

Corrosion of Fixed Orthodontic Appliances

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The orthodontic supply market is a prosperous billion-dollar industry, driven by an increasing demand for orthodontic appliances. The supremacy of metallic first-generation biomaterials is evident for manufacturing brackets, archwires, bands, and other components due to their well-recognized chemical inertness, spontaneous passivation, biocompatibility, and favorable mechanical properties combination. However, the oral cavity is the ultimate corrosion-promoting environment for any metallic material.

Keywords: bioalloys ; biocompatibility ; corrosion ; intraoral aging ; orthodontics

1. Introduction

Orthodontics may be defined as the

“branch of dentistry that is concerned with the supervision, guidance and correction of the growing and mature dentofacial structures. It includes the diagnosis, prevention, interception and treatment of all forms of malocclusion of the teeth and associated alterations in their surrounding structures”.

[1]

Malocclusions—usually referred to as “crooked” or “misaligned teeth”—are a worldwide dental problem [2][3][4][5]. Technically, a malocclusion is not a disease, but rather aesthetical and/or functional misalignments between the dental arches or teeth irregularities (beyond what is considered a normal biological variation). Still, malocclusions can cause susceptibility to trauma and periodontal diseases [2][4][6][7][8][9]. Standard treatments for dental malocclusions involve removable or fixed orthodontic appliances.

Fixed appliances are, in general, more effective than removable ones—especially for more complex situations and/or for adult patients—and incorporate brackets, archwires, tubes, and/or bands, tightened by metallic or polymeric ligatures [10][11]. During treatment, a constant load is transferred from the brackets to the teeth, by using orthodontic archwires (attached to the brackets), obtaining tooth movement while adjacent bone and tissue are remodeled [12].

A standard comprehensive orthodontic treatment may last approximately 2 years [13] and involves three sequential phases: (1st) leveling and aligning; (2nd) correction of molar relationship and space closure; and (3th) detailing and finishing [14].

In contemporary orthodontics, the market supply entails a worldwide billion-dollar industry that is expected to grow in the next few years [15]. Metallic materials are still the first choice for manufacturing fixed appliances due to their balanced set of mechanical, biological, and chemical properties [16]. Up to now, the most commonly used metallic alloys include stainless steel (SS), pure titanium (Ti) and its alloys—especially nickel–titanium (NiTi)—and cobalt–chromium (CoCr) alloys. Other metallic materials can also be found in fixed orthodontic appliances, but with a lower application range.

A clinical concern during orthodontic treatments is intraoral corrosion. Always associated with metallic ion release into the oral cavity, corrosion can be intensified by dental plaque accumulation and/or mechanical actions such as friction and fatigue stress. Several important consequences of this undesirable degradation may arise, namely enamel discoloration and demineralization, hypersensitivity, inflammatory reactions and local pain, and, in more severe cases, toxicity effects [17][18][19][20][21].

The need to modify the orthodontic alloys has been identified. Current research guidelines point in two main directions: (i) to adjust the alloys' bulk composition combined with new and advanced manufacturing processes; or (ii) to modify their surface, while taking advantage of the excellent mechanical properties of the bulk. The composition and microstructure of the surface can be altered by using chemical or physical methods, either by treatment or coating deposition.

2. Metallic Corrosion

This chapter focuses on the main alloys used for the manufacturing of orthodontic appliances, the characteristics of the oral environment, and their effects on the corrosion behavior of metallic alloys.

2.1. Orthodontic Alloys

Metals and alloys thrive in the medical field and are more employed as biomaterials than any other material type [16]. Today, the major metallic alloys used in orthodontic applications include stainless steel (SS), pure titanium (Ti) and its alloys—especially the nickel–titanium (NiTi)—and cobalt–chromium (CoCr) alloys. Some of the main characteristics of these bioalloys, in comparison to human molar tooth enamel, are summarized in **Table 1**.

Stainless steels are iron (Fe)-based alloys containing at least 12% chromium (Cr) and a maximum of 1.2% carbon (C), according to the European Standard EN 10088-1 [22]. SS are outstanding materials for manufacturing brackets, bands, tubes, and ligatures [11][23][24], namely the austenitic 3xx series-AISI (American Iron and Steel Institute: 302, 303, 304L, and 316L), the precipitation hardening (PH) steels, as well as the duplex steels (SAF 2205) [10][25][26][27][28][29]. Together with Ti alloys, SS archwires are frequently used in an orthodontic treatment, especially during the 2nd and 3rd phases [30][31].

Table 1. Main characteristics of bioalloys used for manufacturing orthodontic components [26][32][33][34][35].

	Main Composition	Young's Modulus (GPa)	Yield Strength (MPa)
Human molar tooth enamel	Calcium phosphate hydroxyapatite	70–115	
Stainless steel (AISI 316L)	Fe–Cr–Ni	160–187	960–1500
Cobalt–chromium	Co–Cr–Fe–Ni	150–217	830–1200
α-Titanium	Ti (grade 4)	104	550
β-Titanium	Ti–Mo–Sn–Zr	60–68	620–690
Ti-6Al-4V	Ti–Al–V (grade 5)	100–110	830–1070
Nickel–titanium	Ni–Ti	32–36	200–500

The major advantages of these Fe–Cr alloys include their good corrosion resistance combined with their outstanding biomechanical behavior and affordable price. The key feature of the corrosion behavior is the Cr content, which is between 16 and 25 wt.% for austenitic (face-centered cubic structure, FCC) Fe–Ni–Cr alloys. The Cr element in the solid solution phase of SS alloys allows the development of the typical external protective chromium oxide (Cr₂O₃) thin film. Other bulk alloying elements of SS include molybdenum (Mo) and nickel (Ni > 8%), which improve the corrosion resistance effectiveness: while Ni promotes the formation of the FCC structure, Mo stabilizes the Cr-based passive layer.

However, some concerns regarding oral corrosion resistance, despite the presence of a small molybdenum (Mo) content, and the overall biocompatibility led to the emergence of alternatives [10][11][26][31]. The high Ni nominal content in SS alloys can cause contact dermatitis (see Section 3), which has been encouraging for the development of new Ni–“free” austenitic stainless steels (see Section 4).

CoCr-based alloys have been used in orthodontics since the 1960s for manufacturing brackets and archwires [26][31][36]. With higher Cr content (>20%), these alloys surpass the SS ones in corrosion resistance—mainly in chloride environments due to the Cr-rich oxide passive layer—and biocompatibility, with higher wear resistance [31]; yet, improved ductility and resilience may be achieved (**Table 1**). The foremost drawbacks reported in the literature include additional heat treatments to improve mechanical performance and a more complex soldering process [10]. Currently, CoCr-based wires are commercially available in four color-coded variations according to the heat treatment applied; the blue one (“soft”) is the most used due to its low yield strength compared to stainless steels [26] (**Table 1**).

Ti and its alloys are among the most biocompatible materials and were introduced in orthodontics in the 1980s, gaining popularity for brackets, tubes, and archwires production [11][37]. This class of metallic materials presents outstanding mechanical properties, excellent corrosion resistance (better than SS), in addition to low density (4.5 against 7.8 g/cm³ for SS), providing a very high strength-to-weight ratio and non-eliciting allergic responses. Commercially pure titanium (α-Ti, Grade 4) and/or Ti-6Al-4V (Grade 5) brackets and β-Ti (including titanium molybdenum alloy—TMA) archwires are

examples of some Ni-free components with outstanding corrosion resistance and biocompatibility [10][38]. Ti-based brackets and tubes reduce bonding failure to enamel, whereas TMA wires are ideal for certain (but not all) orthodontic situations due to the right balance of mechanical properties (e.g., low stiffness and high stringback and formability) and weldability [10][26][31]. The low elastic modulus supports the selection of β -Ti and/or NiTi alloys (**Table 1**) for orthodontic wires. High manufacturing cost is the most negative drawback [26].

Particular attention should be given to additional Ti-based alloys, such as NiTi and Cu–NiTi alloys, due to its high Ni nominal content. Nitinol®—which stands for “Nickel Titanium Naval Ordnance Laboratory”, with near-equiatomic Ni and Ti concentrations—revolutionized orthodontics since its introduction into clinical practice in 1972 [26][39][40]. Due to its distinct mechanical properties, such as shape memory (shape memory alloy—SMA) and superelasticity behavior, this class of metals is now extensively used for the manufacture of orthodontic wires. [31][37][41]. In fact, the initial leveling stage of the orthodontic treatment (**Section 1**) usually involves NiTi archwires [30][31]. While the shape memory effect allows for the spontaneous recovery of the component form after being subjected to deformation higher than its elastic limit (by heating), the superelasticity tolerates a constant stress as the strain increases. After the initial elastic stress region and the stress/strain release, the NiTi alloy springs back to its original shape. Thus, high elasticity, spring back, and stored energy (**Table 1**) enable low-force delivery, even when malocclusions involve extreme teeth crowding. To further increase the alloys’ strength and reduce energy loss, NiTi alloys have been chemically modified by copper addition (5–6% Cu)—the Cu–NiTi alloys—by acquiring a thermally activated behavior [42][43][44]. These wires yield lower loads on the teeth and also on deformation percentage; thus, teeth movement proceeds in a more physiological manner, preventing necrosis, hyalinization areas, and the probability of root resorption [45][46]. Other elements, such as Fe and Cr, are also added to Ni–Ti-based SMA alloys to modify their mechanical properties [47]. All Ti-based alloys spontaneously passivate by generating a titanium oxide protective film that provides good oral corrosion resistance.

Other metallic alloys can be found in fixed orthodontic appliances, but with a lower application range. The use of gold (Au)—precious metal-based alloys—for instance, was widespread before 1950 due to its higher corrosion resistance compared with alternative alloys at that time [10][48]. However, high cost and poor mechanical properties (low hardness) undermine its use, even though Au-based and Au-coated aesthetic components are still available today [10][48][49][50][51][52].

2.2. Intraoral Environment

The human body is an extreme environment for any metallic biomaterial [53], and the mouth is its “portal entry” [54]—an “open ecosystem” [55] in which variations in intraoral parameters are frequent and complex, leading to a unique corrosion-promoting medium.

Human saliva—99.5% water, 0.3% proteins, and 0.2% organic compounds—plays multiple important physiological functions, not only in taste, digestion, and speech but also in teeth and tissue lubrication/protection, pH buffering, and microbiological control [56][57][58][59]. The main functions of saliva and its constituents are presented in **Table 2**. This summary intends to reflect the saliva complexity, which is further exacerbated by other factors.

Table 2. Main functions assigned to saliva and its constituents [57][58][59][60].

Function	Description	Agents
Tissue lubrication, repairing, and protection	Seromucous covering of the oral tissues. Barrier against irritants. Lubrication of hard and soft tissues, and prosthesis. Mastication, speech, and deglutition aid due to lubrication. Selective modulation of microbial adhesion to oral tissues. Modulation of dental plaque metabolism. Faster tissue repair.	Mucins and other proteins.
Clearance and pH maintenance	Acids neutralization (e.g., bicarbonate buffer). Alkalinization of dental plaque’s pH through urea metabolism by its microbiome. pH modulation to prevent reaching optimal conditions for oral colonization by pathogens.	Bicarbonate, phosphate, urea, amphoteric proteins, and enzymes.
Maintenance of dental integrity	Modulation of pathogens activity to control the progression of caries and enamel damage. Maintenance of the enamel mineralization/demineralization equilibrium. The presence of fluoride in saliva enhances mineralization and forms a fluorapatite-like coating, which is more resistant to caries than the original teeth material.	Calcium, phosphate, fluoride, and several proteins (including statherin, histatins, cystatins, and proline-rich proteins).

Function	Description	Agents
Antibacterial activity	Selective action of protein-based immunological and non-immunological agents, allowing the growth of non-cariogenic microorganisms. Among other mechanisms, the non-immunological action involves the adhesion inhibition of colonizers to the oral tissues, namely by aggregation (clumping).	Immunoglobulins, enzymes, and other proteins (including glycoproteins, statherins, agglutinins, histidine-rich proteins, and proline-rich proteins).
Digestion, taste, and smell	Besides lubricating food and tissues, saliva starts the chemical oral digestion, namely by the initial action of the α -amylase (converting complex carbohydrates into simple sugars). The hypotonicity of saliva (low sodium, glycose, bicarbonate, and urea levels) regarding plasma, which enhances the dissolution of the substances. The presence of proteins (such as gustin) is necessary to the growth of gustatory buds.	α -amylase, gustin, lipases and other proteins.

Proteins and glycoproteins from saliva rapidly adhere to teeth enamel and any other surface placed inside the oral cavity to form a thin layer (70–100 nm), making them an important natural lubricant and oral protective film [57][61][62]. The most relevant chemical components of saliva include inorganic ions (e.g., N^+ , K^+ , Cl^- , F^- , CHO_3^- , PO_4^{3-} , ...), antimicrobial factors, nitrogenous compounds, enzymes, immunoglobulins, albumin and other proteins, and glucose, among others [54][57][59][60][63]. Moreover, the chemical composition, temperature, and pH of human saliva vary between individuals and along the course of the day (circadian rhythms), also depending on the person's lifestyle, diet, and health/disease conditions [60][61][64][65][66][67][68].

Intraoral mean temperature usually ranges around 33–37 °C [64], but abrupt variations up to 65 °C can occur (e.g., drinking a hot coffee after eating an ice cream or drinking a glass of ice water) [65][69]. The pH of non-stimulated saliva—i.e., without consuming food or drinks—usually varies between 6 and 7, but may also oscillate from 5.3 to 7.8 [54][64][70]. A pH value below 5.5 facilitates the development of dental caries [70][71][72]. An acidic diet can also reduce intraoral pH to 3, for instance, due to acidic soft drinks and fruit juices (pH from 1 to 6) [56][70][73][74]. Another possible contributor to salivary pH fluctuation is regurgitated stomach acid, which has a typical pH value of 1.2 [56]—one of the intraoral problems of bulimic people and oncological patients.

The oral environment is additionally ideal for the inevitable proliferation of microorganisms. So far, over 700 bacterial species have been identified, as well as numerous fungi and viruses [54][55][61][75]. The oral microbiota co-evolved with humans in a mutualistic or even symbiotic manner: While the host provides excellent physiochemical and nutritional conditions, microorganisms (especially bacteria) play important physiological roles, including digestion, oral mucosa cell differentiation, and protection against exogenous pathogens [76][77].

Planktonic (i.e., non-attached, free-floating) bacteria are 1000 times more vulnerable to antimicrobials than when aggregated. Therefore, some species—the primary colonizers—soon physically associate with and then adhere to the glycoprotein-based film over the teeth and biomaterials' surfaces. Other bacterial species adhere and proliferate along with primary colonizers, forming microcolonies imbedded in an extracellular polysaccharide matrix. At this point, an oral biofilm (the dental plaque) grows: Complex groups of microcolonies positively interact with each other and even form a “primitive circulatory system” [55]. The grown (mature) oral biofilm is therefore advantageous to its inhabitants by providing nutrients to and protecting both aerobic and anaerobic colonizers—even against drugs, antimicrobial factors from saliva, and phagocytic cells [55][77][78].

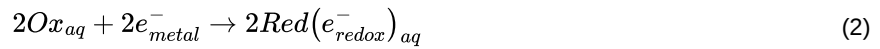
While dental plaque consumes remaining food inside the mouth and protects the teeth against mechanical and chemical injuries (e.g., enamel demineralization), caries and periodontitis may occur if the host/dental plaque relationship is disturbed [61][76][77]. Some species are pathogens, and the microbiological activity of dental plaque releases several by-products into the oral cavity that can modify the chemical composition, oxygenation, and oral pH values [61][76][77]. Saliva and self-cleansing by the cheeks and tongue can naturally control biofilm growth to a certain extent. Nevertheless, oral hygiene procedures are crucial for removing dental plaque, including mechanical brushing with fluoride-containing toothpastes and mouth rinsing with fluorinated mouthwashes and elixirs [66][76][77][79][80].

In short, the intraoral environment is a highly dynamic and complex system—an ultimate degradation-promoting scenario for any biometallic material. Corrosion is a necessary (but not sufficient) condition for causing adverse biologic effects during the use of fixed orthodontic appliances.

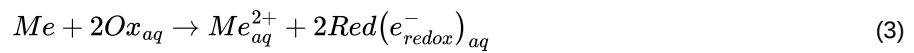
2.3. Corrosion of Metallic Alloys

Metallic corrosion can be expressed as a “*physicochemical interaction between a metal and the environment that results in changes in the properties of the metal, and which may lead to significant impairment of the function of the metal, the environment, or the technical system, of which these form a part*” [81].

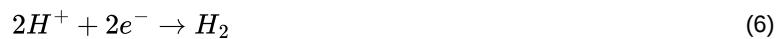
In an aqueous environment, such as the intraoral cavity, corrosion initiates through electrochemical reactions in the metal/solution interface, involving the anodic dissolution of the metal, Me to Me^{2+}_{aq} (oxidation, Equation (1)), and the cathodic reduction of an oxidant from the solution, Ox_{aq} to $Red(e^-_{redox})_{aq}$ (reduction, Equation (2)), that is [82]:



The general charge-transfer reaction for a divalent metal can be written according to Equation (3) [82]:



Dissolved oxygen is usually the cathodic reactant—e.g., according to Equation (4)—with the production of hydroxide ions. However, other mechanisms could be more relevant under acidic conditions since protons may accept electrons produced during the anodic reaction. Typical cathodic reactions under low pH include both Equations (5) and (6), producing water or hydrogen gas, respectively [16][31][78].



The end result of corrosion is the release of metallic ions into the electrolyte, whose extent depends on the electrolyte's nature, including its chemical composition, dissolved oxygen, and pH [31][83]. Moreover, the type of metal or alloy, its manufacturing process, and surface finishing will also influence corrosion [17][28][83][84][85][86].

Most bioalloys—mainly those containing Cr and Ti—rely on the spontaneous formation of a surface protective film. This thin oxide-based layer (some nm thick) may act as a barrier to the movement of ions—a passive film—protecting the metallic substrate against additional electrochemical corrosion [31][81][82]. Passivation is well established, being a spontaneous equilibrium of precipitation and dissolution of ions, with both active and passive films in contact with the electrolyte [87][88].

2.4. Oral Corrosion Forms

Intraoral degradation of metallic appliances is inevitable. Until today, nine basic corrosion types have been reported: uniform, galvanic, crevice, pitting, intergranular, selective leaching, stress, erosion, and microbiologically induced corrosion (MIC), which will be briefly addressed as follows.

2.4.1. Uniform Attack

Uniform corrosion is recognized as general corrosion. This degradation form seems to occur uniformly over the entire surface due to surface electrochemical reactions, almost at the same rate [69][81]. It is the most common type of oral corrosion, affecting all metallic materials at different rates [83], but sometimes it is difficult to detect—only when a significant amount of material is dissolved. All parts of a metallurgical and compositionally uniform surface should be accessible to the electrolyte (saliva) [18].

2.4.2. Galvanic Corrosion

Galvanic corrosion is observed when two different metallic surfaces—with different corrosion potentials—are joined or sufficiently close in an electrolyte solution by establishing a galvanic coupling. The more electropositive (less noble) metal or alloy becomes the anode and preferentially corrodes [16][19][69][81][83].

In orthodontics, contact between dissimilar metallic surfaces might occur in two situations: By simple contact [18][89] or through bonding processes [10][18][90]. In the first case, bracket/wire interactions are inevitable during orthodontic treatment with fixed appliances. Predictably, in certain combinations, such as in the so-common NiTi wire/SS bracket, galvanic corrosion is susceptible to occurring [18], especially in a fluoride-rich environment [89]. Recent research work [48] reported no evidence of galvanic coupling between SS lingual brackets and SS archwires, but the authors suggested caution when using fluoride-containing products during fixed orthodontic treatment with SS brackets and NiTi archwires.

Different parts of brackets or posted archwires are often made of dissimilar alloys, leading to galvanic corrosion [91]. Furthermore, brazing alloys can be used during the manufacturing of orthodontic components [10][18]. Mechanically active welding joints [83] may be reactive, increasing galvanic corrosion susceptibility accompanied by toxic metallic ion release, particularly for silver (Ag)-, copper (Cu)-, and zinc (Zn)-based welding materials [18][92][93]. A recent in vitro study [94] demonstrated that Ag ion release from Ag-soldered SS bands was an order of magnitude higher than other non-soldered SS orthodontic appliances. The authors assigned this effect to the manufacturing process used (welding).

It is generally accepted that galvanic cells can also occur in different locations of the same metallic surface due to non-uniform surface finish (e.g., roughness and chemical composition) and mechanical properties (e.g., work hardening) or even dissimilar properties of the electrolyte (pH and chemical composition) [83]. In the oral cavity, saliva is the main electrolyte, but extracellular fluids such as blood or gingival fluid are also present. Galvanic currents may take place due to the contact of the metallic surface to different biological fluids [61].

2.4.3. Crevice Corrosion

Crevice corrosion is a localized attack occurring in or near constricted places (crevices) formed by two surfaces, of which at least one is metallic [81]. This leads to a local enhancement of aggressive species and depletion of oxygen, in addition to the consequent acidification of the crevice solution due to the hydrolysis of the dissolving metal ions. Generally, metallic materials that show an affinity to pitting also suffer from crevice corrosion. The main causes include differences in metallic ions, fluoride concentration, or oxygenation between the crevice and its surroundings [17][69], associated with a pH decrease and a chloride ion concentration increase [10][18], which deteriorate the protective passive layer—especially on SS alloys [95].

Elastomeric or metallic ligatures are frequently used to fix orthodontic archwires to brackets, establishing ideal sites for crevice attack on brackets [90] (including on 316L SS alloy): Deep craters, fissures, and pores have been detected after long intraoral exposure, as well as extensive deterioration and perforation of the resin-fixed bracket base [17][19][69]. Daems et al. [96] also noticed this type of corrosion at regions of bracket/archwire contact or with plaque and food remnants. Other factors that reportedly cause crevice corrosion comprise the recycling process of the components [18]—not recommended in several countries—surface defects or irregularities [83][96]—including those caused by handling the components by the orthodontist during treatment—and the presence of welding areas [38][97].

2.4.4. Pitting Corrosion

Pitting corrosion is a localized type of corrosion that initiates on metallic surfaces when the protective passive film disrupts due to mechanical and/or electrochemical attack [81][88], leading to the formation of pit holes and/or cavities. This attack has been associated with other corrosion types [95][98], such as the one caused by the well-adherent biofilm that forms during orthodontic treatments. Aggressive ions in saliva, such as chlorine and fluoride [18][31][99]—especially under acidic conditions [100][101][102]—and food additives, such as certain spices [103][104], effectively damage surface protective oxides. Manufacturing defects on orthodontic metallic components may also increase pitting corrosion susceptibility for both SS and NiTi alloys [17][18][19].

The main strategy to improve the pitting resistance of SS alloys is to increase the Cr and Mo nominal content. However, the presence of non-metallic inclusions, such as manganese sulphide (MnS), is of major importance since pits usually initiate at these precipitates [105][106][107]. Usually, the CoCr-based alloys are resistant to pitting; the dissolution of the protective Cr₂O₃ layer into soluble ions (CrO₄²⁻) takes place by oxidation at potentials below the oxygen evolution range [108].

2.4.5. Intergranular Corrosion

As the name suggests, intergranular corrosion occurs in microstructural planar defects along grain boundaries or in the immediate near zones, with minimal or no attack on the alloy grain itself [81][95]. The net result is an alloy fracture along these grain boundaries. SS alloys—used for manufacturing orthodontic brackets and archwires—are particularly vulnerable to this corrosion form, leading to surface staining, weakening the mechanical behavior (strength and ductility), or even failure [93][104]. Special attention should be given to heat treatment of steels [26] (or brazing/welding [83][97][109]—termed weld decay). For a prolonged period above the sensitization temperature [17][18], the formation of small precipitate particles of chromium carbide (Cr_{23}C_6) occurs [95]. Two major consequences arise: the SS brittleness increases and its corrosion resistance decreases, both due to the Cr-depleted zone adjacent to the grain boundary [26][83].

2.4.6. Selective Leaching

Selective leaching or dealloying is found in solid solution alloys, such as Ni–Cr-based or binary alloys containing calcium (Ca) and zinc (Zn) [16], occurring when one element is preferentially removed during the corrosion process [69][95]. This preferential release of a more reactive element from an alloy, regardless of its chemical composition [81], can occur in vivo [16][17]. Still, the effect of selective leaching seems negligible in dentistry [16][69].

2.4.7. Stress Corrosion

Stress corrosion, sometimes termed stress corrosion cracking (SCC), develops due to the influence of both applied tensile stress and a corrosive environment [17][83]. Some alloys that are virtually inert in a particular corrosive medium can become susceptible to this type of corrosion when under loads. This can seriously compromise the mechanical integrity of the material, and failure may eventually occur under low stress levels (compared with alloys in non-corrosive environments) [69][81][95]. Nitinol archwires bonded to brackets are exposed to compressive and tensile stress and might fracture during orthodontic treatment [18][110].

2.4.8. Erosion Corrosion

Erosion corrosion refers to the deterioration of a metallic material due to mechanical abrasion or wear with the combined action of the chemical attack of the corrodent fluid motion. Three subtypes are well known: Erosion, cavitation, and fretting [95]. In orthodontics, fretting corrosion is the most relevant form [69], due to the slight relative motion (vibration and slip) of two contacting metallic surfaces under load [81][95]. Surfaces of both archwires and bracket slots experience load and may undergo a cold-welding phenomenon. In addition, the required small displacements could disrupt the passive films and, consequently, increase corrosion susceptibility (e.g., by pitting) [17][18][83].

2.4.9. Microbiologically Induced Corrosion

As previously mentioned, oral microorganisms can directly or indirectly degrade metallic materials in vivo, either by metabolizing metal from the surface or by modifying the surrounding electrolyte with their metabolic by-products, respectively [83]. This form of corrosion is known as microbiologically induced corrosion (MIC) [61][95][111]. Zarasvand and Rai [78] extensively studied the MIC mechanisms, while Mystkowska et al. [61] described the intraoral process. Accordingly, oral biofilms create differential concentration cells on the metallic surfaces of three main types: oxygen concentration cells, metal concentration cells, and active–passive cells.

Oxygenation cells appear due to a non-uniform biofilm layer—in terms of thickness, ratio of aerobic (oxygen-consuming)/anaerobic microorganisms, or due to the presence of layers of corrosion products—that cause differences in oxygenation throughout the surface. Regions with high oxygen concentrations favor cathodic reactions, and the metallic surface below becomes the cathode. Conversely, in a poorly oxygenated environment, the anodic reaction is enhanced (Equation (1)), and the surface becomes the anode and corrodes. Differences in metallic ion concentration on different sites also occur due to the nature of the extracellular matrix, which has diverse composition and functional groups with different affinities to metallic ions. Under biofilm regions with low affinity to metallic ions, cathodic reactions further progress, whereas anodic dissolution of the metal increases under high-affinity biofilm sites. Finally, if a dense biofilm layer is mechanically or chemically disrupted, the exposed metallic surface corrodes (the anode), while biofilm-covered regions behave as cathodes [61][78]—active–passive cells [81].

Certain anaerobic microorganisms, such as sulfur-reducing bacteria (SRB), release corrosive metabolic products that degrade metallic alloys. The SRB can produce hydrogen gas (H_2), hydrogen sulfide (H_2S), and sulfur difluoride (F_2S , a strong local cathode), while other Gram-negative bacteria release butyric acid ($\text{C}_4\text{H}_8\text{O}_2$) and carbon dioxide (CO_2) [61][78][95]. Besides weakening and retarding the passivation mechanism of the metallic surface, H_2S is highly toxic to cells [112].

and reacts with metals to form metal sulfides and atomic hydrogen. Metal sulfides may precipitate on the surface, generating new active–passive cells, while released atomic hydrogen can cause SCC [61][78][81].

3. Harmful Effects and Clinical Implications

The main consequences of intraoral aging of orthodontic metallic alloys are briefly presented in this chapter, namely the release of metallic ions into the oral cavity, the friction effect between components, and the consequences of using fluoride-based products during treatment with fixed orthodontic appliances.

Aging of metallic alloys is an important issue in orthodontics since both structural and morphological modifications can occur and thus negatively affect the normal clinical treatment progression. Corrosion of metallic surfaces and the presence of biofilm promote metallic ion release and roughness, which may increase friction between brackets and archwires [113][114][115][116][117] and extend the treatment time. Another pointed aging implication is the friction enhancement between the appliance and the mucosa, which causes oral mucosa lesions (from minor wounds to large ulcers), resulting in patients' pain and discomfort [56][118][119][120]. Moreover, aging decreases the resistance to fracture of metallic alloys under repeated cyclic loading [19][115]—fatigue—and could lead to premature failure of archwires [83][121] ruining the in vivo function of the biomaterial.

3.1. Release of Metallic Ions

Corrosion processes ultimately cause the release of metallic ions and particles into the oral cavity [17][87][122][123], which may interact with oral tissues and move to the gastrointestinal tract; even so, their impact on health is not yet fully understood [31][61][83][124]. Biocompatibility concerns raised among clinicians and researchers as hazardous species such as nickel, chromium, cobalt, copper, and vanadium (Ni, Cr, Co, Cu, and V, respectively) can be released from metallic appliances [16][18][123][125][126][127]. Back in 1975, Samitz and Katz [128]—who reviewed data related to Ni released from implanted prostheses—concluded that solubilized metal was found in tissues near implants in laboratory animals.

Multiple researchers have been trying to quantify the release of metallic ions from orthodontic appliances to assess if the concentrations can reach toxic levels for humans, both in vitro and in vivo [123][129][130][131].

The first study found dates back to 1991, by Gjerdet et al. [132], and measured the Ni and Fe contents in patients' saliva up to 3 months of usage. The authors found an initially higher salivary metal content that decreased over treatment time, but values were small when compared with those from dietary intake. Nonetheless, they were already alerted to the large interindividual variability found, as well as to Ni-sensitive patients [132].

Through time, Ni and Cr concentrations are almost always focused, but most studies concluded that the salivary metallic ion concentration is well below toxicity levels. In fact, dietary studies conducted in different countries obtained a daily intake of nickel between 100 and 300 µg/day from food and drinking water. Consuming Ni-enriched food (e.g., processed food) may increase this value up to 900 µg/day [83][133][134][135][136][137][138][139]. Haber et al. [140] estimated a toxicity reference value for Ni-sensitized populations of 4 µg Ni/kg of body weight per day, in addition to Ni in food. Concerning chromium, an average daily intake of 50–280 µg has been proposed [83][141]. However, some authors who analyzed different matrixes (oral mucosa cells, dental plaque, bone, gingiva, hair, and internal organs) found evidence of bioaccumulation that may provoke toxic effects, including DNA damage. In fact, Eliades and Athanasios [17] argued that in vivo studies measuring urinary or serum concentrations of metallic ions in orthodontic patients may give falsely lower Ni levels due to its accumulation in an organ. Further research should therefore persist.

Among the metallic ions released into the oral cavity, Ni raises special health concerns and has been systematically studied [16][133][137][138][140][142][143][144][145][146][147][148], including in orthodontics [122][123][147][149][150][151][152][153][154][155][156][157][158][159][160][161]. The European Union (EU) currently forbids the use of Ni [162]:

- “in any post-assemblies which are inserted into pierced ears and other pierced parts of the human body unless the rate of Nickel release from such post-assemblies is less than 0.2 µg/cm²/week (migration limit)”;
- “in articles intended to come into direct and prolonged contact with the skin (...) if the rate of Nickel release from the parts of these articles coming into direct and prolonged contact with the skin is greater than 0.5 µg/cm²/week”;
- “in articles referred to in point 2 where these have a non-nickel coating unless such coating is sufficient to ensure that the rate of nickel release from those parts of such articles coming into direct and prolonged contact with the skin will not exceed 0.5 µg/cm²/week for a period of at least two years of normal use of the article” [162].

Unfortunately, biometallic alloys lie outside of this EU regulation regarding this matter. The *American Academy of Pediatrics* also expressed concerns regarding the use of Ni-containing alloys, urging the adoption of regulations similar to the EU nickel directive [147]. Dental biomaterials must still comply with several standards and regulations [163].

This transition metal (Ni) is a well-known allergen [164][165], a strong immunologic sensitizer capable of inducing delayed hypersensitive reactions [148][166], triggering cytotoxic, carcinogenic, and mutagenic effects [123][143][167][168], and affecting several cellular functions by long-term exposure to a small amount [123]. Moreover, emphasis has been given to Ni-induced genetic effects, including DNA damage and the inhibition of enzymes involved in DNA reparation [123][159]. The International Agency for Research on Cancer (IARC) classifies Ni (II) and its compounds as carcinogenic or potentially carcinogenic to humans [144].

Chromium is another well-known toxic element. Between the two most stable oxidation states, Cr(III) and Cr(VI), its hexavalent form is toxic and exhibits mutagenic, cytotoxic, and carcinogenic effects in humans [123]. Reportedly, both oxidation states were found in vitro after the corrosion of SS orthodontic brackets in artificial saliva [169].

Ni carcinogenicity, genotoxicity, and allergy are controversial in orthodontics [83][170][171][172][173][174][175][176]. Nonetheless, released Ni from orthodontic components can accumulate in the oral mucosa cells and decrease cell viability [159], while systemic toxicity should not be ignored [177]. Moreover, Kochanowska et al. [178] showed the in vivo effect of long-term exposure to metal orthodontic appliances on both the metallothionein gene expression and the induction of protein synthesis by using animal models (pigs).

Several subtle to severe intra- and/or extra-oral symptoms of allergic reactions to nickel have been reported due to the use of metallic appliances [20][126][171][179][180][181][182][183][184][185]. Symptoms include burning sensation, stomatitis, angioedema, severe gingivitis without dental plaque, gingival hyperplasia, generalized urticaria, and widespread eczema [20][126][182][185][186][187][188]. Besides discomfort and pain for patients, orthodontists may need to replace high Ni-containing components, interrupt the treatment, and/or refer the patient to an allergologist or other specialist for further examination [180][182][183][184].

Ni allergy—namely extreme hypersensitive reactions—is (fortunately) rare in orthodontics [21][170][185], but may be ineffectively diagnosed: Subtle signs are easily misinterpreted as mimicking mechanical injuries or microbiologic activity [83][171][181][189]. Schuster and colleagues [171] reported allergy symptoms related to the presence of fixed appliances during treatment without intraoral signs. Corrosion products induce enamel demineralization, metallic ion incorporation, and color change [190], as well as pain and swelling of oral soft tissues, leading to secondary infections [18]. Pazzini et al. [191] concluded that patients treated with Ni-“free” (0.5–4% Ni) appliances had better gingival health and smaller blood changes when compared with those wearing conventional metallic components (13% Ni). Another possible negative effect is the increase in antibiotic resistance of some bacteria exposed to metals and their potential transfer to medically relevant pathogens [83].

For further comprehension of the toxic effects of metallic ions released during a fixed orthodontic treatment, the reading of the outstanding review works conducted by Martín-Caméan and colleagues [123][192], and by Downarowicz and Mikulewicz [193], is recommended.

3.2. Friction in Orthodontics

Resistance to sliding is present when two surfaces come into contact with each other (e.g., bracket/wire and wire/ligature) [12][26], which is clinically relevant in orthodontics since reduced resistance to sliding can decrease treatment time [194]. Kusy and Whitley [195][196] partitioned resistance to sliding into three components: (i) Friction, “a force that opposes every action that an orthodontist takes to move the teeth”; (ii) binding, when the angle between the bracket slot and the archwire is high enough to promote contact between the bracket corners and the archwire; and (iii) notching, when a permanent deformation of the wire (or bracket) occurs [194][195][196][197][198].

Saliva is the natural intraoral lubricant by forming a protective pellicle [56][57][58][59]—a double layer of proteins [61]—on any material surface and, therefore, reducing the dynamic coefficient of friction [62][199]. While biofilms might have a protective role [54][78][200], microbiological activity most likely contributes to surface degradation by inducing corrosive microcells, rupturing the biofilm, and roughening the appliance surfaces [61]. These effects increase friction, wear, and metallic ions released from the bracket/wire contact pair.

3.3. Oral Hygiene with Fluoride-Based Products

Functional and aesthetic success is essential in orthodontics, but patients must comply with proper oral hygiene during treatment to avoid tooth demineralization and white spot lesions [79][89][201]. Fixed appliances make this task difficult, as the number of oral bacteria related to gingivitis increases shortly after their oral placement [201]. In fact, dental plaque accumulates in several regions, namely in the gingival areas or behind the archwires (e.g., on the bracket slots) [17][96][98][116][202]. To fight dental plaque, orthodontists prescribe fluoride-containing toothpastes, mouth rinses, gels, and varnishes to further control its accumulation and growth, enhance enamel integrity, and prevent dental and gingival diseases [60][79][203].

The downside of using these fluorides is the increased corrosion susceptibility of metallic alloys [18][31][204][205][206][207][208][209][210][211]. Fluoride ions (F^-)—combined with mechanical brushing—easily degrade the protective oxide layers of both SS and Ti-based alloys (see Equations (8) and (9)), increasing localized and general corrosion, promoting metallic ions release [205][212], and negatively impacting their mechanical and surface properties [30][31][206][208][211][213][214][215]—especially at low pH [101][102] and under the simultaneous presence of chloride ions [216].

Walker et al. [30] reported reduced unloading mechanical properties of SS and β -Ti archwires when exposed to neutral or acidulated prophylactic fluoride gels, which may prolong the orthodontic treatment time. On the other hand, Sufarnap and colleagues [44] reported an increase in both surface roughness and Ni and Cu release from Cu–NiTi archwires in NaF solution in vitro without a significant change in the deflection force.

Corrosion of SS bands and brackets [99][102][217][218] also increases in the presence of fluoride ions. Chantarawatit and Yanisarapan [218] argued that acidulated phosphate fluoride gel should not be used in patients wearing fixed metal-based orthodontic appliances.

Since these SS components are the support for NiTi or Cu–NiTi archwires, galvanic coupling risk increased during the 1st orthodontic treatment phase (leveling/aligning) with possible mechanical and/or biocompatibility-related adverse consequences [89][93][213].

References

1. Dental Board of Australia. Dental List of Recognised Specialties, Related Specialist Titles and Definitions. Available online: <https://www.dentalboard.gov.au/Registration-Standards.aspx> (accessed on 10 December 2022).
2. Guo, L.; Feng, Y.; Guo, H.-G.; Liu, B.-W.; Zhang, Y. Consequences of Orthodontic Treatment in Malocclusion Patients: Clinical and Microbial Effects in Adults and Children. *BMC Oral Health* 2016, 16, 112.
3. Zou, J.; Meng, M.; Law, C.S.; Rao, Y.; Zhou, X. Common Dental Diseases in Children and Malocclusion. *Int. J. Oral Sci.* 2018, 10, 7.
4. Lombardo, G.; Vena, F.; Negri, P.; Pagano, S.; Barilotti, C.; Paglia, L.; Colombo, S.; Orso, M.; Cianetti, S. Worldwide Prevalence of Malocclusion in the Different Stages of Dentition: A Systematic Review and Meta-Analysis. *Eur. J. Paediatr. Dent.* 2020, 21, 115–122.
5. Cenzato, N.; Nobili, A.; Maspero, C. Prevalence of Dental Malocclusions in Different Geographical Areas: Scoping Review. *Dent. J.* 2021, 9, 117.
6. Redzepagic Vrazalica, L.; Ilic, Z.; Laganin, S.; Dzemic, V.; Tiro, A. An Epidemiological Study of Malocclusion and Occlusal Traits Related to Different Stages of Dental Development. *S. Eur. J. Orthod. Dentofac. Res.* 2017, 4, 9–13.
7. Mtaya, M.; Brudvik, P.; Astrom, A.N. Prevalence of Malocclusion and Its Relationship with Socio-Demographic Factors, Dental Caries, and Oral Hygiene in 12- to 14-Year-Old Tanzanian Schoolchildren. *Eur. J. Orthod.* 2009, 31, 467–476.
8. Jamilian, A.; Kiaee, B.; Sanayei, S.; Khosravi, S.; Perillo, L. Orthodontic Treatment of Malocclusion and Its Impact on Oral Health-Related Quality of Life. *Open Dent. J.* 2016, 10, 236–241.
9. Proffit, W.R.; Fields, H.W.; Sarver, D.M.; Ackerman, J.L. Malocclusion and Dentofacial Deformity in Contemporary Society. In *Contemporary Orthodontics*; Mosby: St. Louis, MO, USA; Elsevier: Amsterdam, The Netherlands, 2012; pp. 2–18. ISBN 978032308317.
10. Abdallah, M.-N.; Lou, T.; Retrouvey, J.-M.; Suri, S. Biomaterials Used in Orthodontics: Brackets, Archwires, and Clear Aligners. In *Advanced Dental Biomaterials*; Khurshid, Z., Najeeb, S., Zafar, M.S., Sefat, F., Eds.; Elsevier: Amsterdam, The Netherlands, 2019; pp. 541–579. ISBN 978-0-08-102476-8.

11. Proffit, W.R.; Fields, H.W.; Sarver, D.M.; Ackerman, J.L. Contemporary Orthodontic Appliances. In *Contemporary Orthodontics*; Mosby: St. Louis, MO, USA; Elsevier: Amsterdam, The Netherlands, 2012; pp. 347–389. ISBN 978032308317.
12. Proffit, W.R.; Fields, H.W.; Sarver, D.M.; Ackerman, J.L. Mechanical Principles in Orthodontic Force Control. In *Contemporary Orthodontics*; Mosby: St. Louis, MO, USA; Elsevier: Amsterdam, The Netherlands, 2012; pp. 312–346. ISBN 978032308317.
13. Tsihlaki, A.; Chin, S.Y.; Pandis, N.; Fleming, P.S. How Long Does Treatment with Fixed Orthodontic Appliances Last? A Systematic Review. *Am. J. Orthod. Dentofac. Orthop.* 2016, 149, 308–318.
14. Proffit, W.R.; Fields, H.W.; Sarver, D.M.; Ackerman, J.L. The First Stage of Comprehensive Treatment: Alignment and Leveling. In *Contemporary Orthodontics*; Mosby: St. Louis, MO, USA; Elsevier: Amsterdam, The Netherlands, 2012; pp. 530–555. ISBN 978032308317.
15. Business Wire Inc. Business Wire. Available online: <https://www.businesswire.com/news/home/20200728005527/en/Global-Orthodontic-Supplies-Market-Worth-4.6-Billion> (accessed on 10 September 2020).
16. Eliaz, N. Corrosion of Metallic Biomaterials: A Review. *Materials* 2019, 12, 407.
17. Eliades, T.; Athanasiou, A.E. In Vivo Aging of Orthodontic Alloys: Implications for Corrosion Potential, Nickel Release, and Biocompatibility. *Angle Orthod.* 2002, 72, 222–237.
18. Chaturvedi, T.P.; Upadhyay, S.N. An Overview of Orthodontic Material Degradation in Oral Cavity. *Indian J. Dent. Res.* 2010, 21, 275–284.
19. Sifakakis, I.; Eliades, T. Adverse Reactions to Orthodontic Materials. *Aust. Dent. J.* 2017, 62, 20–28.
20. Shukoor, K.M.; Shaj, F.; Shabeer, N.N.; Jayarajan, J. Nickel Allergies in Orthodontic Treatment. *Int. J. Prev. Clin. Dent. Res.* 2016, 3, 143–146.
21. Agarwal, P.; Upadhyay, U.; Tandon, R.; Kumar, S. Nickel Allergy and Orthodontics. *Asian J. Oral Health Allied Sci.* 2011, 1, 61–63.
22. EN 10088-1; Stainless Steels—Part 1: List of Stainless Steels. European Committee for Standardization (CEN): Brussels, Belgium, 2014.
23. Malik, N.; Dubey, R.; Kallury, A.; Chauksye, A.; Shrivastav, T.; Kapse, B.R. A Review of Orthodontic Archwires. *J. Orofac. Res.* 2015, 5, 6–11.
24. Olszewska, A.; Hanć, A.; Barańkiewicz, D.; Rzymiski, P. Metals and Metalloids Release from Orthodontic Elastomeric and Stainless Steel Ligatures: In Vitro Risk Assessment of Human Exposure. *Biol. Trace Elem. Res.* 2020, 196, 646–653.
25. Brüngger, D.; Koutsoukis, T.; Al Jabbari, Y.S.; Hersberger-Zurfluh, M.; Zinelis, S.; Eliades, T. A Comparison of the Compositional, Microstructural, and Mechanical Characteristics of Ni-Free and Conventional Stainless Steel Orthodontic Wires. *Materials* 2019, 12, 3424.
26. Brantley, W.; Berzins, D.; Iijima, M.; Tufekçi, E.; Cai, Z. Structure/Property Relationships in Orthodontic Alloys. In *Orthodontic Applications of Biomaterials*; Eliades, T., Brantley, W.A., Eds.; Elsevier: Amsterdam, The Netherlands, 2017; pp. 3–38. ISBN 9780081003831.
27. Wendl, B.; Wilsche, H.; Lankmayr, E.; Winsauer, H.; Walter, A.; Muchitsch, A.; Jakse, N.; Wendl, M.; Wendl, T. Metal Release Profiles of Orthodontic Bands, Brackets, and Wires: An in Vitro Study. *J. Orofac. Orthop. Fortschritte Kieferorthopädie* 2017, 78, 494–503.
28. Arango, S.; Peláez-Vargas, A.; García, C. Coating and Surface Treatments on Orthodontic Metallic Materials. *Coatings* 2013, 3, 1–15.
29. Arango Santander, S.; Luna Ossa, C.M. Stainless Steel: Material Facts for the Orthodontic Practitioner. *Rev. Nac. Odontol.* 2015, 11.
30. Walker, M.P.; Ries, D.; Kula, K.; Ellis, M.; Fricke, B. Mechanical Properties and Surface Characterization of Beta Titanium and Stainless Steel Orthodontic Wire Following Topical Fluoride Treatment. *Angle Orthod.* 2007, 77, 342–348.
31. Castro, S.M.; Ponces, M.J.; Lopes, J.D.; Vasconcelos, M.; Pollmann, M.C.F. Orthodontic Wires and Its Corrosion—The Specific Case of Stainless Steel and Beta-Titanium. *J. Dent. Sci.* 2015, 10, 1–7.
32. Cuy, J.L.; Mann, A.B.; Livi, K.J.; Teaford, M.F.; Weihs, T.P. Nanoindentation Mapping of the Mechanical Properties of Human Molar Tooth Enamel. *Arch. Oral Biol.* 2002, 47, 281–291.
33. Niinomi, M. Mechanical Properties of Biomedical Titanium Alloys. *Mater. Sci. Eng. A* 1998, 243, 231–236.

34. Bauer, S.; Schmuki, P.; Von Der Mark, K.; Park, J. Progress in Materials Science Engineering Biocompatible Implant Surfaces Part I: Materials and Surfaces. *Prog. Mater. Sci.* 2013, 58, 261–326.
35. Tian, K.; Darvell, B.W. Determination of the Flexural Modulus of Elasticity of Orthodontic Archwires. *Dent. Mater.* 2010, 26, 821–829.
36. Jasso-Ruiz, I.; Velazquez-Enriquez, U.; Scougall-Vilchis, R.J.; Morales-Luckie, R.A.; Sawada, T.; Yamaguchi, R. Silver Nanoparticles in Orthodontics, a New Alternative in Bacterial Inhibition: In Vitro Study. *Prog. Orthod.* 2020, 21, 24.
37. Arango-Santander, S.; Ramírez-Vega, C. Titanio: Aspectos Del Material Para Uso En Ortodoncia. *Rev. Nac. Odontol.* 2016, 12, 63–71.
38. Gioka, C.; Bourauel, C.; Zinelis, S.; Eliades, T.; Silikas, N.; Eliades, G. Titanium Orthodontic Brackets: Structure, Composition, Hardness and Ionic Release. *Dent. Mater.* 2004, 20, 693–700.
39. Uysal, I.; Yilmaz, B.; Atilla, A.O.; Evis, Z. Nickel Titanium Alloys as Orthodontic Archwires: A Narrative Review. *Eng. Sci. Technol. Int. J.* 2022, 36, 101277.
40. Wadood, A. Brief Overview on Nitinol as Biomaterial. *Adv. Mater. Sci. Eng.* 2016, 2016, 4173138.
41. Sifakakis, I.; Bourauel, C. Nickel–Titanium Products in Daily Orthodontic Practice. In *Orthodontic Applications of Biomaterials*; Elsevier: Amsterdam, The Netherlands, 2017; pp. 107–127. ISBN 9780081003831.
42. Gravina, M.A.; Canavaro, C.; Elias, C.N.; Chaves, M.D.G.A.M.; Brunharo, I.H.V.P.; Quintão, C.C.A. Mechanical Properties of NiTi and CuNiTi Wires Used in Orthodontic Treatment. Part 2: Microscopic Surface Appraisal and Metallurgical Characteristics. *Dent. Press J. Orthod.* 2014, 19, 69–76.
43. Parvizi, F. The Load/Deflection Characteristics of Thermally Activated Orthodontic Archwires. *Eur. J. Orthod.* 2003, 25, 417–421.
44. Sufarnap, E.; Harahap, K.; Cynthiana, S.; Reza, M. Nickel and Copper Ion Release, Deflection and the Surface Roughness of Copper-Nickel-Titanium Orthodontic Archwire in Sodium Fluoride Solution. *J. Orthod. Sci.* 2023, 12, 44.
45. Seyyed Aghamiri, S.M.; Ahmadabadi, M.N.; Raygan, S. Combined Effects of Different Heat Treatments and Cu Element on Transformation Behavior of NiTi Orthodontic Wires. *J. Mech. Behav. Biomed. Mater.* 2011, 4, 298–302.
46. Sarul, M.; Kawala, B.; Kawala, M.; Antoszewska-Smith, J. Do the NiTi Low and Constant Force Levels Remain Stable in Vivo? *Eur. J. Orthod.* 2015, 37, 656–664.
47. Farzin-Nia, F.; Yoneyama, T. Orthodontic Devices Using Ti-Ni Shape Memory Alloys. In *Shape Memory Alloys for Biomedical Applications*; Elsevier: Amsterdam, The Netherlands, 2008; pp. 257–296. ISBN 9781845693442.
48. Polychronis, G.; Al Jabbari, Y.S.; Eliades, T.; Zinelis, S. Galvanic Coupling of Steel and Gold Alloy Lingual Brackets with Orthodontic Wires: Is Corrosion a Concern? *Angle Orthod.* 2018, 88, 450–457.
49. Ito, A.; Kitaura, H.; Noguchi, T.; Otori, F.; Mizoguchi, I. Analysis of Coating Loss from Coated Stainless Steel Orthodontic Wire. *Appl. Sci.* 2022, 12, 9497.
50. Toy, E.; Malkoc, S.; Corekci, B.; Bozkurt, B.S.; Hakki, S.S. Real-Time Cell Analysis of the Cytotoxicity of Orthodontic Brackets on Gingival Fibroblasts. *J. Appl. Biomater. Funct. Mater.* 2014, 12, 248–255.
51. Kim, I.-H.; Park, H.-S.; Kim, Y.K.; Kim, K.-H.; Kwon, T.-Y. Comparative Short-Term in Vitro Analysis of Mutans Streptococci Adhesion on Esthetic, Nickel-Titanium, and Stainless-Steel Arch Wires. *Angle Orthod.* 2014, 84, 680–686.
52. Krishnan, M.; Seema, S.; Kumar, A.V.; Varthini, N.P.; Sukumaran, K.; Pawar, V.R.; Arora, V. Corrosion Resistance of Surface Modified Nickel Titanium Archwires. *Angle Orthod.* 2014, 84, 358–367.
53. Hansen, D.C. Metal Corrosion in the Human Body: The Ultimate Bio-Corrosion Scenario. *Electrochem. Soc. Interface* 2008, 17, 31–34.
54. Maruthamuthu, S.; Rajasekar, A.; Sathiyarayanan, S.; Muthukumar, N.; Palaniswamy, N. Electrochemical Behaviour of Microbes on Orthodontic Wires. *Curr. Sci.* 2005, 89, 988–996.
55. Wolf, H.F.; Hassell, T.M. Biofilm—Plaque Formation on Tooth and Root Surfaces. In *Color Atlas of Dental Hygiene-Periodontology*; Thieme: Stuttgart, Germany; New York, NY, USA, 2006; p. 24. ISBN 9783131417619.
56. Zhou, Z.R.; Zheng, J. Tribology of Dental Materials: A Review. *J. Phys. D Appl. Phys.* 2008, 41, 113001.
57. Dawes, C.; Pedersen, A.M.L.; Villa, A.; Ekström, J.; Proctor, G.B.; Vissink, A.; Aframian, D.; McGowan, R.; Aliko, A.; Narayana, N.; et al. The Functions of Human Saliva: A Review Sponsored by the World Workshop on Oral Medicine VI. *Arch. Oral Biol.* 2015, 60, 863–874.
58. Mosca, A.C.; Chen, J. Food-Saliva Interactions: Mechanisms and Implications. *Trends Food Sci. Technol.* 2017, 66, 125–134.

59. de Almeida, P.D.V.; Grégio, A.M.T.; Machado, M.A.N.; de Lima, A.A.S.; Azevedo, L.R. Saliva Composition and Functions: A Comprehensive Review. *J. Contemp. Dent. Pract.* 2008, 9, 72–80.
60. Humphrey, S.P.; Williamson, R.T. A Review of Saliva: Normal Composition, Flow, and Function. *J. Prosthet. Dent.* 2001, 85, 162–169.
61. Mystkowska, J.; Niemirowicz-Laskowska, K.; Łysik, D.; Tokajuk, G.; Dąbrowski, J.R.; Bucki, R. The Role of Oral Cavity Biofilm on Metallic Biomaterial Surface Destruction—Corrosion and Friction Aspects. *Int. J. Mol. Sci.* 2018, 19, 743.
62. Yakubov, G.E.; Macakova, L.; Wilson, S.; Windust, J.H.C.; Stokes, J.R. Aqueous Lubrication by Fractionated Salivary Proteins: Synergistic Interaction of Mucin Polymer Brush with Low Molecular Weight Macromolecules. *Tribol. Int.* 2015, 89, 34–45.
63. Castagnola, M.; Cabras, T.; Vitali, A.; Sanna, M.T.; Messina, I. Biotechnological Implications of the Salivary Proteome. *Trends Biotechnol.* 2011, 29, 409–418.
64. Choi, J.E.; Lyons, K.M.; Kieser, J.A.; Waddell, N.J. Diurnal Variation of Intraoral PH and Temperature. *BDJ Open* 2017, 3, 17015.
65. Moore, R.J.; Watts, J.T.F.; Hood, J.A.A.; Burritt, D.J. Intra-Oral Temperature Variation over 24 Hours. *Eur. J. Orthod.* 1999, 21, 249–261.
66. Kwak, D.Y.; Kim, N.Y.; Kim, H.J.; Yang, S.Y.; Yoon, J.E.; Hyun, I.A.; Nam, S.H. Changes in the Oral Environment after Tooth Brushing and Oral Gargling. *Biomed. Res.* 2017, 28, 7093–7097.
67. Neyraud, E.; Palicki, O.; Schwartz, C.; Nicklaus, S.; Feron, G. Variability of Human Saliva Composition: Possible Relationships with Fat Perception and Liking. *Arch. Oral Biol.* 2012, 57, 556–566.
68. Poles, A.A.; Balcão, V.M.; Chaud, M.V.; Vila, M.M.D.C.; Aranha, N.; Yoshida, V.M.H.; Oliveira, J.M. Study of the Elemental Composition of Saliva of Smokers and Nonsmokers by X-Ray Fluorescence. *Appl. Radiat. Isot.* 2016, 118, 221–227.
69. Upadhyay, D.; Panchal, M.A.; Dubey, R.S.; Srivastava, V.K. Corrosion of Alloys Used in Dentistry: A Review. *Mater. Sci. Eng. A* 2006, 432, 1–11.
70. Hans, R.; Thomas, S.; Garla, B.; Dagli, R.J.; Hans, M.K. Effect of Various Sugary Beverages on Salivary PH, Flow Rate, and Oral Clearance Rate amongst Adults. *Scientifica* 2016, 2016, 5027283.
71. Dental Caries. *Essentials of Oral Pathology and Oral Medicine*; Cawson, R., Odell, E., Eds.; Churchill Livingstone: London, UK, 2008; pp. 40–59. ISBN 978-0443-10125-0.
72. Walsh, L.J. Dental Plaque Fermentation and Its Role in Caries Risk Assessment. *Int. Dent. S. Afr.* 2006, 8, 34–40.
73. Goel, I.; Navit, S.; Mayall, S.S.; Rallan, M.; Navit, P.; Chandra, S. Effects of Carbonated Drink & Fruit Juice on Salivary PH of Children: An in Vivo Study. *Int. J. Sci. Study* 2013, 1, 60.
74. Lubis, H.F.; Simamora, G.H. Release of Nickel Ions and Changes in Surface Microstructure of Stainless Steel Archwire after Immersion in Tomato and Orange Juice. *IOP Conf. Ser. Earth Environ. Sci.* 2021, 912, 012018.
75. He, J.; Li, Y.; Cao, Y.; Xue, J.; Zhou, X. The Oral Microbiome Diversity and Its Relation to Human Diseases. *Folia Microbiol.* 2015, 60, 69–80.
76. Kilian, M.; Chapple, I.L.C.; Hannig, M.; Marsh, P.D.; Meuric, V.; Pedersen, A.M.L.; Tonetti, M.S.; Wade, W.G.; Zaura, E. The Oral Microbiome—An Update for Oral Healthcare Professionals. *Br. Dent. J.* 2016, 221, 657–666.
77. Marsh, P.D.; Head, D.A.; Devine, D.A. Dental Plaque as a Biofilm and a Microbial Community—Implications for Treatment. *J. Oral Biosci.* 2015, 57, 185–191.
78. Alasvand Zarasvand, K.; Rai, V.R. Microorganisms: Induction and Inhibition of Corrosion in Metals. *Int. Biodeterior. Biodegrad.* 2014, 87, 66–74.
79. Øgaard, B. White Spot Lesions During Orthodontic Treatment: Mechanisms and Fluoride Preventive Aspects. *Semin. Orthod.* 2008, 14, 183–193.
80. Weyant, R.J.; Tracy, S.L.; Anselmo, T.T.; Beltrán-Aguilar, E.D.; Donly, K.J.; Frese, W.A.; Hujoel, P.P.; Iafolla, T.; Kohn, W.; Kumar, J.; et al. Topical Fluoride for Caries Prevention. *J. Am. Dent. Assoc.* 2013, 144, 1279–1291.
81. ISO 8044:2015; Corrosion of Metals and Alloys—Basic Terms and Definitions. ISO (International Organization for Standardization): Geneva, Switzerland, 2015. Available online: <https://www.iso.org/obp/ui/#iso:std:iso:8044:ed-4:v1:en> (accessed on 18 May 2018).
82. Sato, N. Basics of Corrosion Chemistry. In *Green Corrosion Chemistry and Engineering: Opportunities and Challenges*; Wiley: Hoboken, NJ, USA, 2011; pp. 1–32. ISBN 9783527329304.

83. House, K.; Sernetz, F.; Dymock, D.; Sandy, J.R.; Ireland, A.J. Corrosion of Orthodontic Appliances-Should We Care? *Am. J. Orthod. Dentofac. Orthop.* 2008, 133, 584–592.
84. Hunt, N.; Cunningham, S.; Golden, C.; Sheriff, M. An Investigation into the Effects of Polishing on Surface Hardness and Corrosion of Orthodontic Archwires. *Angle Orthod.* 1999, 69, 433–440.
85. Strehblow, H.-H. Phenomenological and Electrochemical Fundamentals of Corrosion. In *Materials Science and Technology, Corrosion and Environmental Degradation*, Vol. I.; Schütze, M., Cahn, R., Haasen, P., Kramer, E., Eds.; Wiley-VCH: Weinheim, Germany, 2000; pp. 1–66. ISBN 3-527-29505-4.
86. Eliades, T.; Zinelis, S.; Bourauel, C.; Eliades, G. Manufacturing of Orthodontic Brackets: A Review of Metallurgical Perspectives and Applications. *Recent Pat. Mater. Sci.* 2008, 1, 135–139.
87. Hanawa, T. Metal Ion Release from Metal Implants. *Mater. Sci. Eng. C* 2004, 24, 745–752.
88. Marcus, P.; Maurice, V. Passivity of Metals and Alloys. In *Materials Science and Technology, Corrosion and Environmental Degradation*, Vol. I.; Schütze, M., Cahn, R., Haasen, P., Kramer, E., Eds.; Wiley-VCH: Weinheim, Germany, 2000; pp. 131–169. ISBN 3-527-29505-4.
89. Schiff, N. Galvanic Corrosion between Orthodontic Wires and Brackets in Fluoride Mouthwashes. *Eur. J. Orthod.* 2006, 28, 298–304.
90. Oh, K.T.; Choo, S.U.; Kim, K.M.; Kim, K.N. A Stainless Steel Bracket for Orthodontic Application. *Eur. J. Orthod.* 2005, 27, 237–244.
91. Mendes, B.D.A.B.; Ferreira, R.A.N.; Pithon, M.M.; Horta, M.C.R.; Oliveira, D.D. Physical and Chemical Properties of Orthodontic Brackets after 12 and 24 Months: In Situ Study. *J. Appl. Oral Sci.* 2014, 22, 194–203.
92. Jacoby, L.S.; Junior, V.D.S.R.; Campos, M.M.; de Menezes, L.M. Cytotoxic Outcomes of Orthodontic Bands with and without Silver Solder in Different Cell Lineages. *Am. J. Orthod. Dentofac. Orthop.* 2017, 151, 957–963.
93. Tahmasbi, S.; Ghorbani, M.; Masudrad, M. Galvanic Corrosion of and Ion Release from Various Orthodontic Brackets and Wires in a Fluoride-Containing Mouthwash. *J. Dent. Res. Dent. Clin. Dent. Prospects* 2015, 9, 159–165.
94. 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, 4156.
95. Schweitzer, P.A. *Fundamentals of Metallic Corrosion*, 2nd ed.; CRC Press: Boca Raton, FL, USA, 2006; ISBN 9780429127137.
96. Daems, J.; Celis, J.-P.; Willems, G. Morphological Characterization of As-Received and in Vivo Orthodontic Stainless Steel Archwires. *Eur. J. Orthod.* 2009, 31, 260–265.
97. Saporeti, M.P.; Mazzeiro, E.T.; Sales, W.F. In Vitro Corrosion of Metallic Orthodontic Brackets: Influence of Artificial Saliva with and without Fluorides. *Dent. Press J. Orthod.* 2012, 17, 24e1–24e7.
98. Fróis, A.; Mendes, A.R.; Pereira, S.A.; Louro, C.S. Metal Release and Surface Degradation of Fixed Orthodontic Appliances during the Dental Levelling and Aligning Phase: A 12-Week Study. *Coatings* 2022, 12, 554.
99. Zhang, Y. Corrosion Resistance of Passive Films on Orthodontic Bands in Fluoride-Containing Artificial Saliva. *Int. J. Electrochem. Sci.* 2017, 12, 292–304.
100. Hedberg, Y.S.; Odnevall Wallinder, I. Metal Release from Stainless Steel in Biological Environments: A Review. *Biointerphases* 2016, 11, 018901.
101. Walker, M.P.; White, R.J.; Kula, K.S. Effect of Fluoride Prophylactic Agents on the Mechanical Properties of Nickel-Titanium-Based Orthodontic Wires. *Am. J. Orthod. Dentofac. Orthop.* 2005, 127, 662–669.
102. Kao, C.-T.; Huang, T.-H. Variations in Surface Characteristics and Corrosion Behaviour of Metal Brackets and Wires in Different Electrolyte Solutions. *Eur. J. Orthod.* 2010, 32, 555–560.
103. Mahato, N.; Sharma, M.R.; Chaturvedi, T.P.; Singh, M.M. Effect of Dietary Spices on the Pitting Behavior of Stainless Steel Orthodontic Bands. *Mater. Lett.* 2011, 65, 2241–2244.
104. Chaturvedi, T. Corrosion of Orthodontic Brackets in Different Spices: In Vitro Study. *Indian J. Dent. Res.* 2014, 25, 630.
105. Chiba, A.; Muto, I.; Sugawara, Y.; Hara, N. Pit Initiation Mechanism at MnS Inclusions in Stainless Steel: Synergistic Effect of Elemental Sulfur and Chloride Ions. *J. Electrochem. Soc.* 2013, 160, C511–C520.
106. Yang, S.; Zhao, M.; Feng, J.; Li, J.; Liu, C. Induced-Pitting Behaviors of MnS Inclusions in Steel. *High Temp. Mater. Process.* 2018, 37, 1007–1016.
107. Alnajjar, M.; Christien, F.; Barnier, V.; Bosch, C.; Wolski, K.; Fortes, A.D.; Telling, M. Influence of Microstructure and Manganese Sulfides on Corrosion Resistance of Selective Laser Melted 17-4 PH Stainless Steel in Acidic Chloride

108. Hodgson, A.W.E.; Kurz, S.; Virtanen, S.; Fervel, V.; Olsson, C.-O.A.; Mischler, S. Passive and Transpassive Behaviour of CoCrMo in Simulated Biological Solutions. *Electrochim. Acta* 2004, 49, 2167–2178.
109. Bagatin, C.R.; Ito, I.Y.; Andrucio, M.C.D.; Nelson-Filho, P.; Ferreira, J.T.L. Corrosion in Haas Expanders with and without Use of an Antimicrobial Agent: An in Situ Study. *J. Appl. Oral Sci.* 2011, 19, 662–667.
110. Wang, J.; Li, N.; Rao, G.; Han, E.; Ke, W. Stress Corrosion Cracking of NiTi in Artificial Saliva. *Dent. Mater.* 2007, 23, 133–137.
111. Kameda, T.; Oda, H.; Ohkuma, K.; Sano, N.; Batbayar, N.; Terashima, Y.; Sato, S.; Terada, K. Microbiologically Influenced Corrosion of Orthodontic Metallic Appliances. *Dent. Mater. J.* 2014, 33, 187–195.
112. Jiang, J.; Chan, A.; Ali, S.; Saha, A.; Haushalter, K.J.; Lam, W.-L.M.; Glasheen, M.; Parker, J.; Brenner, M.; Mahon, S.B.; et al. Hydrogen Sulfide—Mechanisms of Toxicity and Development of an Antidote. *Sci. Rep.* 2016, 6, 20831.
113. Kumar, A.; Khanam, A.; Ghafoor, H. Effects of Intraoral Aging of Arch-Wires on Frictional Forces: An Ex Vivo Study. *J. Orthod. Sci.* 2016, 5, 109.
114. Cury, S.; Aliaga-Del Castillo, A.; Pinzan, A.; Sakoda, K.; Bellini-Pereira, S.; Janson, G. Orthodontic Brackets Friction Changes after Clinical Use: A Systematic Review. *J. Clin. Exp. Dent.* 2019, 11, e482–e490.
115. Eliades, T.; Bourauel, C. Intraoral Aging of Orthodontic Materials: The Picture We Miss and Its Clinical Relevance. *Am. J. Orthod. Dentofac. Orthop.* 2005, 127, 403–412.
116. Regis, S.; Soares, P.; Camargo, E.S.; Guariza Filho, O.; Tanaka, O.; Maruo, H. Biodegradation of Orthodontic Metallic Brackets and Associated Implications for Friction. *Am. J. Orthod. Dentofac. Orthop.* 2011, 140, 501–509.
117. Bandeira, A.M.B.; dos Santos, M.P.A.; Pulitini, G.; Elias, C.N.; da Costa, M.F. Influence of Thermal or Chemical Degradation on the Frictional Force of an Experimental Coated NiTi Wire. *Angle Orthod.* 2011, 81, 484–489.
118. Lima, A.A.S.; de Grégio, A.M.T.; Tanaka, O.; Machado, M.Â.N.; França, B.H.S. Tratamento Das Ulcerações Traumáticas Buciais Causadas Por Aparelhos Ortodônticos. *Rev. Dent. Press Ortod. Ortop. Facial* 2005, 10, 30–36.
119. Pires, L.P.B.; de Oliveira, A.H.A.; da Silva, H.F.; de Oliveira, P.T.; dos Santos, P.B.D.; Pinheiro, F.H. de S.L. Can Shielded Brackets Reduce Mucosa Alteration and Increase Comfort Perception in Orthodontic Patients in the First 3 Days of Treatment? A Single-Blind Randomized Controlled Trial. *Am. J. Orthod. Dentofac. Orthop.* 2015, 148, 956–966.
120. Kluemper, G.T.; Hiser, D.G.; Rayens, M.K.; Jay, M.J. Efficacy of a Wax Containing Benzocaine in the Relief of Oral Mucosal Pain Caused by Orthodontic Appliances. *Am. J. Orthod. Dentofac. Orthop.* 2002, 122, 359–365.
121. Bourauel, C.; Scharold, W.; Jäger, A.; Eliades, T. Fatigue Failure of As-Received and Retrieved NiTi Orthodontic Archwires. *Dent. Mater.* 2008, 24, 1095–1101.
122. Petoumeno, E.; Arndt, M.; Keilig, L.; Reimann, S.; Hoederath, H.; Eliades, T.; Jäger, A.; Bourauel, C. Nickel Concentration in the Saliva of Patients with Nickel-Titanium Orthodontic Appliances. *Am. J. Orthod. Dentofac. Orthop.* 2009, 135, 59–65.
123. Martín-Cameán, A.; Jos, Á.; Mellado-García, P.; Iglesias-Linares, A.; Solano, E.; Cameán, A.M. In Vitro and in Vivo Evidence of the Cytotoxic and Genotoxic Effects of Metal Ions Released by Orthodontic Appliances: A Review. *Environ. Toxicol. Pharmacol.* 2015, 40, 86–113.
124. Wang, J.J.; Sanderson, B.J.S.; Wang, H. Cyto- and Genotoxicity of Ultrafine TiO₂ Particles in Cultured Human Lymphoblastoid Cells. *Mutat. Res. Toxicol. Environ. Mutagen.* 2007, 628, 99–106.
125. Messer, R.L.W.; Bishop, S.; Lucas, L.C. Effects of Metallic Ion Toxicity on Human Gingival Fibroblasts Morphology. *Biomaterials* 1999, 20, 1647–1657.
126. Chakravarthi, S.; Chitharanjan, A.; Padmanabhan, S. Allergy and Orthodontics. *J. Orthod. Sci.* 2012, 1, 83.
127. Primožič, J.; Poljšak, B.; Jamnik, P.; Kovač, V.; Čanadi Jurešić, G.; Spalj, S. Risk Assessment of Oxidative Stress Induced by Metal Ions Released from Fixed Orthodontic Appliances during Treatment and Indications for Supportive Antioxidant Therapy: A Narrative Review. *Antioxidants* 2021, 10, 1359.
128. Samitz, M.H.; Katz, S.A. Nickel Dermatitis Hazards from Prostheses: In Vivo and in Vitro Stabilization Studies. *Br. J. Dermatol.* 1975, 92, 287–290.
129. 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, 241–256.
130. Macedo de Menezes, L.; Cardoso Abdo Quintão, C. The Release of Ions from Metallic Orthodontic Appliances. *Semin. Orthod.* 2010, 16, 282–292.

131. Urbutyte, K.; Barčiute, A.; Lopatienė, K. The Changes in Nickel and Chromium Ion Levels in Saliva with Fixed Orthodontic Appliances: A Systematic Review. *Appl. Sci.* 2023, 13, 4739.
132. Gjerdet, N.R.; Erichsen, E.S.; Remlo, H.E.; Evjen, G. Nickel and Iron in Saliva of Patients with Fixed Orthodontic Appliances. *Acta Odontol. Scand.* 1991, 49, 73–78.
133. Cempel, G.N.M. Nickel: A Review of Its Sources and Environmental Toxicology. *Pol. J. Environ. Stud.* 2006, 15, 372–382.
134. Smart, G.A.; Sherlock, J.C. Nickel in Foods and the Diet. *Food Addit. Contam.* 1987, 4, 61–71.
135. WHO (World Health Organization). Nickel in Drinking Water. In Background Document for Development of WHO Guidelines for Drinking-Water Quality; (WHO/SDE/WSH/04.08/55); World Health Organization: Geneva, Switzerland, 2005.
136. Becker, W.; Kumpulainen, J. Contents of Essential and Toxic Mineral Elements in Swedish Market-Basket Diets in 1987. *Br. J. Nutr.* 1991, 66, 151–160.
137. CCME (Canadian Council of Ministers of the Environment). Scientific Criteria Document for Canadian Soil Quality Guidelines for the Protection of Environmental and Human Health: Nickel; Canadian Council of Ministers of the Environment: Winnipeg, MB, Canada, 2015.
138. PHE (Public Health England). Nickel. In Toxicological Overview; Version 1; Toxicology Department, CRCE, Public Health England: London, UK, 2009.
139. WHO (World Health Organization). Nickel. In Air Quality Guidelines for Europe; Regional Office for Europe, Ed.; World Health Organization: Copenhagen, Denmark, 2000; ISBN 9789289013581.
140. Haber, L.T.; Bates, H.K.; Allen, B.C.; Vincent, M.J.; Oller, A.R. Derivation of an Oral Toxicity Reference Value for Nickel. *Regul. Toxicol. Pharmacol.* 2017, 87, S1–S18.
141. WHO (World Health Organization). Chromium. In Air Quality Guidelines for Europe; Regional Office for Europe, Ed.; World Health Organization: Copenhagen, Denmark, 2000; ISBN 9789289013581.
142. Duda-Chodak, A.; Blaszczyk, U. The Impact of Nickel on Human Health. *J. Elem.* 2008, 13, 685–696.
143. Forgacs, Z.; Massányi, P.; Lukac, N.; Somosy, Z. Reproductive Toxicology of Nickel—Review. *J. Environ. Sci. Health Part A* 2012, 47, 1249–1260.
144. IARC (International Agency for Research on Cancer). Nickel and Nickel Compounds; Academic Press: New York, NY, USA, 2011; Volume 100C, pp. 169–218.
145. World Health Organization. Guidelines for Drinking-Water Quality, 4th ed.; World Health Organization: Valletta, Malta, 2011.
146. Genchi, G.; Carocci, A.; Lauria, G.; Sinicropi, M.S.; Catalano, A. Nickel: Human Health and Environmental Toxicology. *Int. J. Environ. Res. Public Health* 2020, 17, 679.
147. Silverberg, N.B.; Pelletier, J.L.; Jacob, S.E.; Schneider, L.C.; Cohen, B.; Horii, K.A.; Kristal, C.L.; Maguiness, S.M.; Tollefson, M.M.; Weinstein, M.G.; et al. Nickel Allergic Contact Dermatitis: Identification, Treatment, and Prevention. *Pediatrics* 2020, 145, e20200628.
148. Das, K.K.; Das, S.N.; Dhundasi, S.A. Nickel, Its Adverse Health Effects & Oxidative Stress. *Indian J. Med. Res.* 2008, 128, 412–425.
149. Sahoo, N.; Kailasam, V.; Padmanabhan, S.; Chitharanjan, A.B. In-Vivo Evaluation of Salivary Nickel and Chromium Levels in Conventional and Self-Ligating Brackets. *Am. J. Orthod. Dentofac. Orthop.* 2011, 140, 340–345.
150. De Souza, R.M.; De Menezes, L.M. Nickel, Chromium and Iron Levels in the Saliva of Patients with Simulated Fixed Orthodontic Appliances. *Angle Orthod.* 2008, 78, 345–350.
151. Ağaoğlu, G.; Arun, T.; Izgü, B.; Yarat, A. Nickel and Chromium Levels in the Saliva and Serum of Patients with Fixed Orthodontic Appliances. *Angle Orthod.* 2001, 71, 375–379.
152. Masjedi, M.; Niknam, O.; Haghighat Jahromi, N.; Javidi, P.; Rakhshan, V. Effects of Fixed Orthodontic Treatment Using Conventional, Copper-Included, and Epoxy-Coated Nickel-Titanium Archwires on Salivary Nickel Levels: A Double-Blind Randomized Clinical Trial. *Biol. Trace Elem. Res.* 2016, 174, 27–31.
153. Yassaei, S.; Dadfarnia, S.; Ahadian, H.; Moradi, F. Nickel and Chromium Levels in the Saliva of Patients with Fixed Orthodontic Appliances. *Orthodontics* 2013, 14, e76–e81.
154. Haleem, R.; Ahmad Shafai, N.; Mohd Noor, S. Perspective on Metal Leachables from Orthodontic Appliances: A Scoping Review. *J. Int. Oral Health* 2021, 13, 539–548.

155. Dwivedi, A.; Tikku, T.; Khanna, R.; Maurya, R.P.; Verma, G.; Murthy, R.C. Release of Nickel and Chromium Ions in the Saliva of Patients with Fixed Orthodontic Appliance: An in-Vivo Study. *Natl. J. Maxillofac. Surg.* 2015, 6, 62–66.
156. Kocadereli, L.; Ataç, A.; Kale, S.; Özer, D. Salivary Nickel and Chromium in Patients with Fixed Orthodontic Appliances. *Angle Orthod.* 2000, 70, 431–434.
157. Fors, R.; Persson, M. Nickel in Dental Plaque and Saliva in Patients with and without Orthodontic Appliances. *Eur. J. Orthod.* 2006, 28, 292–297.
158. Olms, C.; Yahiaoui-Doktor, M.; Remmerbach, T.W. Contact Allergies to Dental Materials. *Swiss Dent. J.* 2019, 129, 571–579.
159. Hafez, H.S.; Selim, E.M.N.; Kamel Eid, F.H.; Tawfik, W.A.; Al-Ashkar, E.A.; Mostafa, Y.A. Cytotoxicity, Genotoxicity, and Metal Release in Patients with Fixed Orthodontic Appliances: A Longitudinal in-Vivo Study. *Am. J. Orthod. Dentofac. Orthop.* 2011, 140, 298–308.
160. Singh, D.P.; Sehgal, V.; Pradhan, K.L.; Chandna, A.; Gupta, R. Estimation of Nickel and Chromium in Saliva of Patients with Fixed Orthodontic Appliances. *World J. Orthod.* 2008, 9, 196–202.
161. Nayak, R.S.; Khanna, B.; Pasha, A.; Vinay, K.; Narayan, A.; Chaitra, K. Evaluation of Nickel and Chromium Ion Release During Fixed Orthodontic Treatment Using Inductively Coupled Plasma-Mass Spectrometer: An In Vivo Study. *J. Int. Oral Health* 2015, 7, 14–20.
162. European Commission Regulation (EC). 1907/2006 of the European Parliament and of the Council of 18 December 2006 —REACH. Available online: <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32006R1907&from=en> (accessed on 5 June 2023).
163. Mikulewicz, M.; Chojnacka, K. Human Exposure to Trace Elements from Dental Biomaterials. In *Recent Advances in Trace Elements*; Wiley: Hoboken, NJ, USA, 2018; pp. 469–479. ISBN 9781119133780.
164. Büdinger, L.; Hertl, M. Immunologic Mechanisms in Hypersensitivity Reactions to Metal Ions: An Overview. *Allergy Eur. J. Allergy Clin. Immunol.* 2000, 55, 108–115.
165. Saito, M.; Arakaki, R.; Yamada, A.; Tsunematsu, T.; Kudo, Y.; Ishimaru, N. Molecular Mechanisms of Nickel Allergy. *Int. J. Mol. Sci.* 2016, 17, 202.
166. Peltonen, L. Nickel Sensitivity. *Int. J. Dermatol.* 2008, 20, 352–353.
167. Zambelli, B.; Uversky, V.N.; Ciurli, S. Nickel Impact on Human Health: An Intrinsic Disorder Perspective. *Biochim. Biophys. Acta Proteins Proteom.* 2016, 1864, 1714–1731.
168. Buczko, P.; Szarmach, I.; Grycz, M.; Kasacka, I. Caspase-3 as an Important Factor in the Early Cytotoxic Effect of Nickel on Oral Mucosa Cells in Patients Treated Orthodontically. *Folia Histochem. Cytobiol.* 2017, 55, 37–42.
169. Luz, M.; Souza, A.; Haddad, A.; Tartomano, A.; Oliveira, P. In Vitro Cr(VI) Speciation in Synthetic Saliva after Releasing from Orthodontic Brackets Using Silica-Aptes Separation and GF AAS Determination. *Quim. Nova* 2016, 39, 951–955.
170. Setcos, J.C.; Babaei-Mahani, A.; Di Silvio, L.; Mjör, I.A.; Wilson, N.H.F. The Safety of Nickel Containing Dental Alloys. *Dent. Mater.* 2006, 22, 1163–1168.
171. Schuster, G.; Reichle, R.; Bauer, R.R.; Schopf, P.M. Allergies Induced by Orthodontic Alloys: Incidence and Impact on Treatment. *J. Orofac. Orthop.* 2004, 65, 48–59.
172. Flores-Bracho, M.G.; Takahashi, C.S.; Castillo, W.O.; Saraiva, M.C.P.; Küchler, E.C.; Matsumoto, M.A.N.; Ferreira, J.T.L.; Nelson-Filho, P.; Romano, F.L. Genotoxic Effects in Oral Mucosal Cells Caused by the Use of Orthodontic Fixed Appliances in Patients after Short and Long Periods of Treatment. *Clin. Oral Investig.* 2019, 23, 2913–2919.
173. Loyola-Rodríguez, J.P.; Lastra-Corso, I.; García-Cortés, J.O.; Loyola-Leyva, A.; Domínguez-Pérez, R.A.; Avila-Arizmendi, D.; Contreras-Palma, G.; González-Calixto, C. In Vitro Determination of Genotoxicity Induced by Brackets Alloys in Cultures of Human Gingival Fibroblasts. *J. Toxicol.* 2020, 2020, 1467456.
174. Bass, J.K.; Fine, H.; Cisneros, G.J. Nickel Hypersensitivity in the Orthodontic Patient. *Am. J. Orthod. Dentofac. Orthop.* 1993, 103, 280–285.
175. Kerosuo, H.; Kullaa, A.; Kerosuo, E.; Kanerva, L.; Hensten-Pettersen, A. Nickel Allergy in Adolescents in Relation to Orthodontic Treatment and Piercing of Ears. *Am. J. Orthod. Dentofac. Orthop.* 1996, 109, 148–154.
176. Staerkjaer, L.; Menne, T. Nickel Allergy and Orthodontic Treatment. *Eur. J. Orthod.* 1990, 12, 284–289.
177. Velasco-Ibáñez, R.; Lara-Carrillo, E.; Morales-Luckie, R.A.; Romero-Guzmán, E.T.; Toral-Rizo, V.H.; Ramírez-Cardona, M.; García-Hernández, V.; Medina-Solís, C.E. Evaluation of the Release of Nickel and Titanium under Orthodontic Treatment. *Sci. Rep.* 2020, 10, 22280.

178. Kochanowska, I.E.; Chojnacka, K.; Pawlak-Adamska, E.; Mikulewicz, M. Metallic Orthodontic Materials Induce Gene Expression and Protein Synthesis of Metallothioneins. *Materials* 2021, 14, 1922.
179. Muris, J.; Feilzer, A.J. Micro Analysis of Metals in Dental Restorations as Part of a Diagnostic Approach in Metal Allergies. *Neuro Endocrinol. Lett.* 2006, 27 (Suppl. 1), 49–52.
180. Dunlap, C.L.; Vincent, S.K.; Barker, B.F. Allergic Reaction to Orthodontic Wire: Report of Case. *J. Am. Dent. Assoc.* 1989, 118, 449–450.
181. Ellis, P.E.; Benson, P.E. Potential Hazards of Orthodontic Treatment—What Your Patient Should Know. *Dent. Update* 2002, 29, 492–496.
182. Kolokitha, O.E.; Chatzistavrou, E. A Severe Reaction to Ni-Containing Orthodontic Appliances. *Angle Orthod.* 2009, 79, 186–192.
183. Noble, J.; Ahing, S.I.; Karaikos, N.E.; Wiltshire, W.A. Nickel Allergy and Orthodontics, a Review and Report of Two Cases. *Br. Dent. J.* 2008, 204, 297–300.
184. Ehrnrooth, M.; Kerosuo, H. Face and Neck Dermatitis from a Stainless Steel Orthodontic Appliance. *Angle Orthod.* 2009, 79, 1194–1196.
185. Navarro-Triviño, F.J.; Ruiz-Villaverde, R. Contact Urticaria/Angioedema Caused by Nickel from Metal Dental Braces. *Contact Dermat.* 2020, 83, 425–427.
186. Maheshwari, S.; Verma, S.; Dhiman, S. Metal Hypersensitivity in Orthodontic Patients. *J. Dent. Mater. Tech.* 2015, 4, 111–114.
187. Rahilly, G.; Price, N. Nickel Allergy and Orthodontics. *J. Orthod.* 2003, 30, 171–174.
188. Kolokitha, O.E.G.; Chatzistavrou, E. Allergic Reactions to Nickel-Containing Orthodontic Appliances: Clinical Signs and Treatment Alternatives. *World J. Orthod.* 2008, 9, 399–406.
189. Gursay, U.K.; Sokucu, O.; Uitto, V.J.; Aydin, A.; Demire, S.; Toker, H.; Erdem, O.; Sayal, A. The Role of Nickel Accumulation and Epithelial Cell Proliferation in Orthodontic Treatment-Induced Gingival Overgrowth. *Eur. J. Orthod.* 2007, 29, 555–558.
190. Gurgel Maia, L.H.E.; de Lima Filho, H.L.; Araújo, M.V.A.; de Oliveira Ruellas, A.C.; de Souza Araújo, M.T. Incorporation of Metal and Color Alteration of Enamel in the Presence of Orthodontic Appliances. *Angle Orthod.* 2012, 82, 889–893.
191. Pazzini, C.A.; Pereira, L.J.; Marques, L.S.; Ramos-Jorge, J.; Aparecida da Silva, T.; Paiva, S.M. Nickel-Free vs Conventional Braces for Patients Allergic to Nickel: Gingival and Blood Parameters during and after Treatment. *Am. J. Orthod. Dentofac. Orthop.* 2016, 150, 1014–1019.
192. Martín-Cameán, A.; Jos, A.; Cameán, A.M.; Solano, E.; Iglesias-Linares, A. Genotoxic and Cytotoxic Effects and Gene Expression Changes Induced by Fixed Orthodontic Appliances in Oral Mucosa Cells of Patients: A Systematic Review. *Toxicol. Mech. Methods* 2015, 25, 440–447.
193. Downarowicz, P.; Mikulewicz, M. Trace Metal Ions Release from Fixed Orthodontic Appliances and DNA Damage in Oral Mucosa Cells by in Vivo Studies: A Literature Review. *Adv. Clin. Exp. Med.* 2017, 26, 1155–1162.
194. Burrow, S.J. Friction and Resistance to Sliding in Orthodontics: A Critical Review. *Am. J. Orthod. Dentofac. Orthop.* 2009, 135, 442–447.
195. Kusy, R.P.; Whitley, J.Q. Friction between Different Wire-Bracket Configurations and Materials. *Semin. Orthod.* 1997, 3, 166–177.
196. Kusy, R.P.; Whitley, J.Q. Influence of Archwire and Bracket Dimensions on Sliding Mechanics: Derivations and Determinations of the Critical Contact Angles for Binding. *Eur. J. Orthod.* 1999, 21, 199–208.
197. Articulo, L. Influence of Ceramic and Stainless Steel Brackets on the Notching of Archwires during Clinical Treatment. *Eur. J. Orthod.* 2000, 22, 409–425.
198. Prashant, P.; Nandan, H.; Gopalakrishnan, M. Friction in Orthodontics. *J. Pharm. Bioallied Sci.* 2015, 7, 334.
199. Ranc, H.; Elkhyat, A.; Servais, C.; Mac-Mary, S.; Launay, B.; Humbert, P. Friction Coefficient and Wettability of Oral Mucosal Tissue: Changes Induced by a Salivary Layer. *Colloids Surf. A Physicochem. Eng. Asp.* 2006, 276, 155–161.
200. Lu, C.; Zheng, Y.; Zhong, Q. Corrosion of Dental Alloys in Artificial Saliva with *Streptococcus Mutans*. *PLoS ONE* 2017, 12, e0174440.
201. Reichardt, E.; Geraci, J.; Sachse, S.; Rödel, J.; Pfister, W.; Löffler, B.; Wagner, Y.; Eigenthaler, M.; Wolf, M. Qualitative and Quantitative Changes in the Oral Bacterial Flora Occur Shortly after Implementation of Fixed Orthodontic Appliances. *Am. J. Orthod. Dentofac. Orthop.* 2019, 156, 735–744.

202. Mei, L.; Chieng, J.; Wong, C.; Benic, G.; Farella, M. Factors Affecting Dental Biofilm in Patients Wearing Fixed Orthodontic Appliances. *Prog. Orthod.* 2017, 18, 4.
203. Alavi, S.; Yaraghi, N. The Effect of Fluoride Varnish and Chlorhexidine Gel on White Spots and Gingival and Plaque Indices in Fixed Orthodontic Patients: A Placebo-Controlled Study. *Dent. Res. J.* 2018, 15, 276–282.
204. Pritam, A.; Priyadarshini, A.; Hussain, K.; Kumar, A.; Kumar, N.; Malakar, A. Assessment of Nickel and Chromium Level in Gingival Crevicular Fluid in Patients Undergoing Orthodontic Treatment with or without Fluoridated Tooth Paste. *J. Pharm. Bioallied Sci.* 2021, 13, 1588.
205. Chitra, P.; Prashantha, G.S.; Rao, A. Effect of Fluoride Agents on Surface Characteristics of NiTi Wires. An Ex Vivo Investigation. *J. Oral Biol. Craniofacial Res.* 2020, 10, 435–440.
206. Schiff, N.; Grosogeat, B.; Lissac, M.; Dalard, F. Influence of Fluoridated Mouthwashes on Corrosion Resistance of Orthodontics Wires. *Biomaterials* 2004, 25, 4535–4542.
207. Nahidh, M.; MH Garma, N.; Jasim, E.S. Assessment of Ions Released from Three Types of Orthodontic Brackets Immersed in Different Mouthwashes: An in Vitro Study. *J. Contemp. Dent. Pract.* 2018, 19, 73–80.
208. Rincic Mlinaric, M.; Karlovic, S.; Ciganj, Z.; Acev, D.P.; Pavlic, A.; Spalj, S. Oral Antiseptics and Nickel–Titanium Alloys: Mechanical and Chemical Effects of Interaction. *Odontology* 2019, 107, 150–157.
209. Condò, R.; Carli, E.; Cioffi, A.; Cataldi, M.E.; Quinzi, V.; Casaglia, A.; Giancotti, A.; Pirelli, P.; Lucarini, I.; Maita, F.; et al. Fluorinated Agents Effects on Orthodontic Alloys: A Descriptive In Vitro Study. *Materials* 2022, 15, 4612.
210. Pastor, F.; Rodríguez, J.C.; Barrera, J.M.; Delgado García-Menocal, J.A.; Brizuela, A.; Puigdollers, A.; Espinar, E.; Gil, J. Effect of Fluoride Content of Mouthwashes on Superelastic Properties of NiTi Orthodontic Archwires. *Materials* 2022, 15, 6592.
211. Sahoo, N.; Bhuyan, L.; Dhull, K.S.; Dash, K.C.; MD, I.; Mishra, P. In Vitro Effect Of Fluoride Prophylactic Agents On Titanium Molybdenum Alloy And Stainless Steel Orthodontic Wires—Scanning Electron Microscope Study. *Bangladesh J. Med. Sci.* 2023, 22, 47–51.
212. 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, 4.
213. Yanisarapan, T.; Thunyakitpisal, P.; Chantarawatit, P. Corrosion of Metal Orthodontic Brackets and Archwires Caused by Fluoride-Containing Products: Cytotoxicity, Metal Ion Release and Surface Roughness. *Orthod. Waves* 2018, 77, 79–89.
214. Abbassy, M. Fluoride Influences Nickel-Titanium Orthodontic Wires' Surface Texture and Friction Resistance. *J. Orthod. Sci.* 2016, 5, 121.
215. Rajendran, A.; Sundareswaran, S.; Peediyekkal, L.; Santhakumar, P.; Sathyanadhan, S. Effect of Oral Environment and Prescribed Fluoride Mouthwashes on Different Types of TMA Wires—An in-Vivo Study. *J. Orthod. Sci.* 2019, 8, 8.
216. Li, X.; Wang, J.; Han, E.; Ke, W. Influence of Fluoride and Chloride on Corrosion Behavior of NiTi Orthodontic Wires. *Acta Biomater.* 2007, 3, 807–815.
217. Brandão, G.A.M.; Simas, R.M.; de Almeida, L.M.; da Silva, J.M.; Meneghim, M.d.C.; Pereira, A.C.; de Almeida, H.A.; Brandão, A.M.M. Evaluation of Ionic Degradation and Slot Corrosion of Metallic Brackets by the Action of Different Dentifrices. *Dent. Press J. Orthod.* 2013, 18, 86–93.
218. Chantarawatit, P.; Yanisarapan, T. Exposure to the Oral Environment Enhances the Corrosion of Metal Orthodontic Appliances Caused by Fluoride-Containing Products: Cytotoxicity, Metal Ion Release, and Surface Roughness. *Am. J. Orthod. Dentofac. Orthop.* 2021, 160, 101–112.