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Original Article

A Systematic Review on the Effects of Fluoride-Induced Corrosion in Peri-Implantitis

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ABSTRACT

Dental implants are predominantly made from commercially pure titanium (cp-Ti) and Ti-6Al-4V alloys, both of which demonstrate impressive clinical success rates, reaching up to 99% over 10 years. However, the surfaces of these implants can degrade over time, potentially leading to the development of mucositis and peri-implantitis. This systematic review examines the effects of fluoride exposure and pH changes on titanium corrosion. Following the PRISMA guidelines, the review incorporated in vitro studies published in English that evaluated how different pH levels and fluoride concentrations affect the corrosion of titanium discs. The initial search yielded 358 articles, and after applying the inclusion criteria, 6 studies were selected for analysis. The review focused on titanium ion release, surface roughness, discoloration, gloss changes, and open circuit potential (OCP). The findings showed that titanium ion release, surface roughness, discoloration, and gloss deterioration increased with decreasing pH and higher fluoride concentrations. In addition, OCP values dropped as fluoride levels rose and the pH became more acidic. Therefore, the interaction between pH and fluoride concentration plays an important role in titanium corrosion, with lower pH levels requiring less fluoride to trigger corrosion. This corrosion process may contribute to the development of peri-implantitis.

Keywords: Titanium, Fluorides, Corrosion, Periimplantitis.

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Introduction

Implant dentistry has become a widely favored restorative solution in clinical practice. Titanium-based implants have been the primary choice for dental implant manufacturing since around 1981. The most commonly used alloys are commercially pure titanium (cp-Ti) and Ti-6Al-4V, both of which show clinical success rates of up to 99% over 10 years [1]. The titanium oxide layer on the surface of the implant is essential for the biocompatibility of titanium, facilitating osseointegration and protecting the titanium surface from corrosion [2]. Unfortunately, the surface of dental implants changes over time, and if alterations occur, they could trigger processes such as mucositis and peri-implantitis [3].

Epidemiological studies carried out more than seventy years ago laid the foundation for the use of fluoride in caries prevention [4]. The topical and systemic use of fluoride for oral health has significantly reduced the prevalence of dental caries and its associated disability [5]. According to ISO standards, the fluoride content in toothpaste should not exceed one thousand five hundred parts per million [6], while fluoride varnishes can contain fluoride concentrations as high as twentytwo thousand six hundred parts per million [7]. Given the effectiveness of fluoride toothpaste in preventing caries, many individuals with titanium implants or prostheses in the oral cavity frequently use fluoride-containing toothpaste.

Corrosion behavior plays a pivotal role in determining the biocompatibility of metal implants, as it can lead to the release of metal ions that potentially result in a range of harmful effects [1]. Although titanium alloys generally display strong resistance to corrosion, this property can be compromised when exposed to specific factors, such as shifts in temperature, changes in pH, and variations in reactive ion concentrations (e.g., H+, Cl-, F-) [1, 8]. Consequently, it is crucial to assess the potential adverse effects of fluoride and identify the conditions that trigger such reactions. This study aims to thoroughly examine the impact of different fluoride concentrations and pH levels on titanium corrosion, to enhance our understanding of how these variables interact and influence the long-term durability and effectiveness of titanium-based implants.

Materials and Methods

This systematic review followed the principles outlined in the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. A protocol was developed and registered with PROSPERO, located at the Centre for Reviews and Dissemination at the University of York, before the study's initiation. The protocol's unique identifier is CRD42023409747.

Clinical question

The clinical question was developed using the participant, intervention, comparison, and outcome (PICO) framework [9]. Does the variation in pH and fluoride concentration influence the corrosion of titanium disks? (See **Table 1**).

Table 1. Formulation of PICO question

P (Population)	Titanium disks
I (Intervention)	Immersion of titanium disks in solutions with varying pH levels and fluoride concentrations.
C (Control)	-
O (Outcome)	Assessment of corrosion on titanium disks: ion release, surface texture alterations, color changes, gloss modifications, and open circuit potential.
PICO	Do variations in pH levels and fluoride concentration affect the corrosion of titanium disks?

Inclusion Criteria

The following criteria were used for inclusion: In vitro studies published in English from 2014 to 2024; fluoride concentration measured in ppm; evaluation of pH's effect on titanium corrosion; use of titanium alloys, specifically cp-Ti or Ti-6Al-4V; and assessment of at least 1 of the following variables: surface roughness, titanium elution, discoloration, gloss change, or open circuit potential.

Exclusion Criteria

Exclusion criteria include editorials, literature reviews, letters, in vivo studies, case reports, animal studies, case series, meta-analyses, systematic reviews, and abstracts.

Search Strategy and Study Selection

Following PRISMA guidelines [10], a thorough electronic search of the literature was carried out independently by 3 researchers (G.M., M.M., and D.L.) across Science Direct, PubMed, and the Cochrane Library databases. Specific keywords like "fluoride," "fluorides," "fluoride ions," "corrosion," and "periimplantitis" were used in the search. The process involved two main phases: an initial screening based on titles and abstracts, followed by a detailed review of the full-text articles that met the inclusion criteria identified in the first phase. Duplicates and studies not meeting the inclusion criteria were excluded during both stages. The selected articles were compared, and any discrepancies were resolved through discussions among the researchers. If consensus could not be reached, seasoned researchers (G.G. and G.J.) were consulted to help resolve the issues.

Risk of Bias Assessment

The risk of bias was independently assessed by 3 researchers (G.M., M.M., and D.L.) using the QUIN tool, a quality assessment tool designed for in vitro studies [11]. Any discrepancies in their evaluations were discussed to reach an agreement. If consensus could not be achieved, third-party experts (G.G. and G.J.) were consulted to assist in resolving any differences.

Results and Discussion

Study selection

The process of reviewing, which includes abstracts, articles, and full-text publications, is illustrated in the PRISMA flow diagram (**Figure 1**).

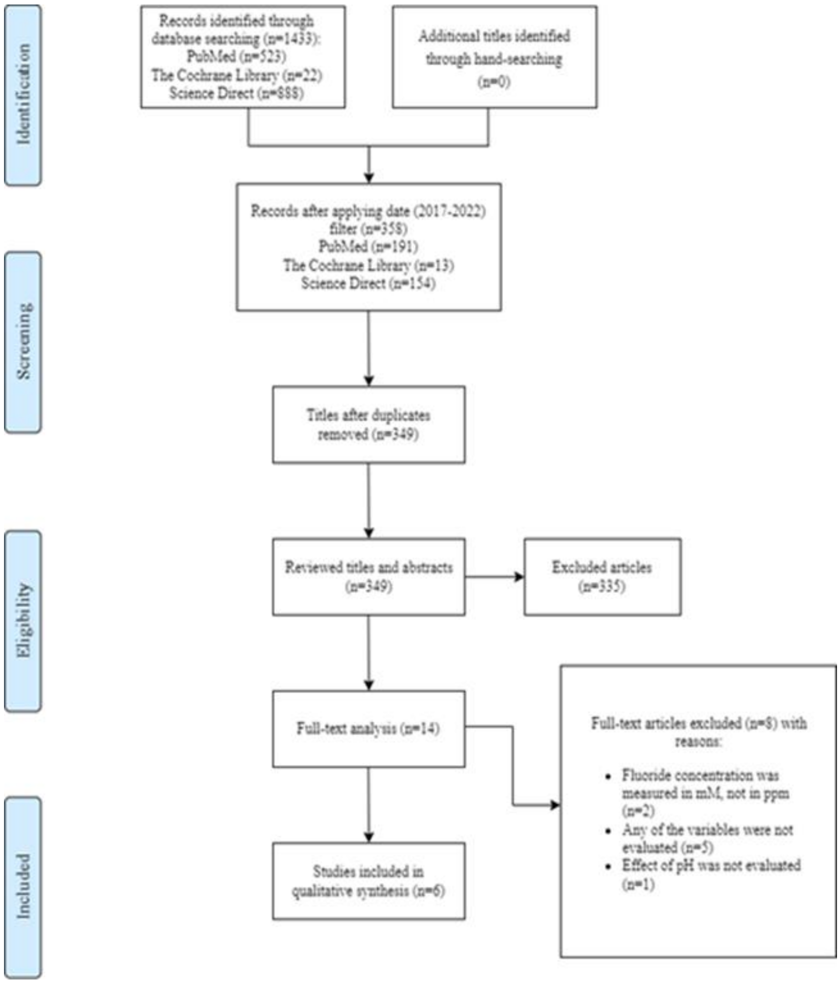

Figure 1. Prisma flowchart

Characteristics of the included studies

A total of 6 studies were incorporated into the qualitative analysis. Out of these, 5 studies employed cp-Ti alloy [8, 12-15], while 2 studies utilized the commercial titanium alloy Ti-6Al-4V [8, 16]. Fluoride concentrations ranged from 0.04 to 9000 ppm NaF, and the pH levels varied between 3 and 7.3. Corrosion assessment was conducted using various methods, including plasma spectrometry [12-15], scanning electron microscopy [8, 14, 16], laser microscope shape analysis [13], and electrochemical measurements [12]. All the studies included were in vitro research published between 2014 and 2024 (**Table 2**).

Table 2. Characteristics of the included studies

Study	Titanium alloy	Solutions	Research method	Investigated variables (+ yes, - no)			
				Elutet titanium	Surface roughness	Discoloration and change in gloss	Open circuit potential
Huang *et al.* [16]	Ti-6Al-4V	Solution A, pH 4.46/260 ppm fluoride; solution B, pH 4.41/178 ppm fluoride; solution C, pH 6.30/117 ppm fluoride; and solution D, pH 4.17/3.92 ppm fluoride); SALINE pH 6,24/3,56 ppm fluoride	Field-emission scanning electron microscope (FE-SEM)	-	+	-	+

Fukushima *et al*. [12]	Cp-Ti	NaF solution (225 or 900 ppm F; pH 4.2 or 6.5)	Electrochemical measurements; plasma mass spectrophotometer	+	-	+	-
Peñarrieta-Juanito *et al*. [8]	Cp-Ti and Ti-6Al-4V	1.23% NaF (5,591 ppm) pH 4	Scanning electron microscope (SEM)	+	+	-	-
Suzuki *et al*. [13]	Cp-Ti	2% NaF (pH = 7.3) and 9,000 ppm (pH = 5.3)	Electron microscope; plasma spectrometer	+	+	-	-
Chen *et al*. [14]	Cp-Ti	A- HBSS; B- HBSS + 0.04 ppm NaF (pH = 7.3); C - HBSS + 0.4 ppm NaF (pH = 7.3); D – HBSS + 0.04 ppm NaF (pH = 5.0); E – HBSS + 0.4 ppm NaF (pH = 5.0)	Scanning electron microscope (SEM); plasma atomic emission spectrometer	+	+	-	+
Furiya-Sato *et al*. [15]	Cp-Ti	Artificial saliva, 1 M H2O2, 1 M H2O2 with catalase; 1000 ppm (pH = 6.5); 1M H2O2 1000 ppm (pH = 6.5); 1M H2O2 9000 ppm (pH = 5.3)	Plasma mass spectrometer	+	-	+	-

Risk of bias assessment

The visual presentation of the results derived from the assessment of bias risk is displayed below in **Table 3**.

Table 3. Risk of bias assessment using QUIN tool (Abbreviations: NA = not applicable)

Study \ Criteria	1	2	3	4	5	6	7	8	9	10	11	12	Final score
Huang *et al*. [16]	2	0	NA	2	2	0	NA	2	0	0	2	2	60%
Fukushima *et al*. [12]	2	0	NA	2	2	1	NA	2	0	0	2	2	65%
Peñarrieta-Juanito *et al*. [8]	2	0	NA	2	2	1	NA	2	0	0	2	2	65%
Suzuki *et al*. [13]	2	0	NA	2	2	2	NA	2	2	0	2	2	80%
Chen *et al*. [14]	2	0	NA	2	2	0	NA	2	0	0	2	2	60%
Furiya-Sato *et al*. [15]	2	0	NA	2	2	0	NA	2	0	0	2	2	60%

The criteria were evaluated using a scoring system with the following ratings: adequately specified (score = 2), inadequately specified (score = 1), not specified (score = 0), and not applicable (NA). After calculating the final scores, results above 70% indicated a low risk of bias, scores between 50% and 70% reflected a medium risk of bias, and scores below 50% pointed to a high risk of bias.

Among the studies included, one showed a low risk of bias [13], while the others exhibited a medium risk of bias [8, 12, 14-16]. This occurred because none of the studies provided an adequate explanation for the sample size calculation or fully addressed the blinding of outcome assessors. Additionally, certain studies [14-16] did not specify the operators or their training, or the information was inadequately presented in other studies [8, 12]. Moreover, the studies [8, 12, 14-16] did not provide sufficient details about the outcome assessors.

Results of Individual Studies

The results of individual studies were grouped according to the specific types of titanium corrosion observed. Four distinct categories were identified: surface roughness, eluted titanium, discoloration, and changes in gloss and open circuit potential.

Titanium Elution

Five studies investigated the release of Ti ions [8, 12-15]. Suzuki *et al.* [13] and Furiya-Sato *et al.* [15] found significant titanium elution in an acidic environment (pH = 5.3) with a fluoride concentration of 9,000 ppm, using cp-Ti ($P < 0.05$). Similarly, Fukushima *et al.* [12] reported increased titanium elution after immersing titanium samples in NaF solution, particularly at low pH levels (pH = 4.2), regardless of NaF concentrations (225 or 900 parts per million) ($P < 0.01$). Chen *et al.* [14] observed a statistically significant increase in Ti ion release in both acidic and neutral environments. In general, cp-Ti released a significantly higher amount of Ti ions at pH 5.0 compared to pH 7.3 ($P < 0.05$). Peñarrieta-Juanito *et al.* [8] found that a 1.23% sodium fluoride solution led to a higher concentration of released Ti, Al, and V ions. The mean values of ion release were lower in the hydrogen peroxide group at pH 7 compared to the fluoride group ($P < 0.05$).

Surface Roughness

4 studies focused on surface roughness [8, 13, 14, 16]. Suzuki *et al.* [13] found that immersion in a NaF solution didn't affect the surface of titanium, with no corrosion observed after 7 days. In contrast, immersion in an acidulated phosphate fluoride (APF) solution at 9,000 ppm and pH 5.3 caused significant surface roughening within just 24 hours due to corrosion ($P < 0.05$). Chen *et al.* [14] observed that in fluoride-free neutral and acidic conditions, no localized corrosion pits were present, and the surface of cp-Ti disks remained smooth. However, micro pits appeared and increased in size with higher fluoride concentrations in serum. Fluoride exposure in acidic environments led to more pronounced micro pit corrosion, resulting in deeper and more significant damage than exposure in neutral conditions. Huang *et al.* [16] reported that Ti-6Al-4V samples subjected to solutions with high fluoride concentrations and low pH showed more defects, including crevice corrosion and pitting, compared to other samples ($P < 0.05$). Peñarrieta-Juanito *et al.* [8] demonstrated that titanium alloys like Ti-6Al-4V were more vulnerable to corrosion than commercially pure titanium when exposed to fluoride ($P < 0.05$).

Discoloration and Gloss Changes

Two studies explored the effects of discoloration and gloss alterations [12, 15]. Research by Fukushima et al. [12] and Furiya-Sato *et al.* [15] found that no significant changes in color or gloss were observed in any commercially pure titanium samples, except when exposed to highly acidic fluoride solutions with high concentrations (specifically, 9,000 parts per million NaF at pH = 5.3 and 900 parts per million NaF at pH = 4.2, respectively).

Open Circuit Potential

A decline in the open circuit potential (OCP) of a metallic material in a given environment suggests an increased chemical reactivity and a higher risk of corrosion. Two studies examined open circuit potential [14, 16]. Both studies revealed that the open circuit potential values of Ti-6Al-4V [16] and cp-Ti [14] gradually decreased as fluoride concentrations in the serum increased, with more pronounced decreases observed in solutions with lower pH levels.

The two most widely used titanium alloys, cp-Ti, and Ti-6Al-4V, are known for their strong osseointegration properties. These alloys demonstrate bioactivity, which aids in bone formation when in direct contact with their metallic surface [1]. When titanium interacts with biological tissues, an oxygen-rich layer forms on its surface, which helps prevent corrosion, thereby making the metal inert. However, no metal or alloy is completely inert in vivo, as electrochemical reactions can result in the release of metal ions when exposed to interstitial fluids. While the titanium oxide layer can regenerate, ongoing wear, exposure to chemical agents like acidic or fluoride-based compounds used in dental treatments, bacterial activity, and their byproducts, as well as an acidic environment, can compromise the integrity of the oxide layer and trigger the corrosion process [17, 18]. In the oral environment, titanium surfaces are coated with proteins such as albumin. Studies suggest that albumin may reduce titanium corrosion, with the possibility that its adsorption on the titanium surface could prevent fluoride-induced corrosion or that albumin's buffering capacity may raise the pH near the titanium material [13].

The primary objective of this study was to assess the influence of fluoride on the corrosion of titanium. A review of the relevant literature led to the inclusion of six studies [8, 12-16]. All studies were carried out in vitro, applying different fluoride concentrations to titanium plates (cp-Ti and Ti-6Al-4V). Five studies focused on cp-Ti, while two examined Ti-6Al-4V alloy.

Furiya-Sato *et al.* [15] reported that immersing cp-Ti in a 1000 ppm fluoride NaF solution at pH 6.5 did not result in any noticeable changes in the titanium's electrochemical corrosion behavior. However, when titanium was immersed in a 9000 ppm fluoride NaF solution at pH 5.3, significant corrosion occurred. Hydrogen fluoride (HF) is known to promote titanium corrosion by disrupting the protective oxide layer, and HF can form from fluoride ions in acidic conditions. Therefore, the neutral pH of 1000 ppm NaF did not induce corrosion [15]. It is important to highlight that even lower fluoride concentrations may lead to corrosion if the environment becomes more acidic, such as through the consumption of food and beverages. Additionally, the biofilm on the titanium surface can generate an acidic environment due to the metabolic activity of sugar. Fukushima *et al.* [12] found that the presence of Streptococcus mutans cells on titanium surfaces weakened the material's corrosion resistance. In contrast, corrosion was notably enhanced by 9000 ppm fluoride NaF, where hydrogen fluoride (HF) was efficiently produced due to the combination of higher fluoride concentration and acidic pH [15].

In a study by Shuto *et al.* [19], which examined the effects of fluoride and abrasive toothpaste on titanium surfaces, the most significant changes in surface roughness, color, and gloss were observed when pure titanium discs were brushed with a toothpaste slurry containing both fluoride and abrasives (fluoride+/abrasive+), followed by a fluoride-free, abrasive-only toothpaste slurry (fluoride–/abrasive+). The study demonstrated that fluoride presence had a noticeable effect on the texture of the titanium surface. Goutam *et al.* [20] reported that the corrosion potential (Ecorr/V) of titanium implants in artificial saliva was measured at -0.42, whereas in artificial saliva containing 0.25% NaF, it dropped to -0.63. For Ti-6Al-4V, the Ecorr/V in artificial saliva was -0.56, and in the presence of 0.25% NaF, it was -0.60. These variations were statistically significant ($P < 0.05$), indicating that fluoride significantly influenced the corrosion behavior of titanium implants.

Chen *et al.* [21] utilized polarization analysis to show that in fluoride-containing oral environments with neutral pH, the Ti-6Al-4V alloy exhibited inert properties. However, its susceptibility to severe corrosion was observed in the presence of crevices. This corrosion was primarily caused by localized acidification, leading to the formation of hydrogen fluoride (HFO) due to the interaction of hydrogen ions (H^+) and fluoride ions (F^-).

Previous systematic reviews have indicated that fluoride can reduce the corrosion resistance of metallic implants. This happens as fluoride ions in the oral cavity's electrolytic environment interact with the titanium oxide layer, promoting its dissolution [3, 18, 22-25].

Around 70% of failures in implant-supported restorations are attributed to inflammatory reactions [22]. Modern dental professionals face the challenge of managing peri-implant mucositis that, if not addressed, can progress to peri-implantitis. This progression may lead to marginal bone loss and, ultimately, implant failure [17, 22].

Systematic reviews of in vitro studies have highlighted the tendency of titanium ions or particles to trigger toxicological and pro-inflammatory responses [3, 17, 18, 22-26]. When titanium corrodes, particles are released from Ti-based implants and can accumulate in the surrounding tissues and organs, where they act as immunogenic agents. Additionally, surface alterations such as discoloration, changes in gloss, and increased roughness may be noted [27]. Titanium has been identified as the primary foreign body found in peri-implantitis biopsies, where it is surrounded by inflammatory cells. These particles are ingested by macrophages, which then release pro-inflammatory cytokines that activate osteoclasts. Metal oxide nanoparticles, especially TiO_2, are known for their antimicrobial properties. Titanium debris may disrupt the balance between bone formation and resorption, potentially leading to osteolysis and bone loss [18, 23-25]. Thus, titanium ions may contribute to inflammatory processes that are associated with bone loss in peri-implant mucositis and peri-implantitis.

Furthermore, an increase in the concentration of titanium ions in affected areas may result from corrosion driven by inflammatory cells and bacteria present in peri-implantitis lesions. This process leads to a decrease in pH levels within the peri-implant environment. The accumulation of bacteria and biofilm further lowers the pH, which accelerates titanium corrosion, even at lower fluoride concentrations. These findings suggest that inflammation alters both the structure and function of biofilms, contributing to titanium corrosion [23, 24].

Conclusion

Both pure titanium and titanium alloys are prone to corrosion in acidic environments, even with low concentrations of fluoride. The combined effects of acid and fluoride are essential in initiating titanium corrosion, as lower pH levels require smaller amounts of fluoride to promote corrosion. These findings underscore the risk that fluoride exposure may contribute to the corrosion of dental implants, potentially leading to the development of mucositis and peri-implantitis.

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