European Journal of Prosthodontics and Restorative Dentistry (2024) **32**, 314–325

Effect of Surface Treatment on Titanium Surface Free Energy and its Relation to Bacterial Activity: A Systematic Review

Keywords

Dental Implants
Surface Properties
Bacteria
Titanium

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ABSTRACT

The surface properties of titanium dental implants, such as wettability and surface free energy, influence the adhesion of microorganisms responsible for inflammation and infection of peri-implant tissues. This systematic review aimed to investigate the relationship of titanium surface treatments, surface free energy/wettability property and its relationship with bacterial activity. This systematic review followed PRISMA 2020 (Preferred Reporting Items for Systematic Review and MetaAnalysis) guidelines and was registered in the OpenScience Framework (osf.io/ejnct). PubMed, ScienceDirect, Embase, and Scopus library databases were used from custom search strategies. Inclusion criteria were research articles that studied titanium or its alloys for wetting property and its correlation with adhesion. Of the 697 articles initially identified, 27 were selected after full-text reading and application of the eligibility criteria. In general, the evaluated studies showed that regardless of the surface treatment, there was an increase in titanium hydrophilicity and concomitant reduction in bacterial adhesion. The surface treatment of titanium results in higher surface free energy and lower bacterial adhesion. Hydrophilic titanium surfaces prevent adhesion of hydrophobic bacteria in early stages.

INTRODUCTION

Titanium and its alloys are used as biomaterials for medical and dental purposes. For dental implants, there are attempts to optimize their surfaces, either by changes in physical, topographical, biological, or chemical conditions, to promote higher resistance to corrosion and bacterial contamination, or by surface modifications that provide a strong bone-implant connection, by increasing wettability, which can promote better interaction with cells, tissues and biological fluids, and higher surface free energy, which the higher it is, the higher the bioactivity of the surface is found, as it favors the adsorption of proteins and bone cells, besides reducing bacterial adhesion by decreasing the sites of colonization.[1-4]

The optimization of these properties provides better conditions for cell activity related to osseointegration and may hinder the adhesion of microorganisms responsible for inflammation and infection of peri-implant tissues,[1,2] and consequent complications related to dental implant failure. A highly wettable surface with adequate surface-free energy facilitates bone cell adhesion and proliferation, thus promoting bone formation around

Received: 17.10.2023
Accepted: 28.04.2024
doi: 10.1922/EJPRD_2609Soares12

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the implant and long-term stability. Moreover, an optimized surface also hinders the adhesion of microorganisms, such as bacteria, to reduce the risk of inflammation and infection of peri-implant tissues.[3] It is reported that up to 14.5% of patients affected by this disease present moderate to severe complications, and in 7.5% of cases implant loss occurs.[4]

Biofilm formation on oral cavity substrates is a complex process that begins with the adhesion of primary colonizers, such as *Streptococcus spp*. and *Actinomyces spp*. through interaction with saliva.[5] Authors have demonstrated the importance of surface textures in initial biofilm formation, especially when it occurs in situ.[2,3,5-8] A hydrophobic and rougher titanium surface has been observed to favor the adhesion of species such as *S. sanguinis*, which easily aggregates with other hydrophobic species such as *A. actinobacillus*, *A. actinomycetemcomitans*, and *Porphyromonas gingivalis*. This interaction between different bacterial species may induce peri-implantitis.

Besides the effects on bacterial adhesion, the hydrophobicity of titanium surfaces may also lead to protein accumulation. These proteins adsorbed on the surface act as specific binding sites for some bacteria, promoting their adhesion and biofilm formation. Therefore, hydrophobic surfaces may contribute to bacterial colonization and the development of complications in peri-implant tissues.[7] On the other hand, increasing the surface free energy or making titanium more hydrophilic may have significant benefits, as more hydrophilic surfaces have a higher affinity for water molecules and biological fluids, which may improve the biocompatibility of the dental implant.[8] This greater hydrophilicity may favor cell interaction with the substrate and surrounding medium, so as to stimulate cell differentiation and bone matrix deposition around the implant.[8]

Surface treatments of dental implants play a crucial role in promoting hydrophilicity and resistance to bacterial colonization. Materials with higher surface-free energy have been shown to be more effective in preventing bacterial adhesion, thereby reducing the risk of implant-associated complications.[10] A common approach to promote hydrophilicity is the application of chemical coatings based on biocidal substances that are deposited sequentially to form multilayers that act as protective barriers on the metal surface of the implant,[10] which may include antibiotics, heavy metals, quaternary ammonium-based components, or antimicrobial peptides,[11] or by other physical, chemical, or mechanical processing methods, which include techniques such as surface roughness modification, laser treatments, electrochemical oxidation, plasma deposition, and others.[11,12]

Titanium surface properties, such as wettability and surface free energy, have been studied to understand their influence on bacterial adhesion and biofilm formation.[6,7] Surface treatments aim to modify these properties to prevent bacterial colonization and promote osseointegration of dental implants through increased initial stability.[11,12] Thus, this systematic review aims to investigate the relationship between surface treatments, titanium surface free energy, and bacterial activity, providing a scientific basis for the development of effective surface treatment strategies for dental implants.

MATERIAL AND METHODS

The present systematic review sought an answer to the question, "What is the influence of different titanium surfaces on surface-free energy and its correlation with bacterial adhesion?" This review was constructed according to PRISMA 2020 (preferred reporting items for the systematic review and meta-analysis). In addition, the protocol was registered with the Open Science Framework (osf.io/s7jze). The search strategy used for population, intervention, comparison, outcome, and outcome (PICOS) is described in Table 1.

Table 1. The Population, Intervention, Comparison, Outcome and Study Design (PICOS) strategy for this systematic review.

PICOS	Description
Population	Titanium surface
Intervention	Surface Treatment
Comparison	Control Group (Titanium surface that did not receive a surface treatment)
Outcome	Assessment of free energy of surface and bacterial adhesion
Study Design	*In vitro* studies

PICOS, Population, Intervention, Comparison, Outcome and Study Design.

This review included articles that evaluated the surface-free energy/wettability and bacterial activity properties of titanium and its alloys. For this purpose, articles with *in vitro* analyses were used. After the exclusion criteria were defined, articles that did not use titanium surfaces, did not perform surface treatments, and did not describe the relationship between wettability/surface-free energy and bacterial adhesion were removed. Studies with only *in vivo* analyses, systematic reviews, book chapters, short communications, conference abstracts, case reports, and personal opinions were also excluded.

The search strategy was applied to the following electronic databases: PubMed, Scopus, Science Direct, and Embase (Supplementary Table 1, available online) on June 24th, 2023. Furthermore, an additional search was performed in the reference and citation lists of the included articles to find new possible inclusions.

The first reading of the articles was performed by 1 author (V.M.S.). The findings were attached to the Rayyan digital platform and then evaluated by 2 independent authors (V.M.S, M.L.C.V.) who were responsible for analyzing the articles according to the pre-established inclusion and exclusion criteria. The remaining studies were read in full.

The reviewers independently tabulated data in a Microsoft Excel spreadsheet according to Author, year; Population (alloy, groups); Intervention (surface treatment); Investigation (Assay and Microrganisms); Outcome for antibacterial activity (Results); the outcome for bacterial activity (assay, cell, and result), energy free surface/wettability and, conclusion were detailed in Table 2.

Table 2. Characteristics of studies that evaluated bacterial activity on the titanium alloy surface after surface treatment.

Article	Alloy	Surface Treatment	Microorganism And Assessment Method	Main Results
Akhavan et al., 2018	Ti	Ion-assisted plasma polymerization	*Candida albicans* Static biofilm assay by Chandra et al., 2008. *S. aureus* Fluorescence Confocal Microscopy Wettability	Surface treatment significantly altered Ti's SFE (53.7±0.5mJ/m²) compared to untreated surface (65.9±0.1). The coating exhibited favorable antimicrobial activity, reducing *C. albicans* adhesion by 10x compared to uncoated material.
Lee et al., 2017	Ti and Ti-Ag	Non-thermal Atmospheric Pressure Plasma Jet (NTAPPJ)	*S. sanguinis* FCM Wettability	The N2 NTAPPJ functionalization of Ti and Ti-Ag samples resulted in increased SFE due to hydrophobicity, leading to reduced bacterial adhesion and the most significant reduction in bacterial count.
Matos et al., 2017	Ti	Micro-arc oxidation (MAO) and Glow Discharge Plasma (GDP)	*S. sanguinis* *A. naeslundii* *F. nucleatum* SEM and CLSM Wettability	The GDP provided hydrophobicity and higher SFE compared to the control groups (sandblasted and no treatment) and MAO. The surface treatments did not influence biofilm formation, except for the MAO group, which reduced *F. nucleatum* adhesion.
Valverde et al., 2019	Ti-6Al-4V	Laser + Layer-by-Layer (LbL) Hyaluronic Acyd/ Chitosan (HA/CHI)	*S. aureus* Viability and Adhesion assays Wettability	The laser treatment resulted in increased hydrophilicity. However, after the LbL coating, the surfaces became hydrophilic, which facilitated loading with triclosan. The HA/CHI treatment without loading achieved 28% reduction in bacterial viability, while those loaded with triclosan resulted in complete bacterial inactivation.
Linklater et al., 2019	Ti	Mask-less plasma etching (5', 10', 20', 30', 40') + Two-dimensional Fast-Fourier Transforms (2D-FFT)	*P. aeruginosa* *S. aureus* CLSM Wettability	Hydrophilicity decreased as time increased, reaching 111° after 30 minutes. Along with the increased roughness, there was an increase in the hydrophobicity of the samples after 30 minutes. The maximum efficiency of bacterial inactivation was achieved at 30 minutes (87±2%).
Unosson et al., 2015	Ti	Sputter-deposition. (gradient coating Ag-Ti)	*S. aureus* CFU Wettability	The light exposure treatment increased the hydrophilicity on the porous side of Ag deposition and reduced SFE on the Ti deposition side. UV light exposure resulted in superhydrophilicity and lower surface roughness. CFU analysis across the surface showed a 99.6% reduction in the Ag-rich region compared to the control, and between 17% and 58% reduction in the Ti-rich region.
Chrzanowski et al., 2010	Ni-Ti	Thermal Treatment (200, 400, 600°C) OR Alkali treatment + thermal treatment (600°C) OR Plasma electrolysis (spark oxidation)	*Staphylococcus aureus* Colony Forming Unity (CFU) Wettability	Increasing temperature reduced SFE: 600°C showed the most hydrophobicity. Light activation reduced CFU count and increased SFE. Despite the higher CFU count observed in the 600°C samples, light activation led to a reduction in bacterial adhesion.
Dini et al., 2020	Ti	Plasma eletrolytic oxidation (PEO) OR UV light application	*S. sanguinis* CFU SEM Wettability	PEO treatment showed hydrophilicity and higher protein adsorption capacity. UV light application enhanced hydrophilicity, protein adsorption, and bacterial reduction in the initial phase of biofilm formation. The combination of UV light and PEO treatment improved both surface and biological characteristics of the material.

Table 2 continued...

Table 2. Characteristics of studies that evaluated bacterial activity on the titanium alloy surface after surface treatment continued...

Zhang et al., 2019	Ti	Acid corrosion (oxalic acid 6% solution) + Spin-coating (AgNW)	*S. aureus* *E. coli* CFU Wettability	The surface treatments (NaT and AgNaT) resulted in more hydrophilic behavior (38.6°±5.5° and 32.3°±3.7°) than the control and AgNW incorporation. The AgNaT surface showed resistance to bacteria (no colonies were formed on the surface, and almost all bacteria present were killed within 24 hours).
Kim et al., 2018	TIPS-Ti Ag-TIPS-Ti	DC Magnetron Sputtering + TIPS (Ta target)	*E. coli* *S. aureus* UFC Wettability	The TIPS-Ti surface enhance the hydrophilicity (from 61° to 6°). The hydrophilicity decreased with surface stabilization by Ag, but still exhibited higher wettability than the control. Ti and TIPS-Ti showed high bacterial viability and biofilm-forming capacity. The Ag-TIPS-Ti surface inactivated *E. coli* and *S. aureus*.
Liu et al., 2017	Ti-LBL-Zn	Layer-by- Layer (chitosan/gelatin pair with zinc ions)	*S. aureus* *E. coli* UFC Wettability	The Zn-coated film enhance the hydrophilicity compared to the control (85.50°). Ti-LBL-Zn10 decreased to the lowest value obtained (54.60°). The counting of *E. coli* and *S. aureus* recuced (544±26 and 171±13 to 256±20 and 90±).
Shao et al., 2020	Ti-NW-Zn	Zinc incorporation	*S. aureus* *P. gingivalis* *A. actinomycetemcomitans* UFC Wettability	The Ti-SLA exhibited high hydrophobicity (≥90°), while the Ti-NW and Ti-NW-Zn showed excellent hydrophilicity (≤10°). The UFC counting of Ti-NW and Ti-NW-Zn were significantly lower than Ti-SLA. The number of live bacteria was lower in Ti-NW-Zn, and almost no *P.g* and *A.a* were observed.
Cunha et al., 2016	Ti	Laser-induced texture	*S. aureus* UFC Wettability SFE	The treatment increased the hydrophilicity of the samples 48.2º±3.1º to 12.6º±3.1º (water), and the diiodomethane contact angle decreased from 43.7º±0.7º to 15.5º±3.5º (diiodomethane). The treatment reduced *S.a* adhesion. The average fraction of the area covered by microorganisms decreased from 25% to 7%.
Shaikh et al., 2018	Ti	Laser-induced texture (femtosecond laser)	*S. aureus* *P. aeruginosa* *E. coli* UFC;SEM Wettability	The Bioactive Glass enhance the hydrophilicity (73±1° to 34±3°). The adhesion of *S.a* was significantly reduced in S3 (10% adhesion area) and obstructed the adhesion of *A. aeruginosa* and *E. coli*.
Truong et al., 2010	Ti	Equal Channel Angular Pressing (ECAP)	*S. aureus* *P. aeruginosa* UFC Wettability	The wettability and SFE did not differ significantly in control (Ti) and treatment (ECAP). *S.a* and *P.a* showed preference to adhere on the treated surface. Surface architecture was suggested as the reason for bacterial attachment.
Sarker et al., 2019	Ti6Al4V	SLM (10°, 45°, 90°)	*S. aureus* SEM FCM Crystal violet assay Wettability and SFE	All samples (10°, 45°, and 90°) were found to be hydrophobic (95.3°, 108.5°, and 114.5°), respectively. SFE followed the inverse order (13.81, 9.13, 7.76 mJ/m²). Higher manufacturing angles were associated with increased roughness, hydrophobicity, and *S. aureus* adhesion (11.5%, 13.6%, 20.3%).
Ozdemir et al., 2016	Ti	Chemical-Mechanical Polishing (CMP)	*C. sakazaki* UFC Wettability	The CMP 3% H_2O_2 on a polyester pad showed the highest hydrophilicity (34.3±2.6), while control (84.4±0.7). Bacterial growth was limited to the thickness of the oxide protective layer, and bacterial adhesion was attributed to the increase in surface roughness.

Table 2 continued...

Table 2. Characteristics of studies that evaluated bacterial activity on the titanium alloy surface after surface treatment continued...

Agarwalla et al., 2019	Ti + Graphene	Vacuum assisted transfer technique (graphene coating)	S. mutans E. faecalis *P. aeruginosa* *C. albicans* Violet Crystal assay CLSM Wettability and SFE	The treatment increased the hydrophobicity and higher contact angles were obtained with more layers of treatment. SFE decreased with the increase in treatment layers, respectively: 38.3; 18.1; 13.8; 12.1 mN/m. The lowest biofilm formation was observed on the double layer, which was statistically correlated with the lower SFE.
Cordeiro et al., 2018	Ti15Zr	Plasma eletrolytic oxidation (PEO)	*S. sanguinis* CLSM Wettability SFE	The PEO resulted in the most hydrophilic surface (30°) and highest SFE compared to SLA (104°) and machined surfaces (89°). The CFU count had the best results for PEO along with better protein adsorption., SLA and Machined group, respectively.
Ferraris et al., 2016	Ti	Hydrofluoric acid + Controlled oxidation in hydrogen peroxide	- SEM XPS FTIR AFM Wettability	The blasting step prior to the proposed treatment made the surface hydrophobic. However, the use of H_2O_2 made the surface hydrophilic. The proposed treatment shows potential for minimizing bacterial adhesion, but microbiological tests were not conducted.
Al-Radha et al., 2012	Ti	Polished partially stabilized zircionia (PZ) OR Zirconia blasting (TBZ) Zirconia blasting OR acid etching (TBZA)	*S. mitis* *P. nigrescens* FCM Wettability SFE	TBZA exhibited the highest hydrophilicity (131.51±5.0). PZ, TBZ, and TBZA showed the lowest values of SFE (33.4°±0.30°; 31.34°±0.31°; 36°±0.60°, respectively). PZ and TBZA provided lower bacterial adhesion than PT, which was related to the presence of zirconia and lower SFE.
Wojcieszak et al., 2016	Si and SiO_2 glass	Magnetron sputtering method (Ti-Ag and Nb-Ag coatings)	*B. subtilis* *P. aeruginosa* *E. coli* *E. hirae* *K. pneumoniae* *S. aureus* *C. albicans* Wettability UFC	Ti-Ag and Nb-Ag exhibited hydrophilic characteristics (55.7° and 60.6°, respectively). Ti-Ag was resistant to *B. subtilis* and *S. aureus*, while Nb-Ag eliminated them only after 6 hours. Within 6 hours, *B. subtilis*, *P. aeruginosa*, *E. coli*, *S. aureus*, and *C. albicans* were eliminated. *E. hirae* and *K. pneumoniae* were eliminated after 24 hours.
Konatu et al., 2021	Ti-15Zr	Oxidation process (TiO_2 nanotubes)	S. epidermidis UFC	The surface did not differ from the control in terms of colony number. After annealing (450°C), the anatase phase was formed, which promoted greater cell adhesion and reduced bacterial adhesion.
Hoyos-Nogués et al., 2018	Ti	PEG eletrodeposition (polyethylene glycol bis terminated)	*S. sanguinis* UFC	The plasma provided the most hydrophilic surface, with PEG exhibiting greater hydrophobicity than the plasma, but not than the control. PEG promoted a reduction in protein adsorption. No bacterial colonies were observed on PEG and PEG+PTF surfaces (indicating their ability to prevent bacterial attachment and act as bactericides).

Table 2 continued...

Table 2. Characteristics of studies that evaluated bacterial activity on the titanium alloy surface after surface treatment continued...

Neto et al., 2024	Ti-6Al-4V	Machined (DU); Machined+Hydroxyapatite (DUHAp); Machined+acid-alkati treatment (DUAA); Additive Manufacturing (DMA).	*S. aureus* MEV EDS DRX UFC Wettability	DUAA and DUHAp showed similar hydrophobicity (P=0.831). DMA exhibited superhydrophilicity (36.02°±6.82°), while DU showed hydrophilicity (40.17°±3.64°). A higher UFC value was observed in DMA. DUHAp and DUAA showed a lower UFC value, influenced by better wettability and SFE.
Choi et al., 2023	Ti	Sandblasting with 50-µm alumina particles at a pressure of 2 bar	*S. gordonii* *F. nucleatum* *P. gingivalis* UFC; CLSM; Violet crystal assay; SEM; Wettability.	The treatment provided increased surface hydrophilicity (72.0°±1.6°) compared to the control (38.0°±4.8°). For all evaluated species, biofilm formation and adhesion were significantly higher on the treated surface.
Priyanka et al., 2023	Ti-6Al-4V	TiN-Ag coating	*S. aureus* XPS XRD SEM Wettability.	TiN-Ag polished and TiN-Ag textured surfaces exhibited hydrophilicity (88.7° and 77.3°, respectively). Antibacterial behavior was efficient for both (84.7% and 85.2%, respectively), but bacterial adhesion was significantly lower on the polished surface than on the textured one.

Surface Free Energy (SFE); Scanning Electron Microscopy (SEM); Confocal Laser Scanning Microscopy (CLSM); Fluorescence Confocal Microscopy (FCM); Colony Forming Units (CFU); X-ray Photoelectron Spectroscopy (XPS); Infrared Spectroscopy (FTIR); Atomic Force Microscopy (AFM); Dispersive X-ray Spectroscopy (EDS).

RESULTS

Figure 1 describes the study selection strategy. A total of 697 results were found, of which 298 were duplicates. After reading the titles and abstracts and applying the inclusion and exclusion criteria, 27 studies were selected for full reading. After reading, all 27 articles were included in the present review. Meta-analysis was not possible due to the lack of homogeneity of the results found in the included articles. Thus, the results were based on a descriptive analysis of the data.

The risk of bias was assessed using the Joanna Briggs Institute (JBI) adapted quasi-experimental study assessment tool. The results obtained after assessing the quality of the studies are shown in Figures 2 and 3. All 27 studies used in this systematic review have a low risk of bias.

For the criterion “Was there a control group?” most studies showed a low risk of bias. The exception was the study by Valverde *et al.*[10] which did not clearly show the control group. In the criterion “Was appropriate statistical analysis used?” approximately 12.5% of the studies[10,20,27] showed a high risk of bias and approximately 8.3% of the studies[15,23] was classified as uncertain. This result is justified by the absence of the statistical procedures or methods used.

This systematic review consists of 27 articles that evaluated different surface treatments, including photoactivation,[12-14] deposition of silver- and zinc-based nanostructures,[15-18] laser application,[10,19,20] mechanical texturing,[11,21,22,34,35] polishing techniques,[21,23] construction of surface gradients from the deposition of various chemical coatings,[6,10-12,17,24-29,36] and application of plasma coatings.[4,8,11,29]

In the studies by Unosson *et al.*,[12] Chrzanowski *et al.*,[13] and Dini *et al.*[14] photoactivations of titanium surfaces were used, and there was a significant correlation (P<0.05) between the applied treatment, surface free-energy, and bacterial adhesion, with decreased contact angle and increased hydrophilicity (P<0.001), as well as a significant reduction in the number of *Staphylococcus aureus* and *Streptococcus sanguinis* bacteria adhered to the surface (P<0.05).

Zhang *et al.*[15] and Kim *et al.*[16] studied the effects of incorporating silver nanostructures into previously treated and untreated titanium surfaces. Zhang *et al.*[15] reported lower contact angle values on surfaces that received acid-base conditioning and silver-based nanostructures (AgNWs) (38.6°±5.5 and 32.3°±3.7, respectively). Kim *et al.*[16] observed that the surfaces modified by Ag-sputtering time (30Ag-TIPST and 120Ag-TIPS-Ti) showed smaller contact angles, thus higher hydrophilicity, and high bactericidal properties. The two authors considered that the incorporation of silver nanostructures to the material was able to inhibit the development of *E. coli* and *S. aureus* species.[15,16]

Liu *et al.*[17] and Shao *et al.*[18] found smaller contact angles after zinc incorporation in pure titanium samples at different times, suggesting better wettability after the application of this type of surface treatment. In the study by Liu *et al.*,[17] the Ti-LBL-Zn10 surface (layer-by-layer deposition of Zn on Ti) showed the lowest contact angle (54.60°), higher surface roughness, and lower

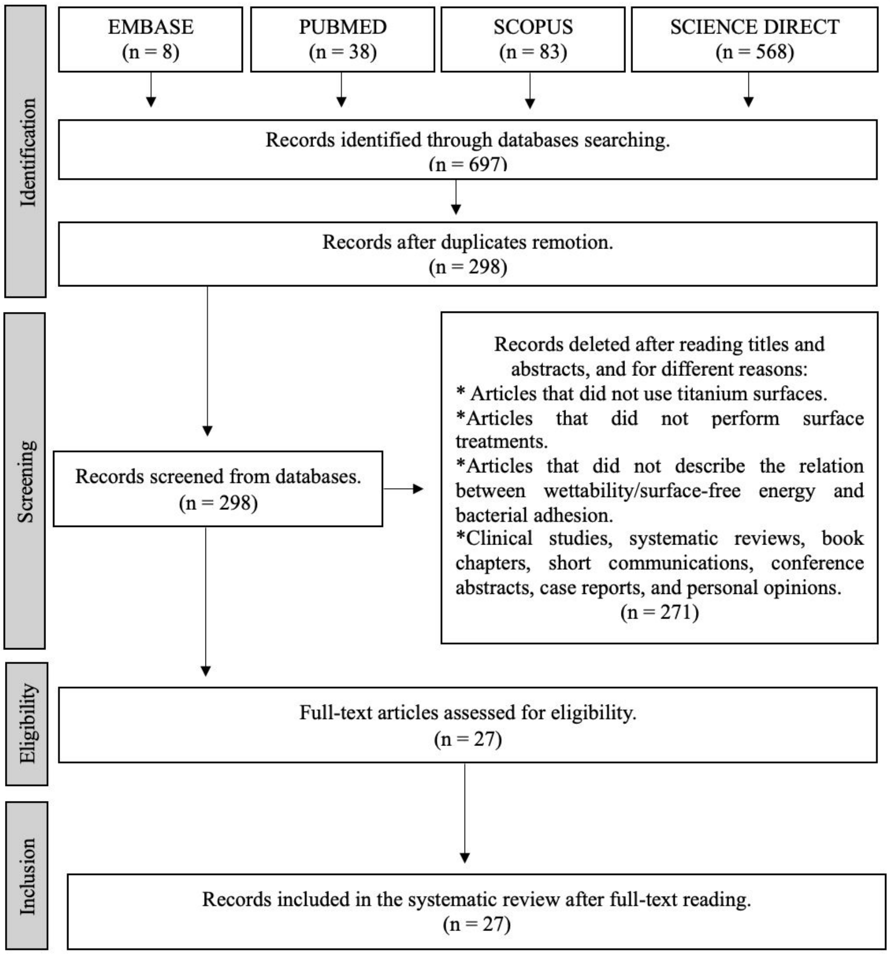


Figure 1: Flow of information through the different phases of the systematic review.

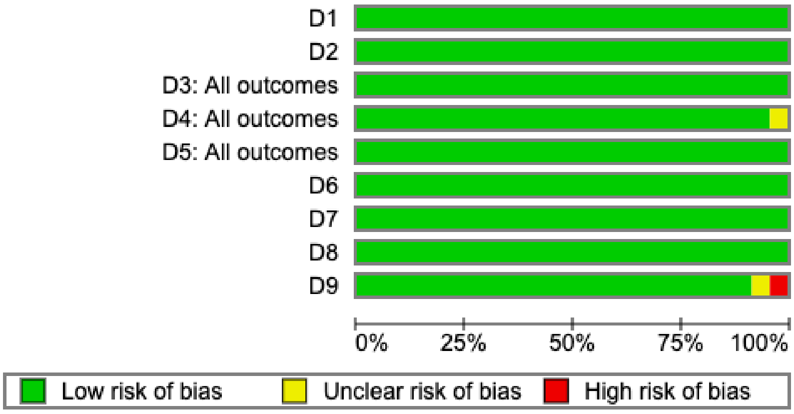
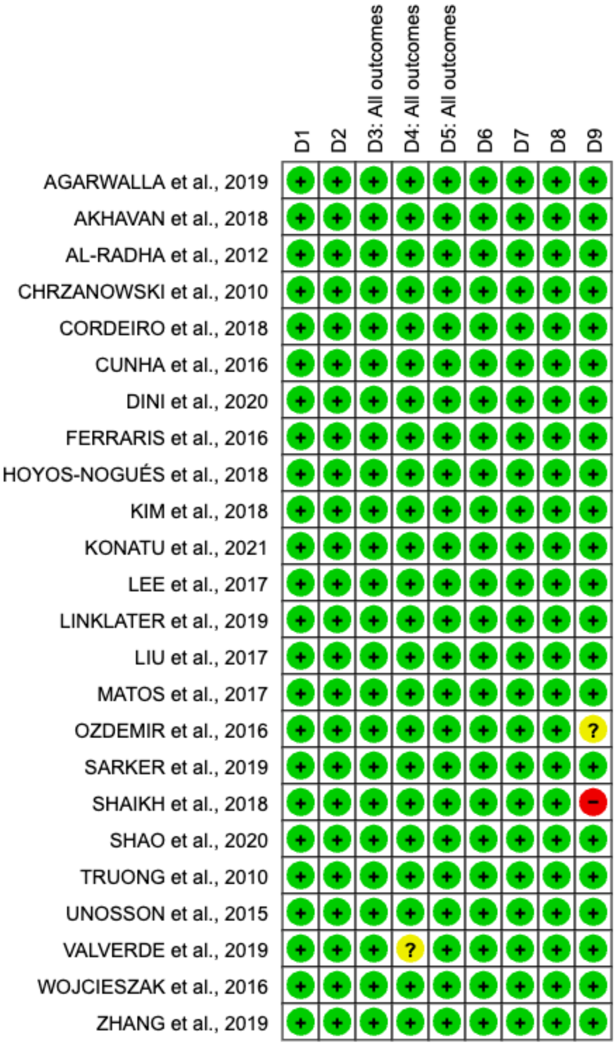


Figure 2: Qualitative analysis with adapted the quasi-experimental studies appraisal tool by the Joanna Briggs Institute.

bacterial viability (*S. aureus and E. coli*) compared to the control group (P<0.01). Shao *et al.*[18] found that surfaces composed of titanium nanostructures (Ti-NW) and, after zinc incorporation (Ti-NW-Zn), showed excellent hydrophilicity and contact angles less than 10°.[18] In the study by Priyanka *et al.*[36] the incorporation of TiN-Ag into the textured surface inhibited the growth of *S.aureus* and provided satisfactory hydrophilicity (77.30°).[36]

Valverde *et al.*,[10] Cunha *et al.*,[19] and Shaikh *et al.*[20] found that laser treatment of surfaces significantly increases the hydrophilicity of specimens. Cunha *et al.*[19] found, from contact angles measured by the sessile drop method, on polished surfaces (48.2°±3.1), and on laser-induced periodic surface structures (LIPSS) (12.6°±3.1) and textured ones (32.1°±9.0).

Linklater *et al.*[11] observed that the wettability of the surface decreases dramatically according to the chemical conditioning time employed: initial contact angle of 55° and after 30 minutes it increases to 111°. In these cases, the adhesion of *P. aeruginosa* species compared to *S. aureus* species was higher due to their hydrophobic characteristics.[11] Neto *et al.*[34] transformed the hydrophobic surface (71.31°±5.97°) into a hydrophilic one



	D1	D2	D3: All outcomes	D4: All outcomes	D5: All outcomes	D6	D7	D8	D9
AGARWALLA et al., 2019	+	+	+	+	+	+	+	+	+
AKHAVAN et al., 2018	+	+	+	+	+	+	+	+	+
AL-RADHA et al., 2012	+	+	+	+	+	+	+	+	+
CHRZANOWSKI et al., 2010	+	+	+	+	+	+	+	+	+
CORDEIRO et al., 2018	+	+	+	+	+	+	+	+	+
CUNHA et al., 2016	+	+	+	+	+	+	+	+	+
DINI et al., 2020	+	+	+	+	+	+	+	+	+
FERRARIS et al., 2016	+	+	+	+	+	+	+	+	+
HOYOS-NOGUÉS et al., 2018	+	+	+	+	+	+	+	+	+
KIM et al., 2018	+	+	+	+	+	+	+	+	+
KONATU et al., 2021	+	+	+	+	+	+	+	+	+
LEE et al., 2017	+	+	+	+	+	+	+	+	+
LINKLATER et al., 2019	+	+	+	+	+	+	+	+	+
LIU et al., 2017	+	+	+	+	+	+	+	+	+
MATOS et al., 2017	+	+	+	+	+	+	+	+	+
OZDEMIR et al., 2016	+	+	+	+	+	+	+	+	?
SARKER et al., 2019	+	+	+	+	+	+	+	+	+
SHAIKH et al., 2018	+	+	+	+	+	+	+	+	−
SHAO et al., 2020	+	+	+	+	+	+	+	+	+
TRUONG et al., 2010	+	+	+	+	+	+	+	+	+
UNOSSON et al., 2015	+	+	+	+	+	+	+	+	+
VALVERDE et al., 2019	+	+	+	?	+	+	+	+	+
WOJCIESZAK et al., 2016	+	+	+	+	+	+	+	+	+
ZHANG et al., 2019	+	+	+	+	+	+	+	+	+

Figure 3: Qualitative analysis with adapted the quasi-experimental studies appraisal tool by the Joanna Briggs Institute per studies.

(19.68°±6.22°) through an acid-alkaline treatment using 85% H_3PO_4, reducing the number of CFU compared to the control, influenced by better surface free energy and wettability.

Matos *et al.*[8] Akhavan *et al.*,[4] Linklater *et al.*,[11] and Hoyos-Nogués *et al.*[30] found that plasma treatments result in smaller contact angles than those recorded for control (Ti) groups. Akhavan *et al.*[4] found smaller contact angles on titanium surfaces that received plasma coating when compared to the control group in both water and diiodomethane (47.3±0.8° and 17.8±0.2°), as well as higher surface free energy (65.9± 0.1 mJ m-2), with lower bacterial (*S. aureus*) and fungal (*C. albicans*) adhesion rates on plasma-coated surfaces.

Hoyos-Nogués *et al.*[30] reported that in samples coated by electrodeposition of polyethylene glycol (PEG) layers, the percentage of dead bacteria increased 8.6% in the coated areas and 10.4% in PEG+PTF samples, so peptides (PTF) strengthened the antibacterial effect. The titanium surfaces in the used control group also showed increased hydrophilicity after surface treatment with PEG. In the study by Matos *et al.*,[8] it was observed that Glow Discharge Plasma (GDP) treatment with the smallest contact angle (20°) showed the lowest bacterial adhesion rates after the longest elapsed time (16.5 h).

However, Truong *et al.*[21] found adhesion of *P. aeruginosa* species at low values of contact angle (43.3°), and both the disc belonging to the control group (Ti) and the Equal channel angular pressing (ECAP)/polished showed low levels of adhesion of this species, as it presents higher hydrophilicity.[21] Ozdemir *et al.*[23] observed that, after applying Chemical-Mechanical Polishing (CPM), the oxide layer covering the titanium discs is removed, resulting in a significant decrease in the contact angle (from 85° to 45°), and a concomitant increase in hydrophilicity.[23] CHOI *et al.*[35] performed sandblasting with 50-μm alumina particles, which provided hydrophilicity (38.0°±4.8° to 72.0°±1.6°), but also greater adhesion of bacterial biofilm.[35]

Regarding the polishing of titanium disks, Ozdemir *et al.*,[23] Truong *et al.*,[21] and Sarker *et al.*[22] reported that high values of contact angle are verified in titanium disks belonging to the control group, considered hydrophobic, due to the air that is trapped between the pores of the oxide layer covering the surface of the disk. Sarker *et al.*[22] verified in their study that all Ti-6Al-4V samples, manufactured by Selective Laser Melting (SLM), presented hydrophobic behavior, whose recorded contact angles were 95.3°, 108.5° and 114.5°. After applying the polishing and mechanical texturing techniques, significant increases in the hydrophilicity of the material and decreased adhesion of bacterial species considered hydrophobic (*S. sanguinis*) were observed.[22]

Al Radha *et al.*[28] found in their study that zirconia (PZ) and titanium-incorporated zirconia (TBZ) surfaces show lower values of surface free energy and percentage of bacterial adhesion when compared to the control group, consisting of pure titanium (PT).[28] Konatu *et al.*[29] reported that cell adhesion is favored after anodization at 20 V for 6 hours associated with subsequent annealing of the material at 450°C. Lee *et al.*[6] found that *S. sanguinis* species, considered hydrophobic, does not easily adhere to the surfaces of Ti and Ti-Ag disks subjected to Non-Thermal Atmospheric Pressure Plasma Jet (NTAPPJ).

Lee *et al.*[6] reported a significant change in the contact angle of the Ti and Ti-Ag samples used in their study (P<0.05), with the surface free energy of the NTAPPJ-treated samples, determined by the Owens-Wendt method, quadrupled when compared to the non-functional ones. In the study by Wojcieszak *et al.*,[28] the surface of the Nb-Ag-based metal specimen showed lower wettability compared to Ti-Ag, so the material composition and surface topography significantly influenced the antimicrobial activity (P<0.05).

Cordeiro *et al.*[25] reported that treatment with Plasma Electrolytic Oxidation (PEO) significantly increased the surface free energy and hardness of Ti15Zr alloys when compared to the control group (P<0.05). The contact angles for the machined, PEO-treated, and Blasting followed by Acid Etching (SLA) surfaces were 89°, 30°, and 104°, respectively. Microbiological analysis revealed that both SLA and PEO showed a significant decrease in CFU when compared to the control (P<0.05). Although Agarwalla *et al.*[24] observed an increase in contact angles of graphene-coated specimens compared to the control group, surfaces that received twice the graphene coating (TiGD) showed a decrease in biofilm accumulation of all tested species and a significant decrease in *C. albicans* and *S. mutans* species (CFU) when compared to the control group (P<0.05).

Ferraris *et al.*[26] observed an approximately half reduction in the contact angle of polished or sandblasted titanium surfaces after chemical treatment (attack with hydrofluoric acid followed by oxidation with hydrogen peroxide), showing greater wettability (static and dynamic conditions). Furthermore, according to the authors, the treatment promotes greater corrosion resistance, bioactive behavior, and the ability to minimize bacterial adhesion.

DISCUSSION

Surface treatments play a role in modifying titanium properties such as wettability, surface-free energy, roughness, and chemical composition. These modifications can selectively impact the response of bone cells and bacteria, promoting osseointegration or inhibiting their adhesion. This ability to modulate cellular activity is crucial to stimulate the integration process of the implant with the surrounding bone. Furthermore, surface treatments can hinder the adhesion of bacteria, preventing the development of inflammation or infection that can lead to peri-implantitis and peri-implant bone loss, to ensure the health and longevity of dental implants.[3,4,6,7,10]

Although surface treatments are widely used to improve the properties of titanium in dental implants, some methods, such as etching, have limitations. This can damage the surface, making it more prone to bacterial adhesion and the growth of unwanted microorganisms. Another example is the process known as SLA (Sandblasted with Large Grits and Acid-Etched), which uses sandblasting and acid-etching to create a suitable surface texture, while this is effective in improving osseointegration, it can leave residual sand particles on the implant surface that is highly reactive to oxygen and can promote bacterial growth. However, research is ongoing to develop alternative approaches, such as plasma, laser, and antimicrobial coatings technologies, which aim to overcome limitations and improve the safety and effectiveness of surface treatments on dental implants.[31]

It was observed that studies[6,10-12,17,24-28,32,36] that used some kind of physical-chemical bactericidal treatment on initially hydrophobic surfaces, in addition to making them hydrophilic, promoted a relevant reduction in the number of adhered microorganisms and established more effective intercellular relationships through the predominant action of electrostatic forces and ionic bonds (polar) over Van der Waals forces (apolar).

The minimum value of surface free energy, determined by Chrzanowski *et al.*[13] for bacterial adhesion, is 25 mN m^{-2}, so that adhesion increases for higher values and decreases for values below this limit. Based on the literature,[2,6,18,26,32] it is possible to state that surfaces with high free energy, i.e., more hydrophilic, stimulate cell interaction with the substrate, facilitate protein adsorption processes, and tend to interact with the environment and absorb low-energy components, resulting in increased bioactivity, i.e., promote a greater biological response, and in the rate of mineral formation. This is beneficial in many biomedical applications and tissue engineering, where the promotion of cell adhesion and mineralization is desired.

On the other hand, in addition to surface free energy, surface roughness also plays an important role in bacterial adhesion, as stated by authors such as Wang *et al.*[32] Studies by Ferreira *et al.*[2] and Annunziata *et al.*[33] corroborate this statement, highlighting that rough surfaces are more susceptible to bacterial accumulation, especially those with mean Ra roughness values greater than 2 mm. It should be noted that certain physicochemical conditions can increase surface roughness,[6,10,15] which can lead to an increase in hydrophobicity,[1,11,22,33] i.e., the surface becomes less hydrophilic and more prone to repel water. The combination of high roughness and increased hydrophobicity can create a favorable environment for bacterial adhesion, as bacteria can find niches and anchorage areas in complex microtopographies and in hydrophobic regions of the surface. Thus, one should consider not only surface-free energy but also surface roughness and hydrophobicity when studying bacterial adhesion, as understanding how these factors interact and influence the interaction between bacteria and surfaces is essential for developing infection prevention strategies and optimizing dental implants.

The explanation for this is that bacteria tend to attach preferentially in places that are protected from shear forces, i.e., in areas where there is not a strong enough fluid flow to remove the newly attached bacteria. This allows time for the bacteria to change their attachment state from reversible attachment (where they can be easily removed) to irreversible attachment (where they become more resistant to mechanical removal). In addition, rough surfaces with a larger surface area and diffuse depressions provide more favorable sites for bacterial colonization because surface irregularities create protected microenvironments in which bacteria can hide from host defense mechanisms and from the action of antimicrobial agents, which contributes to the rapid growth of biofilm, represented by a complex microbial community composed of bacteria attached to a surface and embedded in a matrix of polymeric substances produced by the bacteria themselves.[3, 33]

Increased hydroxyl ion (OH) concentration or hydroxylation of titanium surfaces are effects observed after photoactivation treatment. This process involves exposure of TiO_2 photocatalytic surfaces to ultraviolet (UV) light, which generates free radicals capable of acting on the mineralization of contaminants such as bacteria, which occurs when free radicals oxidize and degrade contaminants, making them less adherent to the surfaces.[12-14] The creation of a highly hydrophilic surface (which has a higher affinity for water) by this photoactivation mechanism has been proposed as a strategy to inhibit bacterial adhesion and development. According to Ferraris *et al.*,[26] the high hydrophilicity of the surface prevents bacteria from attaching and proliferating because water tends to form a continuous layer on the surface, making it difficult for bacteria to come into direct contact with the implant material.

An alternative approach to studies using photoactivation with ultraviolet light as surface treatment is non-thermal plasma treatment under atmospheric pressure, as highlighted by Lee *et al.*,[6] which has the advantage of significantly reducing the time required to obtain a hydrophilic surface, requiring only a few seconds of treatment compared to hours needed for other methods. Moreover, this method has been shown to have a relevant antibacterial effect, so in addition to improving the hydrophilicity of the implant surface, thermal can help prevent bacterial adhesion and growth, reducing the risk of associated infections.

The concentration of hydroxyl ions (OH), resulting from the increased generation of oxygen free radicals during surface treatment, has been identified as one of the main factors responsible for increasing the wettability, surface reactivity, and biocompatibility of implants. When oxygen free radicals bind to initially hydrophobic surfaces, a significant part of the organic chains are removed from the material, which leads to the formation of an oxide layer with hydrophilic properties that coats the implant surface. Its presence hinders the deposition of lipopolysaccharides (LPS), which are bacterial components found in the outer membrane of certain gram-negative bacteria that play an important role in bacterial adhesion and colonization, and the difficulty in deposing these compounds on the implant surface reduces bacterial adhesion. Moreover, the formation of the oxide layer can also modify the chemical reactivity of the implant surface, since the presence of hydroxyl ions increases the interaction of the surface with surrounding molecules, such as proteins and host body cells, which can promote a favorable biological response and better integration of the implant in the surrounding tissue. [6,10,11,17,19,20,24,27,28,33]

As for the studies that were based on the deposition of silver-based nanostructures on titanium surfaces, it was observed that silver promoted a strong bactericidal effect and increased surface-free energy due to decreased contact angles.[15,16,36] The mechanism of action of silver (Ag) is based on the action of its ions, released after its bonding with an organic layer of the metal surface, in which there is intense generation of oxygen free radicals and removal of carbon atoms. These reactive oxygen species, in addition to increasing the hydrophilicity of the material, so as to reduce the contact angles between the surface and the water, which hinders bacterial adhesion and biofilm formation, can cause damage to bacterial DNA by interfering with the replication and proper functioning of bacteria, which prevents the survival and proliferation of their species, further reducing the risk of infections.[15,16]

Similarly, studies that evaluated the incorporation of zinc nanostructures in titanium specimens also observed a significant increase in hydrophilicity, favorable for protein adsorption and osteoblast cell differentiation, and reduction of three important species in the establishment of peri-implantitis: *S. aureus, P. gingivalis*, and *A. actinomycetemcomitans*. The proposed mechanism for these results is that the zinc ions present in the nanostructures have the ability to suppress bacterial growth, in a manner similar to the mechanism observed in silver deposition. The presence of zinc ions results in the generation of reactive oxygen species, which are toxic to bacteria, causing damage to their DNA and compromising their viability and ability to multiply. Thus, zinc ions act as antimicrobial agents, inhibiting bacterial growth and colonization on titanium implant surfaces.[17,18]

Laser surface treatments[10,19,20,33] also promoted a significant increase in the hydrophilicity of the samples and a stronger bactericidal effect when compared to polishing techniques. Cunha *et al.*[19] found in their study that *S. aureus* deposits on laser-treated surfaces were lower, with only 7% of the titanium surface covered by bacteria compared to 25% on polished surfaces. The explanation for this stronger bactericidal effect is related to the physical and chemical changes induced by laser treatment, which can create microstructures on the surface of the material, such as microscopic roughnesses and grooves, that hinder bacterial adhesion. In addition, it can generate regions of high surface energy and increase the chemical reactivity of the surface, making it less favorable for bacterial adhesion and colonization.[19]

In addition to the clear influence of surface treatments, the adhesion of bacteria to a hydrophilic or hydrophobic surface is also determined by the species' own characteristics, because some bacterial species have hydrophobic properties, while others have hydrophilic characteristics and this determines the affinity of the bacteria for surfaces with a similar nature.[3,6,11] For example, *S. sanguinis* and *P. aeruginosa* species are considered hydrophobic compared to other species, such as *S. aureus* and *E. coli*. This means that these bacteria have a lower affinity for hydrophilic surfaces and are more easily adhered to surfaces with hydrophobic characteristics.

Hydrophobic bacteria, such as *S. sanguinis* and *P. aeruginos*[3,5,6,9,11] is seen as primary colonizers that adhere to the substrate through weak and reversible chemical bonds, mediated by protein receptors called adhesins. These are responsible for recognizing and binding to specific surface components, allowing hydrophobic bacteria to initially attach. Once adhered, these bacteria can facilitate the coaggregation of other bacterial species in successive stages. This coaggregation is a process in which different bacterial species aggregate and organize themselves into communities, forming what is known as a biofilm. Therefore, the strategy to slow down bacterial colonization on surfaces is to prevent the establishment of these hydrophobic bacteria in the early stages. This is important because once these bacteria settle and form an initial layer, they can facilitate the adhesion and coaggregation of other bacterial species, resulting in a more robust biofilm that is difficult to remove.[6,10,24,25,32]

In this context, the increase in surface energy promoted by surface treatments favors the establishment of greater cellular interactions of microorganism species with the substrate; however, hydrophobic bacteria responsible for initial biofilm adhesion are inhibited, resulting in a significant reduction in the number of colonies forming units.[3,6,8,10,11,14,16,18,20,22,24,25,27,28,30,32]

Although the literature is extensive regarding titanium surface changes in an attempt to improve the surface characteristics of dental implants in terms of osseointegration and microbiological behavior, the great heterogeneity of the articles found in this review prevents an adequate correlation of the results obtained for a precise conclusion.

CONCLUSIONS

Based on the results of this systematic review, it is concluded that:

1) Surface treatments can increase the surface free energy of titanium and decrease bacterial adhesion.

2) Increased surface free energy inhibits the adhesion of hydrophobic species (*S. sanguinis* and *P. aeruginosa*) early in the bacterial adhesion process.

3) Titanium surfaces should preferably be hydrophilic, as the primary colonizing bacteria responsible for peri-implantitis have an affinity for hydrophobic surfaces.

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SUPPLEMENTARY TABLE

Supplementary **Table 1.** Database search strategies.

Database	Search	Found
PubMed April 10th, 2024	titanium AND "surface treatment" AND (wettability OR "surface free energy") AND (bacterial adhesion)	38
Scopus April 10th, 2024	titanium AND "surface treatment" AND (wettability OR "surface free energy") AND "bacterial adhesion"	83
Science Direct April 10th, 2024	titanium AND "surface treatment" AND (wettability OR "surface free energy") AND "bacterial adhesion"	568
Embase April 10th, 2024	titanium AND "surface treatment" AND (wettability OR "surface free energy") AND "bacterial adhesion"	8