani G. The effect of temperature on the mechanical behavior of nickel-titanium orthodontic initial archwires. Angle Orthod. 2013;83(2):298–305.
17. Azizi A, Jamilian A, Nucci F, Kamali Z, Hosseinikhoo N, Perillo L. Release of metal ions from round and rectangular NiTi wires. Prog Orthod. 2016;17(1):10.
18. Mirjalili M, Momeni M, Ebrahimi N, Moayed MH. Comparative study on corrosion behaviour of Nitinol and stainless steel orthodontic wires in simulated saliva solution in presence of fluoride ions. Mater Sci Eng C. 2013;33(4):2084–93.
19. Castro SM, Ponces MJ, Lopes JD, Vasconcelos M, Pollmann MCF. Orthodontic wires and its corrosion—The specific case of stainless steel and beta-titanium. J Dent Sci. 2015;10(1):1–7.
20. Salve RS, Khatri JM. Allergies and its management in orthodontics. Int J Appl Dent Sci. 2022;8(1):15–9.
21. Zigante M, Rincic Mlinaric M, Kastelan M, Perkovic V, Trinajstic Zrinski M, Spalj S. Symptoms of titanium and nickel allergic sensitization in orthodontic treatment. Prog Orthod. 2020;21(1):17.
22. Wever DJ, Veldhuizen AG, Sanders MM, Schakenraad JM, Van Horn JR. Cytotoxic, allergic and genotoxic activity of a nickel-titanium alloy. Biomaterials. 1997;18(16):1115–20.
23. Urbutytė K, Barčiūtė A, Lopatienė K. The changes in nickel and chromium ion levels in saliva with fixed orthodontic appliances: A systematic review. Appl Sci. 2023;13(8):4739.
24. Singh RK, Gupta N, Goyal V, Singh G, Chaudhari A. Allergies in orthodontics: From causes to management. Orthod J Nepal. 2019;9(2):71–6.
25. Kolokitha OE, Chatzistavrou E. Allergic reactions to nickel-containing orthodontic appliances: Clinical signs and treatment alternatives. World J Orthod. 2008;9(4):399–406.
26. Di Spirito F, Amato A, Di Palo MP, Ferraro R, Cannatà D, Galdi M, et al. Oral and extraoral manifestations of hypersensitivity reactions in orthodontics: A comprehensive review. J Funct Biomater. 2024;15(4):175.
27. Mikulewicz M, Suski P, Tokarczuk O, Warzyńska-Maciejewska M, Pohl P, Tokarczuk B. Metal ion release from orthodontic archwires: A comparative study of biocompatibility and corrosion resistance. Molecules. 2024;29(16):5685.
28. Haleem R, Shafiai NAA, Noor SNFM. An assessment of the pH changes and metal ions released into artificial saliva by fake orthodontic braces. BMC Oral Health. 2023;23(1):669.
29. Aiswareya G, Verma SK, Khan S, Owais M, Farooqi IH, Naseem S. Metal release and cytotoxicity of different orthodontic bracket-wire combinations: An in vitro study. J Int Soc Prev Community Dent. 2023;13(5):469–76.
30. Jamilian A, Moghaddas O, Toopchi S, Perillo L. Comparison of nickel and chromium ions released from stainless steel and NiTi wires after immersion in Oral B®, Orthokin® and artificial saliva. J Contemp Dent Pract. 2014;15(3):403–6.
31. Mikulewicz M, Chojnacka K. Release of metal ions from orthodontic appliances by in vitro studies: A systematic literature review. Biol Trace Elem Res. 2011;139(3):241–56.
32. Furlan TR, Barbosa J, Basting R. Nickel, copper, and chromium release by CuNi-titanium orthodontic archwires is dependent on the pH media. J Int Oral Health. 2018;10(4):224–9.
33. Senkutvan R, Jacob S, Charles A, Vadgaonkar V, Jatol-Tekade S, Gangurde P. Evaluation of nickel ion release from various orthodontic arch wires: An in vitro study. J Int Soc Prev Community Dent. 2014;4(1):12–7.
34. Ağaoğlu G, Arun T, Izgi B, Yarat A. Nickel and chromium levels in the saliva and serum of patients with fixed orthodontic appliances. Angle Orthod. 2001;71(5):375–9.
35. Mikulewicz M, Chojnacka K. Trace metal release from orthodontic appliances by in vivo studies: A systematic literature review. Biol Trace Elem Res. 2010;137(2):127–38.
36. Anuradha P, Varma NKS, Balakrishnan A. Reliability performance of titanium sputter coated Ni–Ti arch wires: Mechanical performance and nickel release evaluation. Bio-Med Mater Eng. 2015;26(1–2):67–77.
37. Katić V, Buljan ZI, Špalj S, Ćurković HO. Corrosion behavior of coated and uncoated nickel-titanium orthodontic wires in artificial saliva with short-term prophylactic fluoride treatment. Int J Electrochem Sci. 2018;13(5):4160–70.
38. Mortazavi SMJ, Paknahad M, Khaleghi I, Eghlidospour M. Effect of radiofrequency

electromagnetic fields (RF-EMFs) from mobile phones on nickel release from orthodontic brackets: An in vitro study. Int Orthod. 2018;16(4):562–70.
39. Venkatachalapathy S, Rajendran R, Thiyagarajan B, Jeevagan S, Chinnasamy A, Sivanandham M. Effect of mobile phone with and without earphones usage on nickel ion release from fixed orthodontic appliance. J Contemp Dent Pract. 2023;24(4):303–7.
40. Imani M, Mozaffari H, Ramezani M, Sadeghi M. Effect of fixed orthodontic treatment on salivary nickel and chromium levels: A systematic review and meta-analysis. Dent J. 2019;7(2):21.
41. Cioffi M, Gilliland D, Ceccone G, Chiesa R, Cigada A. Electrochemical release testing of nickel–titanium orthodontic wires in artificial saliva using thin layer activation. Acta Biomater. 2005;1(6):717–24.
42. Petković Didović M, Jelovica Badovinac I, Fiket Ž, Žigon J, Rinčić Mlinarić M, Čanadi Jurešić G. Cytotoxicity of metal ions released from NiTi and stainless steel orthodontic appliances, part 1: Surface morphology and ion release variations. Materials. 2023;16(11):4156.
43. Pastor F, Rodriguez JC, Barrera JM, García-Menocal JAD, Brizuela A, Puigdollers A, et al. Effect of fluoride content of mouthwashes on metallic ion release in different orthodontic archwires. Int J Environ Res Public Health. 2023;20(3):2780.
44. Ganidis C, Nikolaidis AK, Gogos C, Koulaouzidou EA. Determination of metal ions release from orthodontic archwires in artificial saliva using ICP-OES. Main Group Chem. 2023;22(3):201–12.
45. Laird C, Xu X, Yu Q, Armbruster P, Ballard R. Nickel and chromium ion release from coated and uncoated orthodontic archwires under different pH levels and exposure times. J Oral Biosci. 2021;63(5):450–4.
46. Jusufi Osmani Z, Tariba Knežević P, Vučinić D, Alimani Jakupi J, Reka AA, Can M, et al. Orthodontic alloy wires and their hypoallergenic alternatives: Metal ions release in pH 6.6 and pH 5.5 artificial saliva. Materials. 2024;17(10):5254.
47. Al-Jmmal A. Metal ion release from Ni–Cr alloy with different artificial saliva acidities. Al-Rafidain Dent J. 2014;14(2):266–71.
48. Chikhale R, Akhare P, Umre U, Jawlekar R, Kalokhe S, Badole N, et al. In vitro comparison to evaluate metal ion release: Nickel-titanium vs. titanium-molybdenum orthodontic Archwires. Cureus. 2024;16(9):e56595.
49. Kao C-T, Ding S-J, He H, Chou MY, Huang T-H. Cytotoxicity of orthodontic wire corroded in fluoride solution in vitro. Angle Orthod. 2007;77(2):349–54.
50. Mikulewicz M, Chojnacka K, Wołowiec P. Release of metal ions from fixed orthodontic appliance: An in vitro study in continuous flow system. Angle Orthod. 2014;84(1):140–8.
51. Mirhashemi A, Jahangiri S, Kharrazifard M. Release of nickel and chromium ions from orthodontic wires following the use of teeth whitening mouthwashes. Prog Orthod. 2018;19(1):4.
52. Zubaidy ZNA, Hamdany AKA. Evaluation of nickel ion release and surface characteristics of stainless steel orthodontic archwires after using magnetically treated water as a mouthrinse. J Res Med Dent Sci. 2022;10(7):197–202.
53. Erwansyah E, Susilowati, Pratiwi C. Effect of snakefruit extract (Salacca zalacca) in inhibiting release of chromium and nickel ions from stainless steel orthodontic wire. Int J Appl Pharm. 2019;11(5):33–6.
54. Durgo K, Orešić S, Rinčić Mlinarić M, Fiket Ž, Jurešić GČ. Toxicity of metal ions released from a fixed orthodontic appliance to gastrointestinal tract cell lines. Int J Mol Sci. 2023;24(8):9940.
55. Thiyagarajan A, Magesha V, Sreenivasagan S, Sundramoorthy AK. Electroanalysis of nickel ions released in artificial saliva from three orthodontic arch wires: Stainless steel, NiTi, and CuNiTi. Int J Health Sci. 2023;7(9):1737–47.
56. Ghazal ARA, Hajeer MY, Al-Sabbagh R, Alghoraibi I, Aldiry A. Evaluation of two types of nickel-titanium wires in terms of micromorphology and nickel ion release following oral environment exposure. Prog Orthod. 2015;16(1):9.
57. Velasco-Ibáñez R, Lara-Carrillo E, Morales-Luckie RA, Romero-Guzmán ET, Toral-Rizo VH, Ramírez-Cardona M, et al. Evaluation of the release of nickel and titanium under orthodontic treatment. Sci Rep. 2020;10(1):22280.
58. Almasry R, Kosyreva TF, Skalny AA, Katbeh I, Abakeliya KG, Birukov AS, et al. Nickel ions release from orthodontic wires into the oral cavity during orthodontic treatment. Endodontia Today. 2022;20(3):79–84.
59. Bass JK, Fine H, Cisneros GJ. Nickel hypersensitivity in the orthodontic patient. Am J Orthod Dentofac Orthop. 1993;103(3):280–5.

60. Lages RB, Bridi EC, Pérez CA, Basting RT. Salivary levels of nickel, chromium, iron, and copper in patients treated with metal or esthetic fixed orthodontic appliances: A retrospective cohort study. J Trace Elem Med Biol. 2017;40(1):67–71.
61. Amini F, Jafari A, Amini P, Sepasi S. Metal ion release from fixed orthodontic appliances—an in vivo study. Eur J Orthod. 2012;34(1):126–30.
62. Petrov V, Andreeva L, Petkov G, Gueorguieva M, Stoyanova-Ivanova A, Kalitzin S. Modelling of nickel release dynamics for three types of nickel-titanium orthodontic wires: Nickel release dynamics assessment. In: Proc 2nd Int Conf on Applications of Intelligent Systems. Las Palmas, Spain: ACM; 2019. p. 1–5.
63. Georgieva M, Petkov G, Petrov V, Andreeva L, Martins JNR, Georgiev V, et al. Dynamic reconstruction of the nickel ions' behavior in different orthodontic archwires following clinical application in an intraoral environment. Materials. 2024;18(1):92.
64. Kovac V, Poljsak B, Bergant M, Scancar J, Mezeg U, Primozic J. Differences in metal ions released from orthodontic appliances in an in vitro and in vivo setting. Coatings. 2022;12(2):190.
65. Matusiewicz H. Potential release of trace metal ions from metallic orthodontic appliances and dental metal implants: A review of in vitro and in vivo experimental studies. World J Adv Res Rev. 2023;19(1):32–90.