TITLE PAGE

Title:

Efficacy of biofilm decontamination methods of dental implant surfaces: A systematic review of in vitro studies

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Running title:

Implant surface decontamination

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Abstract:
This systematic review examines the decontamination techniques used to clean titanium (Ti) implant surfaces covered with in vitro bacterial biofilms. The selected studies were gathered from the PubMed and Web of Science databases. These include in vitro studies investigating decontamination methods used to clean Ti implant surfaces coated with bacterial biofilms until January 2024. The determined studies were filtered according to the PRISMA guidelines and the Science in Risk Assessment and Policy (SciRAP) was used to assess the reporting and methodological quality of the included studies. A total of 634 full-length peer-reviewed articles were identified. After excluding duplicate papers between the databases and screening according to the predefined inclusion and exclusion criteria, 13 studies were selected. Various decontamination methods, including mechanical, chemical, and physical, were assessed as a single or combined approach. Significant variability was observed among the included studies. Combining the mechanical and physical methods with a chemical yielded the most significant reduction in both single- and multiple-species biofilms. The current results do not indicate that any single decontamination technique is more effective than others in eradicating bacterial biofilm from Ti surfaces; the combined approach was more advantageous than the single ones.

Keywords: peri-implantitis, bacteria, biofilm, implant, titanium, re-osseointegration, debridement.

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Introduction

Replacing missing teeth with dental implants is an effective method with a high cumulative survival rate of up to 94 % after 15 years [1]. Despite this high success rate, peri-implant supporting tissues are susceptible to diseases. Peri-implant diseases are classified into peri-implant mucositis and peri-implantitis (PI), with an incidence of 11.9% and 7.1% after 8-10 years, respectively [1]. There has been debate regarding the exact pathological mechanism of PI; however, it is accepted that it is a plaque-correlated multifactorial disease with subsequent progressive supporting bone loss [2]. Findings obtained from failed dental implants indicate that periodontal bacterial pathogens, such as *Staphylococcus* spp., *Capnocytophaga* spp., *Fusobacterium* spp., *Porphyromonas gingivalis (P. gingivalis)*, Gram-negative anaerobic rods, *Prevotella intermedia (P. intermedia)*, and *Aggregatibacter actinomycetomcomitans (A actinomycetomcomitans),* may play a role in developing PI. These bacterial species have been cultivated from failed dental implants more significantly than expected for their healthy counterparts [3,4]. Accordingly, most proposed therapeutic approaches focus on eradicating dysbiotic biofilm from the implant surface [5,6], followed by restoring the lost supporting peri-implant tissues [7].

One of the primary challenges in PI therapy is the various implant body-related features, thread design, and implant microstructure, which hinder the accessibility of decontaminating biofilm with various treatment protocols. These challenges are evident, especially in non-surgical therapy settings, where the biofilm regions are not visible to the operator [8]. Additionally, the morphology of various shapes of PI bone defects affects the accessibility for decontamination and, consequently, their potential for regeneration [9]. Therefore, non-surgical therapy alone may result in inadequate outcomes and necessitate surgical intervention [10]. Various mechanical (e.g., curettes, sonic and ultrasonic devices, air powder abrasion, titanium (Ti) brushes, and implantoplasty), chemical (e.g., chlorhexidine -CHX, citric acid, topical or systemic antimicrobials), and physical (e.g., laser, photodynamic therapy) decontamination methods have been suggested, either individually or in combination [11–14]. Nevertheless, there is no golden standard method for decontaminating infected implant surfaces, and most available treatment options demonstrate limited effectiveness. [5,15].

Re-osseointegration will, however, likely occur around thoroughly cleaned implants, where direct structural and functional attachment is expected between the previously infected implant surface and bone [16]. In contrast, residual bacterial byproducts on the implant surface are thought to promote fibrous encapsulation. Therefore, the pivotal role of effective decontamination techniques in achieving successful re-osseointegration cannot be overstated. Identifying reliable methods to eradicate bacterial biofilm from the implant surface is critical in treating peri-implantitis (PI) and improving its success rate.

In vitro studies are crucial in finding new treatment strategies and evaluating their effectiveness. Hence, this systematic review assessed current methods for decontaminating Ti discs/implant surfaces biofilms. The review evaluated the efficacy of various decontamination methods, including mechanical, chemical, and physical, either as a single or combined approach, in achieving biofilm eradication on implant surfaces.

Materials and Methods

Research question

The research question was as follows: "Among the various decontamination protocols available for decontaminating infected implant surfaces, which approach demonstrates the best effectiveness in eradicating bacterial biofilm and exhibiting superior antibacterial properties?"

Data sources

A comprehensive literature search of electronic databases, including PubMed-MEDLINE and Web of Science, was conducted until January 2024. The keywords used in the search are indicated in Table (1)

Eligibility criteria

A literature search was performed on published in vitro studies investigating Ti surface decontamination. The published studies met the following criteria: (1) type of study (in vitro); (2) type of intervention (decontamination implant surface biofilm); (3) control (intact biofilm or other suitable methods); (4) principal outcomes (bacterial count in colony forming units)

Inclusion and exclusion criteria

Clinical studies and case report series investigating the effect of implant surface decontamination on clinical healing outcomes are excluded. Review articles, animal studies, or in vitro studies in which the type of bacterial biofilm was not specified were also excluded. Articles not written in English or articles without full text were not considered.

Study selection

Three reviewers read the titles and abstracts separately. Full-text articles were also reviewed in case the abstracts did not provide enough information to decide. Two reviewers assessed the full texts of the remaining articles and set inclusion and exclusion criteria based on the PICO strategy. The determined studies were screened using Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. A third reviewer was consulted if there was a conflict between the reviewers. After the full-text screening, the necessary information was extracted, and the potential articles were selected (Fig 1).

Data extraction

Two reviewers independently extracted data from qualified studies after reading their full text, and the following variables were derived from each study: 1) year of publication; 2) type of biofilm; 3) type of substrate; 4) surface type; 5) decontamination methods and controls; 6) incubation time after decontamination; 7) study outcomes; and 9) trial duration.

Quality assessment

The Science in Risk Assessment and Policy (SciRAP) resource [17] was used to assess the quality of the included studies. The SciRAP provides various tools designed to evaluate the reliability and relevance of studies in ecotoxicity, in vitro toxicity, in vivo toxicity, and epidemiology for scientific evaluations. As described by Corvino et al. [18] , this tool was adopted to assess the methodological and reporting quality of in vitro studies separately. SciRAP tool is classified into "Reporting quality," "Methodological quality," and "Relevance," with sets of criteria for each one separately. The "relevance" category was not considered as it is related to toxicity assessment of human health hazards. The reporting and methodological criteria for evaluating the selected studies are assessed as "fulfilled," "partially fulfilled," or "not fulfilled," based on the descriptions provided for each item in the selected studies. In terms of reliability, four criteria were excluded from the reporting quality assessment (n = 23) and another four from the methodological quality assessment (n = 15), as they were not applicable to the in vitro studies included in this review. The SciRAP score has a value ranging from 0 (indicating all criteria are judged as "not fulfilled") to 100 (indicating all criteria are judged as "fulfilled").

Results

Study selection

The leading search was conducted in January 2024, resulting in a total of 634 studies: 346 from PubMed and 288 from the Web of Science. A total of 112 duplicate articles were removed by an automated tool (EndNote, Find Duplicate). After the title and abstract screening of 522 articles, 490 were excluded. Following a full-text screening of 32 articles, 19 articles were excluded for the following reasons: no bacterial biofilm was used in the study (n = 4); the types of bacteria in the biofilm are not specified (n = 2); substrate is not identified (n = 1); insufficient or no incubation of the substrate after decontamination (n = 4); no quantitative bacteria data (n = 2); unclear methodology (n = 2); duplicate studies (n = 2); and full text is not available (n = 2). A total of 13 studies were included in the analysis. All included studies were in vitro studies that evaluated Ti surface microbial biofilm decontamination in which their results were expressed in CFU.

Study quality assessment

All the included studies defined the type of substrate, used either negative or positive controls, and reported decontamination results in mean CFU. The SciRAP resource assessment results demonstrated a mean reporting quality score of 86.50 ± 5.47/100 and a mean methodologic quality score of 9.19 ± 4.59/100. Table 2 illustrates the reporting and methodological quality scores assessment for the included studies.

Study characterization

Nine of the studies included in the analysis investigated the effect of decontamination on single-species biofilms, specifically *Streptococcus mutans (S. mutans)* [19,20], *Streptococcus sanguinis (S. sanguinis)* [21], *Staphylococcus aureus (Staph. aureus)* [22], *Streptococcus gordonii* (*S. gordonii*) [23], *A actinomycetomcomitans* [24–26], and *Tannerella forsythia (T. forsythia)* [27]. The remaining four studies focused on multi-species biofilms. Abushahba et al. [28] examined a dual-species biofilm of *F. nucleatum* and *P. gingivalis.* Misischia et al. [27] also utilized a biofilm

comprising three bacterial species: *S. mutans*, *Streptococcus oralis (Staph oralis)*, and *A. actinomycetomcomitans*. In the Citterio et al. [30] study, the biofilm used contains *Staph aureus*, *Staphylococcus epidermidis (Staph. Epidermidis)*, *Streptococcus anginosus (S. anginosus), Streptococcus salivarius (S. salivarius), Streptococcus mitis (S. mitis)*, *F. nucleatum,* and *Capnocytophaga ochracea*. Meanwhile, Stein et al. [31] investigated a biofilm composed of *A. actinomycetomcomitans*, *Actinomyces oris, F. nucleatum, Streptococcus sanguinis (S. sanguinis),* and *S. oralis* in addition to *Candida albicans.*

Most of the included studies used Ti discs as a substrate for the biofilm [20,22–29,31]. In contrast, two studies used commercially available (Osseotite Biomed 3i) dental implants coated with biofilms in an in vitro laboratory environment and placed in simulated circumferential bone defects [21,30], and one study used sandblasted and acid-etched (SLA) implants [19].

Ti curette and stainless-steel ultrasonic scaler tips were used in one study [31]. Air particle abrasion was used in five studies with various abrasive materials, including bioactive glasses [20,28], glycine, amorphous silica [21,30], sodium bicarbonate [21], and erythritol [30,31]. One study [23] tested airflow containing amino acid glycine compared to sodium chloride (NaCl), alkaline electrolyzed water, and hydrogen peroxide (H_2O_2). Four studies used photodynamic therapy (PDT) to decontaminate the bacterial biofilm from SLA and polished Ti surface [22,24,25,27]. Various types of lasers were also used, including semiconductor lasers like diode lasers (DL)[25], neodymium-doped yttrium aluminum garnet (Nd:YAG) [27,29], erbium, chromium-doped yttrium, scandium, and gallium garnet (Er,Cr:YSGG) [29] and erbium-doped yttrium aluminum garnet (Er:YAG) [31] (Table 3).

Descriptive results

Mechanical debridement

Curettes and ultrasonic scalers

In Polizzi et al. [19] study, ultrasonic scalers with various tips, EMS steel, EMS Peek, and IS-Tip_STS_3E tips, were used to decontaminate implant surface *S. mutans* biofilm. After decontamination, the implants were incubated for 3 h. A significant reduction in the *S. mutans* count was reported for the implants cleaned with the EMS Peek or IS-Tip_STS_3E tips. Using the EMS steel did not reduce the bacterial count; instead, it led to an increase after 3 h of incubation. Stein et al. [31] also used ultrasonic scalers with stainless steel tips to decontaminate Ti discs covered with *A. actinomycetomcomitans*, *Actinomyces oris, F. nucleatum, S. sanguinis, S. oralis,* and *Candida albicans* biofilms. No significant decrease in the microbial count was observed on the discs. However, a significant reduction of rRNA count, which represents microbial activity, was observed on the substrates. The same study also tested the effectiveness of Ti curette; however, no significant reduction was observed in the bacterial or rRNA counts (Table 3).

Air particle abrasion (APA)

APA with chemical

Quintero et al. [21] used Airflow Perio and Cavitron Jet Plus to deliver a combination of water and glycine, amorphous silica, sodium bicarbonate, and mint flavored with sodium saccharin to decontaminate *S. sanguinis* biofilm from OSSEOTITE (BIOMET *3i*) dental implant surfaces. Using either air-abrasion instrument demonstrated a significant reduction in the viable bacteria compared to the control. Citterio et al. [30] have also evaluated air-abrasion in decontaminating OSSEOTITE (BIOMET *3i*) dental implant surfaces biofilm composed of seven microbial species. Their study combined air-abrasion with erythritol amorphous silica and 3% CHX, with or without sulfuric/sulfuric acid, compared to air-abrasion without powder. Combining air abrasion with chemicals significantly reduced bacterial count compared to air abrasion without powder. Similarly, in the Ichioka et al. [23] study, airflow combined with amino acid glycine was also used to decontaminate machined Ti discs covered with *S. gordonii* biofilms. After decontamination, the discs were placed in NaCl, alkaline electrolyzed water, or H_2O_2 for 60 s. All treatment groups significantly reduced *S. gordonii* biofilm (Table 3).

APA bioactive substance

Bioactive glasses (BAG), the original Hench glass (45S5), and dopped with zinc (Zn) were used in air-abrasion application to decontaminate SLA discs covered with *S. mutans* [20] or *F. nucleatum* and *P. gingivalis* dual biofilm [28]. After BAG air abrasion, the decontaminated discs were cultivated for 5 h for *S. mutans* and 23 h for the anaerobic bacteria. Significant reduction in *S. mutans* and *F. nucleatum* counts and complete eradication of *P. gingivalis* were reported in either 45S5 BAG or the Zn-containing BAG compared to intact biofilm or discs decontaminated using inert glass controls (Table 3).

Chemical disinfection

Chemical agents such as CHX, H_2O_2, iodine, doxycycline, Sodium hypochlorite (NaOCl), toluidine blue (TBO), and erythrosine (an iodine-containing color) are investigated as a single decontamination approach in the studies included in this review. CHX in 0.12% and 0.2% concentrations was used to decontaminate single species [6,8,9] and multi-species [27,31] biofilms formed on Ti substrates with various surface characteristics. All studies reported significant biofilm disinfection effects of CHX except two studies, in which the effect was insignificant [24,31]. In one study [24], TBO was used to decontaminate *A. actinomycetomcomitans* biofilm from SLA discs, and a significant decrease in the bacterial count was reported compared to the negative control. In the Cho et al. [26] study, erythrosine was used to decontaminate similar discs covered with the same bacterial biofilm but showed no significant effect. In two studies [22,27], H_2O_2 in 3% and 0.2 % concentrations were used, and both studies reported significantly positive effects compared to controls. In Stein et al.'s [31] study, 10% povidone-iodine, 14 % doxycycline, and 0.95% NaOCl were also used to decontaminate the multi-species biofilm from SLA Ti surfaces. No significant effects were observed on all decontamination measures except 0.95% NaOCl, which significantly decreased the rRNA count on the substrates (Table 3).

Photodynamic therapy

PDT was used as a single-treatment approach to decontaminate various bacterial biofilms, including *S. aureus* [22], *P. gingivalis*, and *T. forsythia* [27]. PDT was an effective decontamination method to decontaminate single species *S. aureus* biofilm and showed a significant reduction in the bacterial CFU count on polished and SLA surfaces compared to CHX, H_2O_2, and non-decontaminated controls. PDT was also an effective method to decontaminate polished Ti surfaces covered with *P. gingivalis* and *T. forsythia* dual-species biofilm (Table 3).

Laser

Five studies used a laser as a single or combined decontamination approach [22,25,27,29,31]. These included Nd:YAG [27,29] Er:YAG [29], Er,Cr:YSGG [29], a diode with various wavelengths [22,25,29], and CO_2 [29]. As a single treatment approach, Nd: YAG significantly reduced *T. forsythia* and *P. gingivalis* [27], *S. mutans*, and *A actinomycetomcomitans* [29]. Also, in Stein et al. [31] study, the Er:YAG laser effectively reduced the rRNA count of the 6 multi-species biofilms compared to the non-decontaminated control. Misischia et al. [29] also used Er,Cr:YSGG, and diode laser and showed that both significantly reduced *S. mutans, S. oralis,* and *A actinomycetomcomitans* compared to control. However, in Etemadi et al. [25], using a diode laser for 4 min was ineffective in completely eradicating *A actinomycetomcomitans* (Table 3).

Combined Therapy

In the study by Cai et al. [22], PDT was combined with CHX or H_2O_2 to decontaminate SLA surface bacterial biofilm. Significantly less *Staph. aureus* was observed in the combined treatment approach than the PDT alone. Likewise, in the study by Ghasemi et al. [24], combining TBO with LED PDT was significantly more effective in eradicating SLA *A actinomycetomcomitans* biofilm than TBO alone. However, when TBO was combined with laser PDT, no significant effect was reported compared to TBO alone. In the study by Etemadi et al. [25], combining PDT, DL, and phycocyanin resulted in significantly lower *A actinomycetomcomitans* counts than using them individually in decontaminating Ti SLA surfaces. Similarly. in the study by Cho et al. [26], combining erythrosine with LED light for 30 or 60 sec resulted in a significantly more significant reduction of *A actinomycetomcomitans* on SLA surfaces compared to erythrosine alone (Table 3). A summary of the most effective treatment approaches is given in Table 4.

Discussion

Peri-implant mucositis and PI are inflammatory conditions associated with microbial biofilm, and their treatment has mainly involved decontaminating implant surfaces [32]. The goal of treatment is to eradicate the microbial biofilm, leaving the previously contaminated implant surface suitable for the attachment and proliferation of host cells [15]. However, implant threads, which commonly have a roughened surface to enhance osseointegration, can become exposed to oral microorganisms and hinder implant surface cleaning [33]. Several implant surface decontamination protocols have been suggested; however, a universally accepted protocol or method has yet to exist. This systematic review evaluated the commonly used

mechanical, chemical, and physical decontamination methods as a single or combined approach to decontaminating Ti discs or implants with various surface characteristics.

Peri-implant bone healing occurs in two patterns: contact osteogenesis, which refers to bone formation directly on the implant surface, and distance osteogenesis, which describes new bone formation on the surfaces of the existing host bone [34]. Healing of bone defects around the implant occurs in a series of events that start initially with a blood clot formation, which fills the defect space [35]. The clot is then replaced by a connective tissue matrix, regarded as a scaffold for the woven bone formation. In contact osteogenesis, newly formed woven bone forms on the implant surface without being connected to the parent bone [36,37]. The healing process suggested that contact and distance osteogenesis contributed to the closure of the marginal defects. It is worth noting that healing around the exposed implant surface due to PI may not necessarily follow the pattern for newly inserted implants into the fresh bone. The exposed implant surfaces lack possible inherent osteoconductive properties, essential for stimulating the attachment and proliferation of bone-forming cells, which could impede potential contact osteogenesis. Therefore, following meticulous surface decontamination, various bone graft materials, including autogenous, allogenic, xenogenic, and alloplastic bone materials, have been used to augment bone defects. [38,39].

Despite the reported effectiveness of using ultrasonic instrumentation for implant surface mechanical debridement [19,31], the main problem concerning these devices is their tendency to alter the surface topography of the pristine implant, especially when using tips of hard materials like steel or Ti [40,41]. These topographical changes have been reported to increase roughness to implant surfaces and thus may facilitate bacteria recolonization [4243]. Another concern associated with hard material tips is that the detached Ti particles, due to the instrumentation procedure, remain in the peri-implant tissue, which may cause an immunologic reaction [44]. Softer materials for ultrasonic tips, such as carbon, resin, or polyether ether ketone, have been suggested for implant surface debridement to minimize damage to the original surface morphology [45,46]. Although these softer tips cause less surface alterations than conventional stainless-steel curettes and ultrasonic tips, various studies have shown they are ineffective in eradicating bacterial biofilm [47,48]. Therefore, the adjunctive benefit of chemicals such as CHX and local antibiotics or antimicrobial PDT has been considered [49].

The APA technique has also been used to decontaminate infected Ti/implant surfaces using various abrasive materials, such as amino glycine powder, sodium bicarbonate, hydroxyapatite, and BAG [50,51]. The results of this systematic review indicate that APA is an effective method for eradicating various types of bacterial biofilms. However, research has shown that APA could alter the targeted implant's surface characteristics, such as roughness, wettability, and surface-free energy [52,53]. In contrast, other research demonstrated that the APA effectively cleans bacterial biofilm without altering the morphological characteristics of the implant surface [54,55]. The inconsistency in these results may arise from variables in the abrasive powder's characteristics—such as hardness and particle diameter—as well as the abrasion conditions, including the distance from the implant surface and the air pressure applied.
Abrasive materials can be entrapped in implant surface micropores, potentially affecting implant osseointegration either positively or negatively, depending on the biocompatibility

of the abrasive powder. The retention of glass particles on the surface following the APA process has been investigated. The results revealed that placing the abraded Ti discs in an ultrasonic bath for 15 minutes did not affect the quantity of glass particles attached to the surface [50]. Furthermore, APA using BAG powder, such as 45S5 glass, has demonstrated extended antibacterial effects against gram-positive and gram-negative bacteria [20,28]. This extended effect is related to the remaining glass particles entrapped on the surfaces. In addition, BAG APA has been shown to impart osteogenic properties to abraded Ti surfaces that promote osteoblast cell adhesion and proliferation [53]. Furthermore, BAG APA has also been shown to promote osseointegration of experimentally induced bone defects in rats [56]. There is, however, one reported subcutaneous emphysema case that resulted from the use of APA devices in the management of PI due to the forceful injection of air into the loose surrounding connective tissue [57]. Regardless, emphysema complications have been most associated with the use of high-speed handpieces in tooth extraction[58].

Various chemical agents, such as CHX, H_2O_2, TBO, phycocyanin, erythrosine, phosphoric acid gel, and doxycycline paste, have been utilized to decrease bacterial biofilm on infected implant surfaces as a single therapeutic approach. The studies included in this systematic review showed that CHX and H_2O_2 could effectively reduce *Staph. aureus* [22] and phycocyanin could inhibit the *A actinomycetomcomitans* [25]. However, TBO has a limited effect on *A actinomycetomcomitans* biofilms formed on SLA surfaces [24]. Also, on multi-species biofilms, CHX or NaOCl effectively reduced the bacterial biofilm count compared to intact biofilm control [27,29,31,59]. However, in a study by Dostie et al., [60] 1% CHX has been insufficient in effectively eradicating mature multi-species biofilm from SLA Ti surfaces since it resulted in killing only about 12% of the total bacteria. This may be related to the thickness and maturity of the biofilm used. Despite the controversy over their effectiveness, there are some concerns regarding the use of CHX frequently or at high concentrations. Reports have shown that this may modify the surface topography of dental implants, induce cytotoxic effects on cells, and consistently hinder re-osseointegration, especially when used frequently or at high concentrations [61,62]. This also applies to the use of H_2O_2 since exposure of osteoblast and gingival fibroblast to a very low concentration of H_2O_2 (0.05-µg/ml) resulted in a decrease in cell viability of up to 50% (P <0.05) [63]. Therefore, the frequent use of such chemical solutions as a surface decontaminant in PI cases should be avoided, especially at high concentrations, and alternative antimicrobial agents should be considered [61].

Implant surface wettability plays a critical role not only in the early stages of cell adhesion, proliferation, and differentiation but also in determining how effectively chemical disinfectant compounds used to decontaminate implant surfaces can penetrate and interact with the implant's microstructure [64]. The wettability of implant surfaces varies based on the specific surface modifications used. For example, the contact angle (CA) of machined Ti implant surfaces ranges from 64° to 97°, while that of SLA surfaces ranges from 126° to 150° [64]. Thus, the SLA hydrophobic surface may hinder the penetration of disinfectant to the microstructure of the infected implant surface, therefore affecting its decontamination effectiveness. Recent research has demonstrated that applying 2% dimethyl sulfoxide (DMSO) to a Ti implant surface for 5 min significantly decreased the CA from 67.8° to 18.21°. Therefore, applying such a chemical before using the disinfectant could facilitate its reachability into the implant microstructure[65].

In contrast, PDT is a non-invasive treatment approach that combines low-power lasers with photosensitizers to reduce local microbial biofilms [66,67]. The photosensitizing agent generates highly reactive free radicals, which, at high concentrations, become toxic and cause irreversible oxidative damage to microorganisms by affecting their membrane, mitochondria, and nuclei [68]. The results of this systematic review demonstrated that PDT is an effective method in decontaminating infected Ti surfaces covered by various bacterial species associated with PI. In the Cai et al. [22] study, combining PDT with 0.2% CHX was more effective in eliminating *S. aureus* biofilm than a single treatment alone, indicating that PDT could provide an additional benefit to the chemical approach. Despite the studies that have reported an effect of CHX on Ti implant surfaces [61,62], Saffarpour et al. [69] have shown that combining laser or PDT with CHX on SLA Ti surfaces contaminated with *A actinomycetomcomitans* revealed no changes to the implant's surface characteristics as demonstrated by scanning electron microscopic evaluation.

Numerous types of lasers, including gas lasers, e.g., CO_2, semiconductor lasers, e.g., diode lasers, and solid-state lasers, e.g., Er:YAG, Nd:YAG, and Er,Cr:YSGG, have been used for implant surface biofilm eradication [70]. Studies included in this review demonstrated that all types of lasers effectively decontaminate single- and multi-species bacterial biofilms from various Ti surface topographies, with the best results obtained by using Nd:YAG [25,27,29,31]. These findings align with the results of Kang et al. [58], which indicated that Er,Cr:YSGG laser resulted in more favorable results in managing PI than conventional mechanical debridement methods. However, Renvert et al. [71] and Schwarz et al. [72] have reported controversial results, which showed that Er:YAG and DL have little or no effect in removing bacterial biofilm from the Ti implant surface. In the Etemadi et al. [25] study, DL, PDT, and phycocyanin combined were more effective than individually using any treatment modality. Tonin et al. [73] compared laser to PDT in decontaminating in vitro subgingival periodontal biofilm cultures from periodontitis patients. Their study reported a reduction in bacterial count in both treatment modalities, with a more favorable effect obtained using PDT. These findings align with those reported in this systematic review by Anil et al. [27], which showed a more favorable effect of using PDT over Nd:YAG laser. It is important to note that the laser dose plays a crucial role in implant surface biofilm removal efficiency. Nevertheless, increasing the dose can cause implant surface damage, as reported by Tonin et al. [73]. Their study indicated that the Er:YAG laser could alter the oxide layer of SLA discs and increase surface roughness. Moreover, laser use can raise the temperature, particularly with Nd:YAG, diode, and CO_2 lasers [74,75]. Accordingly, special care is needed to avoid tissue damage during laser application.

Bacterial debris, such as lipoteichoic acids from Gram-positive bacteria and lipopolysaccharides from Gram-negative bacteria, is released mainly after bacteriolysis and can persist on implant surfaces [76] . These bacterial by-products have the potential to activate the immune system, leading to inflammatory responses. If this debris remains on a decontaminated implant, it may hinder reosseointegration, compromising the implant's survival [77]. One notable limitation of this systematic review is that it did not assess the efficacy of decontamination methods in removing these bacterial by-products from implant surfaces. This gap highlights an important area for further research, as there is currently insufficient data assessing the efficacy of available decontamination methods for eliminating

these toxic remnants. It is also worth highlighting that this review specifically focused on studies conducted under in vitro conditions. In vitro studies play an essential role in the early stages of research, as they are essential for identifying and evaluating novel treatment approaches in controlled environments. However, the findings from in vitro studies often require further validation in more complex biological systems. Therefore, a separate systematic review that will focus exclusively on in vivo studies will be considered in the future.

Furthermore, it is important to note that the included studies in this systematic review exhibit notable variability, representing a noteworthy limitation. This heterogeneity may arise from the discrepancies in bacterial biofilms utilized. While some studies used single-species biofilms, others used multi-species biofilms, leading to distinctions in the complexity of the biofilms being investigated. Further, the incubation time between studies varied considerably even when similar bacterial species were used for biofilm formation. These inconsistencies in biofilm composition and incubation protocols affect the complexity and maturation of the biofilm, making it difficult to compare outcomes and draw robust conclusions directly across the studies. In addition, this review did not consider surface properties such as composition, roughness, and wettability, which could affect the retention and cleaning effectiveness of the bacterial biofilm.

Conclusions

The current results do not indicate that any single decontamination technique is more effective than others in eradicating bacterial biofilm from titanium implant surfaces. Air abrasion using bioactive glass seems to provide an extended antibacterial effect that could inhibit bacterial recolonization on titanium surfaces. Combined mechanical or physical methods with a chemical method result in favorable outcomes. In vitro studies are essential in identifying novel treatment approaches. Nevertheless, methodological divergences, such as various biofilm types, limit the ability to systematically evaluate outcomes and identify which methods can be applied in clinical settings. Further studies with fewer variations are needed to thoroughly evaluate the effectiveness of various implant surface decontamination methods.

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Author contributions

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Conflict of interest statement

All authors declare that they have no conflict of interest.

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