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Dental Implant Longevity : A Systematic Review of Innovative Coating Techniques and Their Impact on Cellular Adhesion and Bacterial Colonization.

[Longevidade dos Implantes Dentários : Uma Revisão Sistemática das Técnicas de Revestimento Inovadoras e do Seu Impacto na Adesão Celular e na Colonização Bacteriana.]

Dissertação de Mestrado em Medicina Dentaria

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Orientador :

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Resumo

Os implantes dentários são uma pedra angular da medicina dentária moderna, proporcionando soluções eficazes para a substituição de dentes. As características da superfície dos implantes desempenham um papel crucial no seu sucesso, influenciando a osseointegração e o risco de infecções peri-implantares. Embora os revestimentos tradicionais como o jato de areia, o grão grande e o ataque ácido (SLA) tenham sido amplamente utilizados, os recentes avanços nos biomateriais e na nanotecnologia levaram ao desenvolvimento de técnicas de revestimento inovadoras. Estes novos revestimentos têm como objetivo melhorar as propriedades antimicrobianas, promover a regeneração dos tecidos e melhorar o sucesso global dos implantes.

Os revestimentos inovadores, tais como os revestimentos bioactivos, os revestimentos antimicrobianos, os revestimentos que promovem a regeneração dos tecidos, os revestimentos com eluição de fármacos e os revestimentos biocompostos oferecem melhorias promissoras em relação aos métodos tradicionais. Os revestimentos bioactivos, por exemplo, incentivam a osteointegração, estimulando a formação óssea. Os revestimentos antimicrobianos reduzem a adesão bacteriana e a formação de biofilme, minimizando assim as infecções peri-implantares. Os revestimentos que promovem a regeneração dos tecidos centram-se na melhoria da integração dos tecidos moles, enquanto os revestimentos com eluição de fármacos proporcionam a libertação controlada de agentes terapêuticos. Os revestimentos biocompostos combinam materiais para potenciar propriedades sinérgicas, aumentando a durabilidade e a biocompatibilidade.

O objetivo desta revisão sistemática é comparar estes revestimentos inovadores de uma perspetiva microbiológica. Especificamente, a revisão avaliará o impacto de cada revestimento na adesão bacteriana, na formação de biofilme e na eficácia antimicrobiana. Ao analisar sistematicamente os resultados microbiológicos associados a cada tipo de revestimento inovador, esta revisão tem como objetivo identificar as estratégias mais eficazes para melhorar o sucesso a longo prazo dos implantes dentários.

Palavras-chaves: implantes dentários, revestimentos, tratamento de superfície, bactérias, biofilme.

Abstract

Dental implants are a cornerstone of modern dentistry, providing effective solutions for tooth replacement. The surface characteristics of implants play a crucial role in their success, influencing osseointegration and the risk of peri-implant infections. While traditional coatings like Sandblasted, Large-grit, Acid-etched (SLA) have been widely used, recent advancements in biomaterials and nanotechnology have led to the development of innovative coating techniques. These new coatings aim to enhance antimicrobial properties, promote tissue regeneration, and improve overall implant success.

Innovative coatings such as bioactive coatings, antimicrobial coatings, tissue regeneration-promoting coatings, drug-eluting coatings, and biocomposite coatings offer promising enhancements over traditional methods. Bioactive coatings, for instance, encourage osseointegration by stimulating bone formation. Antimicrobial coatings reduce bacterial adhesion and biofilm formation, thus minimizing peri-implant infections. Tissue regeneration-promoting coatings focus on enhancing soft tissue integration, while drug-eluting coatings provide controlled release of therapeutic agents. Biocomposite coatings combine materials to leverage synergistic properties, enhancing durability and biocompatibility.

The objective of this systematic review is to compare these innovative coatings from a microbiological perspective. Specifically, the review will evaluate the impact of each coating on bacterial adhesion, biofilm formation, and anti-microbial efficacy. By systematically analyzing the microbiological outcomes associated with each type of innovative coating, this review aims to identify the most effective strategies for improving the long-term success of dental implants.

Keywords: dental implants, coatings, surface treatment, bacteria, biofilm

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Abreviations Index

ALP: alkaline phosphatase activity

AO : anodic oxidation

Ag-NP : silver nanoparticles

AgNPs@AMPSISF : silver nanoparticles functionalized with antimicrobial peptides/silk fibroin

BG : bioactive glass

BMP : bone morphogenetic protein

BMSCs : bone marrow stem cells

CFU : colony forming unit

CMD : carboxymethyl dextran

CMS : chymotrypsin

CRP : C-reactive protein

EDS : energy dispersive X-ray spectroscopy

GFs : gingival fibroblasts

HEK : human embryonic kidney

IL-6 : interleukin-6

MAO-Ti : microarc-oxidized titanium

MBG : mesoporous bioactive glass

MC : minocycline

MC@(ODA-CMD)CL : Cross-linked MC-loaded nanomicelles

MMT : montmorillonite

MRSA : methicillin-resistant Staphylococcus aureus

OPN : osteopontin

PDGF : platelet-derived growth factor

PEI : polyethylenimine

PEO : plasma electrolytic oxidation

PLL : poly-L-lysine

PVD : physical vapor deposition

ROS : reactive oxygen species

SEM : scanning electron microscopy

SLA : sandblasting and acid etching

XRD : X-ray diffraction

1. Introduction

Increased life expectancy, an ageing population and a growing interest in aesthetic procedures have all contributed to the popularity of dental implantology, providing a solution that is as close as possible to a natural tooth in terms of aesthetics, sensory feedback and masticatory function. In this regard, implant failures turned out to be a major challenge.

Peri-implantitis remains the post-implant complication with the greatest impact on success rates. This condition being mainly bacterial it is fundamental to look more precisely at the bacteria involved (often common to periodontitis) and their role in the peri-implantitis pathogenesis.

Although we observe common initial colonizers, it is more relevant to look at the later colonizers which are truly characteristic markers of peri implantitis, especially Gram-negative anaerobic species, such as *Porphyromonas gingivalis, Prevotella intermedia, Aggregatibacter actinomycetemcomitans, Tannerellas forsythias, Treponema denticola, Fusobacterium sp., Campylobacter sp., Prevotella nigrescens*, and *Campylobacter* (Pierre et al., 2023).

It is also worth noting the presence of other microorganisms not commonly associated with periodontal diseases, such as, *Candida albicans,* enteric rods *(Escherichia coli)* or microorganisms associated with extra oral infections, such as staphylococci *(Staphylococcus aureus)* which are widely mentioned in the selected studies.

Surface treatment of dental implants plays a crucial role in implants' long-term clinical success by directly influencing their interaction with the oral microbiological environment. Osseointegration is closely linked to the effective management of bacterial colonization on the surface of these medical devices. Traditionally, conventional surface treatment, using sandblasting and acid etching (SLA), has been advocated for its ability to promote increased cell adhesion and enhanced osseointegration.

However, the emergence of new technologies in the field of biomaterials has paved the way for innovative surface coatings, offering new perspectives for controlling peri-implant microbiology. This systematic review aims to compare these emerging methods, with a focus on their impact on peri-implant microbiology. We will evaluate how these different methods influence bacterial adhesion, biofilm formation and antimicrobial efficacy around dental implants.

By providing a critical analysis of microbiological data from relevant studies, this review seeks to enlighten practitioners understanding of the microbiological implications of different surface treatment approaches. Understanding how these methods modify the peri-implant microbial ecosystem will better equip practitioners to select surface coatings that promote optimal biological integration and reduce the risk of peri-implant microbial complications.

1.1 Cellular adhesion and bacterial colonization

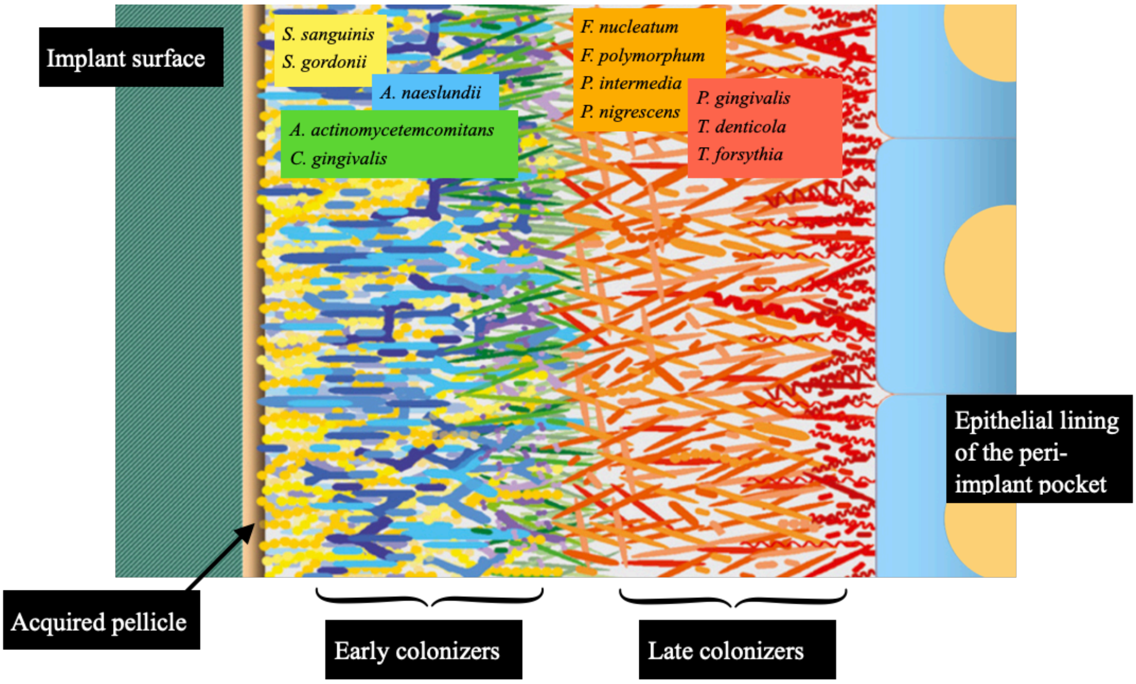
In the oral cavity, many distinct biofilms can be encountered on different surfaces including teeth and dental implants (Belibasakis et al., 2015). Their formation and maturation can trigger peri-implant tissues' inflammation and lead to peri-implantitis the same way the sub-gingival biofilm can be associated with periodontitis (Lang & Berglundh, 2011).

Biofilm formation on teeth and implants follows similar rules due to their shared ecological environment (Schmidlin et al., 2013). On this basis, biofilms feature diverse community of interacting organisms, and a glycocalyx matrix, those complex structures become stable over time, affording a protective environment from host defenses and antimicrobial agents (e.g., antibiotics resistance).

As most studies have found, the submucosal microbiota is composed of a mixed anaerobic infection dominated by Gram-negative bacteria: early colonizers like *Streptococcus sanguinis* and *Actinomyces naeslundii* adhere to the salivary pellicle and begin the process of biofilm development (Fig. 1). Through co-aggregation, the early colonizers grow, affect the surrounding environment, and encourage the adherence of secondary (*F. nucleatum*) and teritary (*P. gingivalis*) colonizers (Marsh, 2005; Socransky & Haffajee, 2005; Kolenbrander et al., 2006).

Figure 1

Schematic representation of the microbial succession that may take place on an implant surface exposed to the oral environment.



Some studies have also found high numbers of other microorganisms not commonly associated with periodontal diseases, such as enteric rods (*E. coli*) and yeasts (*C. albicans*), or microorganisms associated with extraoral infections, such as staphylococci (e.g., *S. aureus* and *Staphylococcus epidermidis*). Indeed, *E. coli* can be used as a model for gram-negative bacteria since many studies involving bacterial adhesion and decontamination carried out on dental implants with *E. coli* bacteria of choice, as well as because it is a readily available and easily cultivated aerobic microorganism (Kubasiewicz-Ross et al., 2020). *S. aureus* has a specific affinity for titanium that is why it often colonize the surface of dental implants, with *C. albicans* as a symbiont, causing severe suppurative infection at the corresponding sites (Liao et al., 2023).

Bacteria can start colonizing an implant as soon as 30 minutes after insertion. The gingival site where a titanium abutment penetrates is particularly susceptible to bacterial attack due to its lack of bacteriostatic properties. Moreover, the absence of Sharpey's fibers and periodontal ligaments in implants weakens the oral mucosa's physical barrier, making it more vulnerable to bacterial invasion (Liao et al., 2023). This can result in implant-associated infections and, potentially, the mobility or dislocation of implants. These findings suggest that maintaining good periodontal health is fundamental for the long-term success of implants.

In this matter, improving the success rate of dental implants is finding a way to reduce bacterial infections, while maintaining implant biocompatibility. That why we decided to focus our research on surface coatings that could resolve the microbiological issues leading to peri-implantitis.

Several changes to the implant surface micro topography (affecting their surface physicochemical properties: roughness, hydrophobicity, surface free energy and wettability) have been developed with the goal of enhancing the dynamics of osseointegration, shortened the time it takes to achieve implant stability and clinical success. Taking in consideration the opportunity given by coatings technique to enhance osseointegration specifically via antimicrobial optimization of the device, our aim is to define which of the existing coating techniques is the more efficient.

1.2 Implants coatings

Dental implant coatings are layers of materials applied to the surface of implants to enhance their performance and integration with surrounding tissues. They serve several important functions that make them essential for improving implant integration (promoting bonding between the implant and surrounding bone to ensure stable and long-lasting fixation), preventing infections (preventing bacterial adhesion and biofilm formation to reduce the risk of infections), and promoting tissue regeneration (encouraging soft tissue growth around the implant for better aesthetic and functional integration). With advanced materials and technologies, these coatings help optimize the performance and longevity of dental implants.

1.2.1 Bioactive coatings

Implant coatings promote osseointegration: the bonding between the implant and the surrounding bone. Materials like hydroxyapatite and bioglass are often used to stimulate the formation of new bone cells, helping to securely anchor the implant in the bone.

1.2.2 Antimicrobials coatings

Antimicrobial coatings play a crucial role in reducing bacterial colonization and biofilm formation. For example, coatings containing silver ions gradually release these ions, which disrupt bacterial cell membranes and inhibit their growth.

1.2.3 Drug-releasing coatings

Drug-releasing coatings are another innovation. These coatings can gradually release medications, such as antibiotics or anti-inflammatory drugs, to prevent infections and reduce inflammation post-implantation.

1.2.4 Tissue regeneration-promoting coatings

Some coatings are specifically designed to promote tissue regeneration. By incorporating growth factors such as PDGF (platelet-derived growth factor) and BMP (bone morphogenetic protein), these coatings stimulate the growth of soft and hard tissues around the implant. Biomimetic materials, which mimic the properties of natural tissues, can also improve the biological response of the surrounding tissues.

2. Development

2.1 Materials and methods

2.1.1 Population, Intervention, Comparison and Outcome (PICO) method

For the present review, the PICO question to be addressed was as follows:

« With which surface treatment do we obtain better outcomes, between the new coating techniques, in patients with dental implants, considering bacterial proliferation and cellular adhesion? ».

2.1.2 Search strategy

A systemic search via PubMed, MDPI and SciELO was performed between October 2023 and March 2024. Articles in English, Portuguese and French were considered.

The following terms and combination were applied :

« Dental implant » OR « dental implantology » AND « coating »

AND « bacteria » OR « biofilm »

AND « Bioactive glasses » OR « Calcium Phosphatase » OR « Silver Ions » OR « Titanium Dioxyde » OR « Drug-releasing coatings » OR « BMP » OR « PDGF » OR « VEGF ».

These terms have been entered and verified by one author in various searches relying on "or".

Reference management software (Mendley 2.112.0) was used.

2.1.3 Eligibility criteria

2.1.3.1 Inclusion criteria

The inclusion criteria were defined as follows:

- Coating methods targeted must be the primary focus of the investigation.
- One study by author (authors' diversification).
- Only reports and articles will be treated.
- Quality of the microbiological assays.
- Articles that are relevant for contextualization.

2.1.3.2 Exclusion criteria

The exclusion criteria were defined as follows:

- Studies over 5 years old i.e., conducted before 2019 (except for relevant reviews serving contextualization).
- Articles that do not permit free full access.

2.1.3.3 Screening process

The selection process was carried out by applying the eligibility criteria and 13 articles were eliminated by applying the inclusion criteria (table 1).

Table 1

Records excluded during the screening process.

Inclusion criteria	**Records excluded**		
Coating methods targeted must be the primary focus of the investigation	Cytotoxicity of hydroxyapatite-tyrosine complex with gray titania coating on titanium alloy surface to L929 mouse fibroblasts	2019	Leelanarathiwat K, Minato K, Katsuta Y et al.
	Biocompatible Nanostructured Silver-Incorporated Implant Surfaces Show Effective Antibacterial, Osteogenic, and Anti-Inflammatory Effects in vitro and in Rat Model	2023	Gao H, Jiang N, Niu Q et al.
	Decontamination methods to restore the biocompatibility of contaminated titanium surfaces	2019	Jin S, Lee E, Park J et al.
	Eradicating infecting bacteria while maintaining tissue integration on photothermal nanoparticle-coated titanium surfaces	2020	Ren X, Gao R, Van Der Mei H et al.
One study / authors (authors' diversification)	Extensive Investigation on the Effect of Niobium Insertion on the Physical and Biological Properties of 45S5 Bioactive Glass for Dental Implant	2023	Hammami I, Gavinho S, Pádua A et al.
	Bioactive Glass Modified with Zirconium Incorporation for Dental Implant Applications: Fabrication, Structural, Electrical, and Biological Analysis	2023	Hammami I, Gavinho S, Pádua A et al.

***Table 1** Cont*

Inclusion criteria	**Records excluded**		
One study / authors (authors' diversification)	Surface characterization, electrochemical properties and in vitro biological properties of Zn-deposited TiO2 nanotube surfaces	2023	Durdu S, Cihan G, Yalcin E et al.
Only reports and articles will be treated.	Ion-Doped Calcium Phosphate-Based Coatings with Antibacterial Properties	2023	Fosca M, Streza A, Antoniac I et al.
	Anti-Periprosthetic Infection Strategies: From Implant Surface Topographical Engineering to Smart Drug-Releasing Coatings	2021	Ghimire A, Song J
	Natural Antibiotic Oregano in Hydroxyapatite-Coated Titanium Reduces Osteoclastic Bone Resorption for Orthopedic and Dental Applications	2020	Vu A, Bose S
Quality of the microbiological assays	Synthesis and characterization of osteoinductive visible light-activated adhesive composites with antimicrobial properties		Moghanian A, Portillo-Lara R, Shirzaei Sani E et al.
	Biocompatibility, Bioactivity, and Antibacterial Behaviour of Cerium-Containing Bioglass®		Gavinho S, Pádua A, Sá-Nogueira et al.
	Novel Strategy for Surface Modification of Titanium Implants towards the Improvement of Osseointegration Property and Antibiotic Local Delivery	2023	Silva I, Barreto A, Seixas R et al.

2.1.4 Risk of bias

The risk of bias were assessed using the Risk Of Bias In Non-Randomized Studies of Interventions (ROBINS-I) tool based on seven domains (Sterne et al., 2016): (1) bias due to confounding, (2) bias due to selection of participants, (3) bias in classification of interventions, (4) bias due to deviation from intended interventions, (5) bias due to missing data, (6) bias in measurement of outcomes and (7) bias in selection of the reported result. In the included studies, the overall risk of bias was classified as "low risk" if there was a low risk of bias across all the domains, "moderate risk" if there was a moderate risk of bias across all or some of the domains, and "serious risk" if there was a serious risk of bias across at least one domain (figure 2 and 3).

Figure 2

Risk of bias assessment using the ROBINS-I tool : wheighted bar plots showing the distribution of risk-of-bias judgments within each bias domain

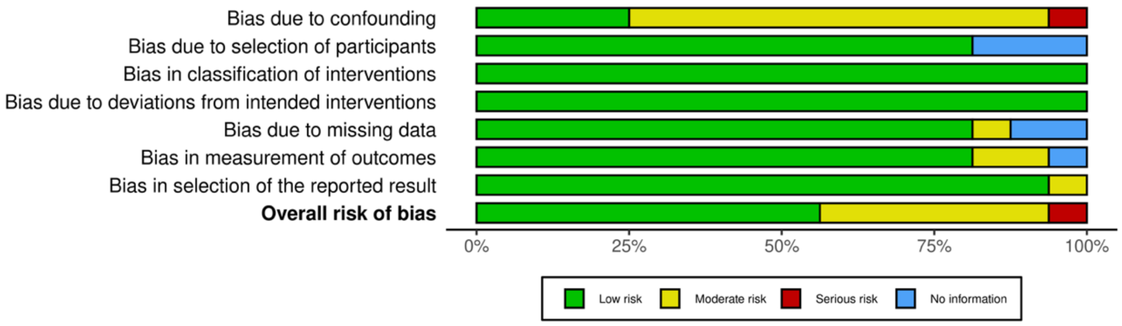
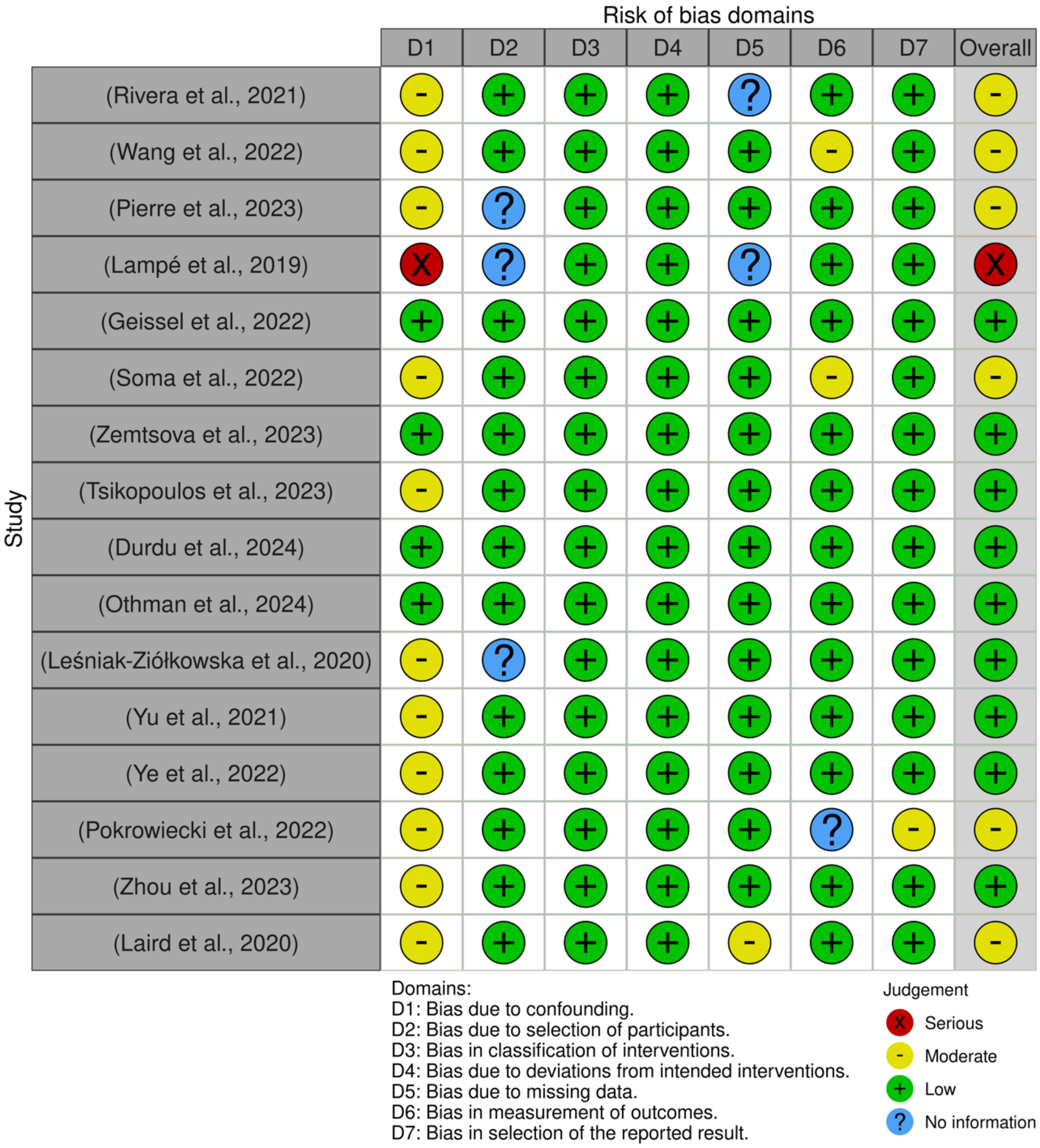


Figure 3

Risk of bias assessment using the ROBINS-I tool : traffic light plots of the domain-level judgments for each study.



Risk of bias domains

Study	D1	D2	D3	D4	D5	D6	D7	Overall
(Rivera et al., 2021)	-	+	+	+	?	+	+	-
(Wang et al., 2022)	-	+	+	+	+	-	+	-
(Pierre et al., 2023)	-	?	+	+	+	+	+	-
(Lampé et al., 2019)	X	?	+	+	?	+	+	X
(Geissel et al., 2022)	+	+	+	+	+	+	+	+
(Soma et al., 2022)	-	+	+	+	+	-	+	-
(Zemtsova et al., 2023)	+	+	+	+	+	+	+	+
(Tsikopoulos et al., 2023)	-	+	+	+	+	+	+	+
(Durdu et al., 2024)	+	+	+	+	+	+	+	+
(Othman et al., 2024)	+	+	+	+	+	+	+	+
(Leśniak-Ziółkowska et al., 2020)	-	?	+	+	+	+	+	+
(Yu et al., 2021)	-	+	+	+	+	+	+	+
(Ye et al., 2022)	-	+	+	+	+	+	+	+
(Pokrowiecki et al., 2022)	-	+	+	+	+	?	-	-
(Zhou et al., 2023)	-	+	+	+	+	+	+	+
(Laird et al., 2020)	-	+	+	+	-	+	+	-

Domains:
D1: Bias due to confounding.
D2: Bias due to selection of participants.
D3: Bias in classification of interventions.
D4: Bias due to deviations from intended interventions.
D5: Bias due to missing data.
D6: Bias in measurement of outcomes.
D7: Bias in selection of the reported result.

Judgement
X Serious
- Moderate
+ Low
? No information

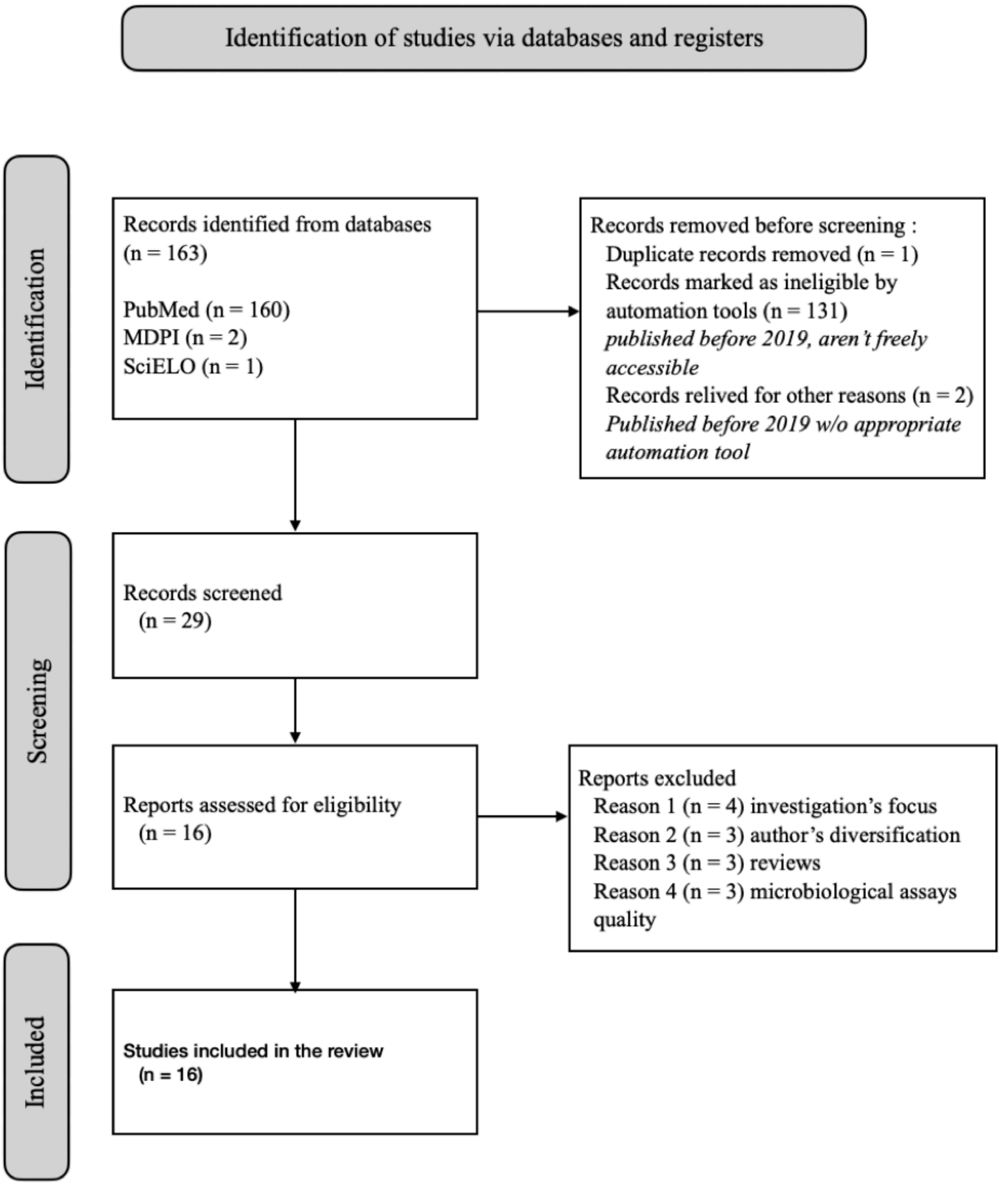
2.2 Results

2.2.1 Study selection

The end point of the search was March 15th 2024. Publications after this date have not been considered. A total of 163 studies have been identified from data bases and 134 were excluded before the screening (fig.4). PRISMA flow diagram was used to summarize the screening process (Page et al., 2021).

Figure 4

PRISMA flow diagram



2.2.2 Study characteristics

An overview of the selected articles is important for future comparison (table 2). The different techniques have been divided into 3 groups according to their purpose and areas of analysis:

- Surface characterization.
- Microbiological tests.
- Biological properties

Table 2

Techniques used in selected studies.

Surface treatment		**Publication**	**Surface characterization**	**Microbiological assays**	**Biological properties**
Bioactive Glasses	Zein Zein/BG Zein/CuBG	(Rivera et al., 2021)	SEM ASTM international standard (tape test : measuring adhesion)	CFU SEM (BF formation)	Cytocompatibility : alamar blue assay OPN and ALP activity (Osteogenic ppties) : real time PCR Pro-angiogenic ppties: CFU, MO and optical digital scanner (blood vessels counting)
	MBG–Ag–coated Ti	(Wang et al., 2022)	XRD spectra FTIR spectra analysis SEM EDX XPS Wettability analysis (contact angle measurement)	Adhesion strength analysis (Burger's test scale range) Antibacterial activity (disk diffusion test)	In vitro bioactivity assays (XRD, SEM, EDS)
Calcium Phosphatase	CaP coating Copper-Doped CaP Coating	(Pierre et al., 2023)	SEM EDX Raman spectre XRD (Cu anti cathode) Electrodeposition time (SEM Screwing / unscrewing test (SEM)	CFU counts	pH
Silver ions	Ag-Np implanted Ti	(Lampé et al., 2019)	SRIM SNMS (INA-X) Ambios XP-I SEM EDS	CFUs	Alamar Blue assay

Table 2 *Cont.*

Surface treatment		**Publication**	**Surface characterization**	**Microbiological assays**	**Biological properties**
Silver ions	xAgSiO2 coatings	(Geissel et al., 2022)	TEM images SEM Nanoparticle crystal size	SEM CFUs	Cytotoxicity (PrestoBlue®)
	HAp-IP6-Ag+–Ti	(Soma et al., 2022)		Antimicrobial activity (formation of inhibition circles, bacterial growth inhibition) Immunohistochemical analysis Phase-contrast microscope NIR-fluorescence bacterial detection probe	ELISA CRP and IL-6 levels Cytototxicity
Ti dioxyde	TiO2/Ag/HAp	(Zemtsova et al., 2023)	SEM EDX XRD	SEM CFUs	MTT Test (Cytotoxicity Assessment) ELISA (ALPK and OPN activity)
	vancomycin-, -Al2O3 nanowire-, and TiO2 nanoparticle-supplemented Resomer®	(Tsikopoulos et al., 2023)	AFM	MIC MBIC XTT SEM	
	TiO2 nanotubes on Ti foam Ti foam surface	(Durdu et al., 2024)	XRD (phase structure) SEM (surface morphology) EDX (elemental composition)	CFUs	
	TiO2-coated TiO2- and ZnO-coated	(Othman et al., 2024)	SEM EDS	Measurement for absorbance	
Drug releasing coatings	GM-PEO, GM-PADA_AMX, GM-PADA_CEF and GM-PADA_VANCO	(Leśniak-Ziółkowska et al., 2020)	SEM XPS H NMR spectroscopy	Inhibition zone measurement CFU counts	Alamar Blue In Vitro Toxicology Assay Kit (cytocompatibility) FLUOstar Omega microplate reader Optical microscope

Table 2 *Cont.*

Surface treatment		**Publication**	**Surface characterization**	**Microbiological assays**	**Biological properties**
Drug releasing coatings	$(MMT/PLL\text{-}VA)_8$	(Yu et al., 2021)	Thickness : spectroscopic ellipsometry Cauchy model SEM Ellipsometry measurement	shake-flask culture method (Inhibition Rate Assays) SEM (antimicrobial activity) zone of bacterial inhibition (ZOI)	Cytocompatibility : MTT assay microplate reader to measure absorbance
	MC@(ODA-CMD)$_{CL}$-Ti	(Ye et al., 2022)	SEM (surface morphology) Atomic force microscopy (roughness) Sessile drop measurement method and EasyDrop Standard instrument (contact angle / hydrophilicity)	Antibacterial rate (AR%) Bacterial viability : CLSM and red total fluorescence ratio (%) Bacterial morphology : SEM Antibacterial performance : CCK8 assay	Cytotoxicity assay : absorbance measurement (microplate reader) Cell viability : absorbance (fibroblasts) Cell adhesion assay : living cells labelling kit, synergy HT reader (fluorescence intensity)
	ZnO+0.1%Ag NPs	(Pokrowiecki et al., 2022)	SEM with InLens and AsB EDS Atomic force microscopy (AFM) Drop shape (wettability) : digital camera and Küss advance computer program	Absorbance measurement (mean absorbance value)	
	AgNPs@AMPs-loaded SF-based coating	(Zhou et al., 2023)	Atomic force microscopy (topological structure / surface roughness) TEM + SEM (surface morphology) EDS (analysing surface element distribution) XPS, XRD and FTIR (chemical composition and binding of the surface) Hydrophilicity (fluorescence)	Colony counting SEM	Ag+ release : inductively coupled plasma mass spectrometry (ICP-MS) Membrane permeability : fluorescence measurement (microplate reader) Protein concentration in the bacterial suspension : Pierce BCA protein detection kit Intracelular production of ROS : fluorescence intensity (DCFH-DA reagent) Osteogenic differentiation : ALP detection kit and BCIP / NBT ALP color development kit (absorbance value) Protein expression : Western Blott Gene expression analysis : RT-PCR Bone implantation : micro CT, SEM, light microscopy
Tissue regeneration-promoting coatings	PDGF	(Laird et al., 2020)	SEM		FACScan (flow cytometer) Forward scatter (FSC) Side scatter (SSC) Green fluorescence Fluorescence microscopy MTS cell proliferation assay reagent enzyme-linked immunosorbent assay (ELISA)

We also wanted to systematically categorize and compare the various studies based on the bacteria they targeted (table 3). This approach allows us to identify patterns, strengths, and potential gaps in the research.

Table 3

Identification of the selected studies and their bacteria of choice

Surface treatment		**Publication**		**Bacteria**
Bioactive Glasses	Zein Zein/BG Zein/CuBG	(Rivera et al., 2021).	Antibacterial, pro-angiogenic and pro-osteointegrative zein-bioactive glass/copper based coatings for implantable stainless steel aimed at bone healing	*E. coli* *S. aureus* *S. epidermidis*
	MBG–Ag–coated Ti	(Wang et al., 2022)	In Vitro Bioactivity and Antibacterial Effects of a Silver-Containing Mesoporous Bioactive Glass Film on the Surface of Titanium Implants	*Aggregatibacter actinomycetemcomitans* *S. mutans*
Calcium Phosphatase	CaP coating Copper-Doped CaP Coating	(Pierre et al., 2023).	Antibacterial Electrodeposited Copper-Doped Calcium Phosphate Coatings for Dental Implants	*S. gordonii* *A. naeslundii* *P. micra* *F. nucleatum* *Aggregatibacter Actinomycetemcomittans* *P. intermedia* *P. gingivalis*
Silver ions	Ag-Np implanted Ti	(Lampé et al., 2019)	Investigation of silver nanoparticles on titanium surface created by ion implantation technology	*S. aureus*
	xAgSiO2 coatings	(Geissel et al., 2022)	Antibiofilm activity of nanosilver coatings against Staphylococcus aureus	*S. aureus*
	HAp-IP6-Ag+–Ti	(Soma et al., 2022)	An ionic silver coating prevents implant-associated infection by anaerobic bacteria in vitro and in vivo in mice	*P. gingivalis* *S. aureus*
Titanium dioxyde	TiO2/Ag/HAp	(Zemtsova et al., 2023)	Creation of a Composite Bioactive Coating with Antibacterial Effect Promising for Bone Implantation	*S. aureus* *P. aeruginosa* *E. faecalis* *K. pneumoniae* *A. naumanniii*
	vancomycin-, -Al2O3 nanowire-, and -TiO2 nanoparticle-supplemented Resomer®	(Tsikopoulos et al., 2023)	Is nanomaterial- and vancomycin-loaded polymer coating effective at preventing methicillin-resistant Staphylococcus aureus growth on titanium disks? An in vitro study	*MRSA*
	TiO2 nanotubes on Ti foam Ti foam surface	(Durdu et al., 2024)	Surface characterization and antibacterial efficiency of well-ordered TiO2 nanotube surfaces fabricated on titanium foams	*S. aureus* *E. coli* *B. subtilis* *P. aeruginosa* *S.typhimurium*

Table 3 *Cont.*

Surface treatment		**Publication**		**Bacteria**
Titanium dioxyde	TiO2-coated TiO2- and ZnO-coated	(Othman et al., 2024)	Antimicrobial behavior of nanocoated orthodontic micro-implants: An in vitro study	*S. aureus* *S. mutans* *P. gingivalis*
Drug-releasing coatings	GM-PEO, GM-PADA_AMX, GM-PADA_CEF and GM-PADA_VANCO	(Leśniak-Ziółkowska et al., 2020)	Antibacterial and cytocompatible coatings based on poly(adipic anhydride) for a Ti alloy surface	*S. aureus* *MRSA*
	$(MMT/PLL\text{-}VA)_8$	(Yu et al., 2021)	Antibiotic-loaded mmt/pll-based coating on the surface of endosseous implants to suppress bacterial infections	*S. aureus*
	$MC@(ODA\text{-}CMD)_{CL}\text{-}Ti$	(Ye et al., 2022)	Carboxymethyl Dextran-Based Nanomicelle Coatings on Microarc Oxidized Titanium Surface for Percutaneous Implants: Drug Release, Antibacterial Properties, and Biocompatibility	*S. aureus*
	ZnO+0.1%Ag NPs	(Pokrowiecki et al., 2022)	Dental Implant Healing Screws as Temporary Oral Drug Delivery Systems for Decrease of Infections in the Area of the Head and Neck	*S. mutans* *S. oralis* *S. aureus* *E. coli*
	AgNPs@AMPs-loaded SF-based coating	(Zhou et al., 2023)	Biomimetic AgNPs@antimicrobial peptide/silk fibroin coating for infection-trigger antibacterial capability and enhanced osseointegration	*S. aureus*
Tissue regeneration-promoting coatings	PDGF	(Laird et al., 2020)	A proof of concept gene-activated titanium surface for oral implantology applications	*« Bacteria »*

2.2.2.1 Rivera et al., 2021

The zein-bioactive glass/copper (zein/CuBG) coatings significantly reduced bacterial biofilm formation compared to copper-free coatings, effectively inhibiting the growth of *S. aureus*, *S. epidermidis*, and *E. coli*.

The antibacterial efficacy of copper was demonstrated both in vitro and in vivo, with a significant reduction in viable bacterial colonies observed on the zein/CuBG coated surfaces.

The zein/CuBG coatings showed good cytocompatibility with human fibroblasts, endothelial cells, and osteoblasts. SEM images confirmed that cells adhered well and spread on the zein/CuBG coatings.

The bioactive glass component in the coatings promoted osteogenic differentiation of human osteoblast progenitor cells during the first days, but the other coatings without BG showed similar support in osteogenesis after 15 days, suggesting similar cell maturation. This was evidenced by the expression of osteogenic genes and the release of alkaline phosphatase (ALP) in the culture medium.

The presence of copper did not interfere with the osteogenic potential of the coatings, suggesting that the zein/CuBG coatings can support bone tissue formation.

The zein/CuBG coatings demonstrated pro-angiogenic properties, promoting the formation of new blood vessels around the implant site in vivo. This is attributed to the ability of copper to stimulate angiogenesis by influencing the stability of the oxygen sensor protein HIF-1α allowing the activation of VEGF and other pro-angiogenic thus initiating the neo- vascularization process

The coatings exhibited good adhesion to the stainless steel substrate and maintained structural integrity under mechanical stress.

In vivo experiments confirmed the antibacterial and pro-angiogenic properties of the zein/CuBG coatings. The coatings successfully inhibited bacterial infection and supported the formation of new tissue and blood vessels at the implantation site.

These findings suggest that zein/CuBG coatings are a promising approach for enhancing the antibacterial, pro-osteogenic, and pro-angiogenic properties of stainless steel implants. The use of these coatings could improve implant integration and reduce the risk of infections, leading to better clinical outcomes. Further research and clinical trials are recommended to validate these results and explore the long-term effects of such coatings in real-world settings.

2.2.2.2.2 Wang et al., 2022

This study shows that MBG-Ag coatings exhibit significant antibacterial activity against early colonizing bacteria such as *Aggregatibacter actinomycetemcomitans* and *S. mutans*. This is evidenced by the inhibition zones observed in disk diffusion tests.

The coatings enhance hydroxyapatite formation when immersed in simulated body fluid (SBF), indicating a potential for better osseointegration.

The study identifies that a lower concentration of silver (1 mol%) in the MBG films provides a balanced improvement in antibacterial properties, wettability, and adhesion strength, making it the most effective composition among those tested.

MBG-Ag films improve the wettability of titanium implants, which is crucial for better integration with biological tissues. Additionally, the adhesion strength tests show that these films adhere well to titanium, with lower silver content showing the best adhesion properties.

The findings suggest that MBG-Ag coatings could be a promising approach to reducing implant-related infections and improving the clinical outcomes of dental implants by providing enhanced antibacterial properties.

These conclusions support the potential use of MBG-Ag coatings as an advanced material for dental implants, offering significant improvements over traditional methods in terms of preventing infections and promoting tissue integration.

2.2.2.3 Pierre et al., 2023

The study concluded that copper-doped CaP coatings on titanium dental implants effectively reduce bacterial colonization and biofilm formation. This is particularly relevant for the prevention of peri-implantitis, as the coatings demonstrated robust antibiofilm properties against both primary and secondary colonizers without cytotoxic effects.

The findings suggest that these coatings could be a promising approach for enhancing the longevity and success of dental implants by preventing post-operative infections and peri-implantitis. The electrodeposition and ion exchange processes used to produce these coatings allow the thickness and copper doping to be adjusted, making them versatile for clinical applications.

In summary, the copper-doped CaP coatings show significant potential in improving the microbiological safety and success of dental implants by effectively reducing bacterial colonization and biofilm formation, thereby preventing peri-implant complications.

2.2.2.4 Lampé et al., 2019

The study concluded that coating titanium surfaces with silver nanoparticles (Ag-NP) is highly effective in imparting antibacterial properties to dental implants. The results demonstrated a significant reduction in *S. aureus* colonization. This substantial antibacterial effect is attributed to the uniform distribution and optimal size of the silver nanoparticles.

Importantly, the silver nanoparticle coatings were found to be non-cytotoxic, ensuring their safety for dental applications. The cytotoxicity tests, conducted using the Alamar Blue assay, confirmed that the coated implants did not harm surrounding tissues. Additionally, the nanoparticles were securely anchored to the titanium surface, preventing them from detaching and entering the bloodstream. This stability is crucial for maintaining both the antibacterial properties and biocompatibility of the implants.

These findings suggest that silver nanoparticle coatings can effectively prevent peri-implantitis, a common cause of implant failure, by reducing bacterial colonization. The study highlights the potential for this coating method to increase the lifespan of dental implants and improve patient outcomes. Furthermore, the techniques used for applying the coatings, ion implantation, and physical vapor deposition (PVD), could be adapted for other types of medical implants where antibacterial properties are needed without compromising biocompatibility.

2.2.2.5 Geissel et al., 2022

The study aimed to develop a homogeneous and adherent calcium phosphate (CaP) antibacterial coating on titanium dental implants to improve osseointegration and limit postoperative peri-implantitis.

Copper incorporation into the CaP coatings was achieved without introducing copper ions directly into the electrolyte solution, utilizing an ion exchange post-treatment instead. This method achieved high copper incorporation rates (up to 27%), which demonstrated significant antibiofilm effects against bacterial strains commonly found in peri-implantitis. Notably, a lower copper incorporation rate (11%) was sufficient to prevent implant colonization without cytotoxic effects.

These findings indicate that CaP coatings doped with copper can effectively impair biofilm formation and bacterial colonization, which are critical factors in preventing peri-implantitis and ensuring the long-term success of dental implants. Further in vivo studies are recommended to confirm biocompatibility and efficacy before clinical application.

2.2.2.6 Soma et al., 2022

The study demonstrated that silver ion coatings on titanium rods effectively inhibit the growth of the anaerobic bacteria *P. gingivalis* both in vitro and in vivo. This suggests that silver-coated implants can prevent infections even in anaerobic conditions, which are typically challenging to treat.

The silver ion-coated implants significantly reduced osteonecrosis caused by infectious osteomyelitis. This was evident from histological analysis showing fewer empty lacunae in bones implanted with silver-coated rods compared to control rods.

The presence of silver ion-coated implants was associated with reduced levels of inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6). These reductions indicate that the implants not only prevent infection but also mitigate the associated inflammatory response.

The antimicrobial activity of the silver ion-coated rods was maintained for at least four years, demonstrating the long-term efficacy of the coating.

The silver ion coatings did not exhibit cytotoxic effects in vitro, suggesting that they are safe for use in clinical applications without harming surrounding tissues.

Overall, the study concludes that silver ion coatings on titanium implants offer a promising solution for preventing implant-associated infections, especially in anaerobic environments, without compromising the safety and functionality of the implants.

2.2.2.7 Zemtsova et al., 2023

The study demonstrated that certain coatings significantly reduce bacterial colonization and biofilm formation compared to uncoated implants. This was particularly evident with coatings that incorporated antimicrobial agents such as silver or chitosan.

The coatings studied were typically biocompatible, showing no adverse effects on the surrounding tissues. Some coatings, like those containing hydroxyapatite, even promoted better integration with the bone.

Coatings with antimicrobial properties, such as those containing silver nanoparticles or chitosan, were particularly effective at preventing bacterial growth and biofilm formation. This suggests their potential to reduce the risk of peri-implantitis and other infections.

The article highlights the need for further research to optimize the formulations and application methods of these coatings. Long-term clinical trials are essential to fully understand their benefits and any potential drawbacks.

2.2.2.8 Tsikopoulos et al., 2023

The study investigates the effectiveness of various coatings in preventing the growth of methicillin-resistant *Staphylococcus aureus* (MRSA) on titanium disks.

Vancomycin-loaded Resomer® coatings demonstrated significant efficacy in preventing MRSA biofilm formation. High-dose vancomycin coatings achieved complete biofilm reduction, while low-dose vancomycin coatings resulted in an 84% reduction. These findings highlight the potential of vancomycin as an effective antimicrobial agent when incorporated into polymer coatings.

Other coatings tested, including Al2O3 nanowires and TiO2 nanoparticles, were less effective compared to vancomycin. A polymer coating without any antibacterial agents reduced biofilm growth by 62%, which was not considered clinically meaningful.

Comparatively, vancomycin, particularly in high doses, was the most effective agent in reducing MRSA biofilm formation among those tested.

The study suggests that bioresorbable vancomycin-supplemented coatings on titanium implants could potentially decrease the incidence of early post-operative surgical site infections. However, the balance between localized toxicity and antibiofilm efficacy should be carefully considered when loading polymers with highly concentrated antimicrobial agents.

In summary, vancomycin-loaded polymer coatings could enhance the antibacterial properties of titanium implants, offering a promising approach to prevent MRSA infections in clinical settings.

2.2.2.9 Durdu et al., 2024

The study successfully fabricated well-ordered titanium dioxide (TiO2) nanotube arrays on titanium foams using anodic oxidation (AO) at 40V for 1 hour. The major elements observed on the AO-coated Ti foam surfaces were titanium (Ti) and oxygen (O), confirming the presence of the TiO2 structure.

The TiO2 nanotube surfaces demonstrated significantly enhanced antibacterial properties compared to bare Ti foam. Specifically, bacterial inhibition was improved by 53.3% for Staphylococcus aureus and 69.4% for *Escherichia coli*.

The findings suggest that TiO2 nanotube array surfaces on Ti foam have strong potential for use in dental and orthopedic implants due to their enhanced antibacterial properties. Future research should focus on investigating the in vivo antibacterial and osteogenic activities of these surfaces.

The study discusses possible mechanisms for the antibacterial action of TiO2 nanotubes, including membrane stretching, charge repulsion, and the generation of reactive oxygen species (ROS) through photocatalysis. These mechanisms contribute to the reduction of bacterial adhesion and proliferation on the implant surfaces.

TiO2 nanotube surfaces are more bioactive (induce a specific biological response at the interface of a material, enabling the formation of a bond between the tissues and the material) than Ti substrates, accelerating the rate of apatite formation and improving bone cell adhesion and proliferation, making them highly suitable for biomedical application.

2.2.2.10 Othman et al., 2024

The study demonstrated the significance of improving the surface of orthodontic micro-implants by coating them with titanium dioxide (TiO2) and zinc oxide (ZnO) nanoparticles. This nanoparticle coating effectively prevents biofilm formation, enhancing osseointegration and reducing peri-implant inflammation. As a result, the probability of micro-implant failure is decreased. The nanoparticle depositions on the titanium surface can be used to design morphological and structural features, promoting cell proliferation and preventing infections caused by pathogenic microbial agents.

2.2.2.11 Leśniak-Ziółkowska et al., 2020

A poly(adipic anhydride) layer loaded with antibiotics was successfully deposited on a Ti alloy surface (Ti–2Ta–3Zr–36Nb, known as Gum Metal) treated with a plasma electrolytic oxidation (PEO) process.

The PEO-treated surfaces exhibited increased surface roughness and wettability, with no observable defects or cracks, indicating a good surface morphology for subsequent polymer coating.

The poly(adipic anhydride) layer containing amoxicillin, cefazolin, or vancomycin was deposited, demonstrating favorable surface microstructure for the adhesion and proliferation of MG-63 osteoblast-like cells.

The antibiotic release from the polymer layer maintained sufficient concentrations for inhibiting bacterial growth for up to 10 hours. The antibacterial effects were confirmed with tests against S. aureus and MRSA.

The study suggests that the surface modification of titanium alloys with fast-degrading poly(adipic anhydride) loaded with antibiotics holds potential for developing dental and orthopedic implants with improved antibacterial properties and biocompatibility.

2.2.2.12 Yu et al., 2021

The study demonstrates that (MMT/PLL-VA)8 multilayer films, created through a layer-by-layer self-assembly process, effectively release vancomycin in response to bacterial presence and CMS concentration changes (which is used to trigger the antibiotic release in response to bacterial infections). This targeted release mechanism enhances the antibacterial activity while maintaining good biocompatibility.

In vitro tests show that these films exhibit high levels of bactericidal activity, significantly reducing the viability of S. aureus bacteria.

In vivo evaluations using rat models indicate that implants coated with (MMT/PLL-VA)8 films result in lower infection rates, reduced inflammation, and improved bone regeneration compared to unmodified implants.

These conclusions highlight the potential of using (MMT/PLL-VA)8 multilayer films for improving the effectiveness of implants in clinical settings, particularly in preventing and treating bacterial infections.

2.2.2.13 Ye et al., 2022

The research developed a carboxymethyl dextran (CMD)-based nanomicelle antibacterial coating on a microarc-oxidized titanium (MAO-Ti) surface, demonstrating that these coatings can effectively incorporate and release minocycline (MC), an antibiotic.

The cross-linked MC-loaded nanomicelles (MC@(ODA-CMD)CL) showed greater stability compared to uncross-linked nanomicelles. The coatings provided a sustained release of the drug over 360 hours, reaching a cumulative release rate of 86.6%.

The CMD-based nanomicelle coatings significantly reduced bacterial adhesion, particularly against Staphylococcus aureus, compared to smooth titanium (S-Ti) sheets. This suggests that the coatings can effectively prevent bacterial contamination and biofilm formation on implants.

The coated titanium surfaces enhanced the viability, adhesion, and morphology of human skin fibroblasts, indicating excellent biocompatibility, which is crucial for clinical applications.

The study concludes that the CMD-based nanomicelle coatings on titanium surfaces hold promising potential for use in percutaneous implants, due to their sustained drug release, excellent antibacterial properties, and biocompatibility.

2.2.2.14 Pokrowiecki et al., 2022

This study presents a detailed examination of the antimicrobial properties and clinical potential of zinc oxide (ZnO) and silver (Ag) nanoparticle coatings on dental implant healing abutments.

The ZnO+0.1% Ag nanoparticle coatings significantly reduced bacterial biofilm formation on titanium healing abutments. The study demonstrated that these coatings effectively inhibited the growth of *Streptococcus mutans, Streptococcus oralis, Staphylococcus aureus*, and *Escherichia coli*.

Scanning Electron Microscopy images revealed that bacterial cells on coated surfaces were fewer, less spread out, and often surrounded by nanoparticles, indicating a strong antibacterial effect.

The nanoparticle coating process increased surface roughness and decreased wettability, which are desirable properties for enhancing antibacterial activity and preventing bacterial adhesion.

The high-power ultrasonic deposition method used for coating was effective and could be applied to standard titanium dental abutments without the need for specialized equipment.

The ZnO+0.1% Ag nanoparticle coatings offer a promising approach for reducing the risk of peri-implant infections, particularly in the early stages of implant integration.

These coatings could be used as temporary drug delivery systems, providing localized antibacterial effects during the critical healing period, thereby improving the overall success rate of dental implants.

2.2.2.15 Zhou et al., 2023

The study developed a silk fibroin-based coating (AgNPs@AMPs/SF) that incorporates silver nanoparticles (AgNPs) and antimicrobial peptides (AMPs). This coating exhibited a protein crown-like structure, enhancing the stability and antibacterial properties of the nanoparticles.

The AgNPs@AMPs/SF coating demonstrated excellent antibacterial capabilities, maintaining an antibacterial rate above 99% against Staphylococcus aureus for up to 21 days. The antibacterial mechanism involved membrane disruption and reactive oxygen species (ROS) generation, effectively killing planktonic bacteria and inhibiting biofilm formation.

In vitro tests showed that the coating promoted the adhesion, proliferation, and osteogenic differentiation of bone marrow stem cells (BMSCs). The coating significantly enhanced the expression of osteogenesis-related genes and proteins, indicating its potential to support bone regeneration.

In vivo studies with rat models demonstrated that implants coated with AgNPs@AMPs/SF showed enhanced bone formation and osseointegration compared to uncoated implants. The coating promoted new bone formation at the implant interface without causing any biosafety issues.

The AgNPs@AMPs/SF coating holds great potential for clinical applications in orthopedic and dental implants due to its dual functions of preventing bacterial infections and promoting osseointegration. This coating could improve the success rate and longevity of implants by addressing common challenges such as infection and insufficient bone integration.

2.2.2.16 Laird et al., 2020

The study successfully developed a gene-activated titanium surface by coating it with polyethylenimine (PEI)-plasmid DNA (pDNA) nanoplexes stabilized with sucrose. This coating was able to transfect human embryonic kidney 293T (HEK293T) cells and human primary gingival fibroblasts (GFs) in culture.

GFs transfected with nanoplexes containing platelet-derived growth factor subunit B (PDGFB)-encoding pDNA secreted PDGF-BB for at least seven days after transfection. This indicates that the gene-activated surface can induce sustained protein production, which could enhance the peri-implant soft tissue seal.

The transfected GFs showed minimal viability loss and increased expression of integrin-α2, an important protein for cell adhesion, four days post-transfection. This suggests that the coating method is biocompatible and supports cellular functions.

The results suggest that using gene-activated titanium surfaces can improve the formation and quality of the peri-implant soft tissue seal, potentially reducing the risk of peri-implantitis and improving implant success rates. The approach could be a viable alternative to using recombinant proteins, offering a more cost-effective and efficient solution for enhancing implant integration.

2.3 Discussion

2.3.1 Summary of findings

2.3.1.1 Microbiological assays

Evaluating the microbiological effectiveness of various coatings on dental implants requires a rigorous understanding of the assays used to measure bacterial growth, biofilm formation, and antimicrobial activity. Each assay offers unique insights and comes with specific advantages and limitations. The table below (table 4) provides a comparative summary of the microbiological assays employed in the reviewed studies, highlighting their descriptions, effectiveness, limitations, and the studies that utilized these assays.

Table 4

Comparative summary of the microbiological assays used in the studies.

Microbiological assays	Description	Effectiveness	Limitations	Studies Using this assay
CFU Counts	Quantifies viable bacteria by counting colonies formed on agar plates	Widely used Provides direct enumeration of bacteria	May not capture all aspects of biofilm complexity	(Rivera et al., 2021) (Pierre et al., 2023) (Lampé et al., 2019) (Geissel et al., 2022) (Zemtsova et al., 2023) (Durdu et al., 2024) (Leśniak-Ziółkowska et al., 2020) (Zhou et al., 2023)
Disk Diffusion Test	Measures the zone of inhibition around a disk containing the antimicrobial agent	Simple Cost-effective Visual measure	May not accurately reflect in vivo conditions	(Tsikopoulos et al., 2023; Wang et al., 2022)
MIC and MBIC	Determines the minimum concentration needed to inhibit bacterial growth/ biofilm	Critical for comparing potency of antimicrobial agents	Limited to laboratory settings	(Tsikopoulos et al., 2023; Wang et al., 2022)

Shake-Flask Culture Method	Evaluates bacterial inhibition in dynamic fluid environments	Provides more realistic assessments of antibacterial efficacy	Limited to specific conditions	(Yu et al., 2021)
Zone of Inhibition (ZOI) measurement	Visual measure of antibacterial activity	Simple, provides clear inhibition zone	Limited scope for in-depth analysis	(Yu et al., 2021) (Leśniak-Ziółkowska et al., 2020)
Bacterial viability assays	Asseses the viability of bacteria post-treatment	Provides insights into the effectiveness over time	Can be complex to interpret	(Rivera et al., 2021) (Ye et al., 2022)
Bacterial Morphology assessment	Uses imaging techniques to observe changes in bacterial structure	Offers qualitative depth to quantitative assays	Requires specialized equipment	(Rivera et al., 2021) (Ye et al., 2022)
Other techniques	Advanced methods like immunohistochemical analysis or NIR-fluorescence	Precise detection and measurement	Often require specialized conditions and equipment	(Soma et al., 2022)

Most coatings significantly reduce bacterial adhesion to the implant surface, which is crucial for preventing initial colonization and subsequent infection. Techniques like SEM and CFU counts are commonly used to assess bacterial adhesion, indicating the coating's effectiveness.

Many coatings are effective in inhibiting biofilm formation, which is fundamental in infections' prevention. Studies often use SEM and CFU counts to evaluate biofilm formation with strong inhibition observed in coatings containing antimicrobial agents like silver, copper and vancomycin.

As evidenced by significant reductions in CFU counts, large inhibition zones in disk diffusion tests and low MIC and MBIC values, some coatings demonstrated high antimicrobial efficacy. Comparing the various studies selected (table 5), we can see that antimicrobial agents like silver, copper and vancomycin are particularly effective in enhancing the antimicrobial properties of the coatings, making them suitable for clinical applications.

Table 5

Comparative Outcomes of Bacterial Adhesion, Biofilm Formation, and Antimicrobial Efficacy in Dental Implant Coatings

Publication	Bacterial Adhesion	Biofilm Formation	Antimicrobial Efficacy
(Rivera et al., 2021)	Significant reduction in bacterial adhesion	Effective inhibition of biofilm formation	High antimicrobial efficacy, demonstrated by significant reduction in CFU counts and inhibition zones
(Wang et al., 2022)	Reduced bacterial adhesion observed	Effective in preventing biofilm formation	High antimicrobial activity with large inhibition zones in disk diffusion tests
(Pierre et al., 2023)	Significant reduction in bacterial adhesion	Strong inhibition of biofilm formation	High antimicrobial efficacy, demonstrated by reduced CFU counts
(Lampé et al., 2019)	Significant reduction in bacterial adhesion	Effective in preventing biofilm formation	Strong antimicrobial effect, significant reduction in CFU counts
(Geissel et al., 2022)	Reduced bacterial adhesion	Effective inhibition of biofilm formation	High antimicrobial efficacy, reduced CFU counts and low cytotoxicity
(Soma et al., 2022)	Significant reduction in bacterial adhesion	Effective in preventing biofilm formation	High antimicrobial efficacy, demonstrated in both in vitro and in vivo settings

Table 5 *Cont.*

Publication	Bacterial Adhesion	Biofilm Formation	Antimicrobial Efficacy
(Zemtsova et al., 2023)	Reduced bacterial adhesion	Effective inhibition of biofilm formation	High antimicrobial efficacy, demonstrated by significant reduction in CFU counts
(Tsikopoulos et al., 2023)	Significant reduction in bacterial adhesion	Strong inhibition of biofilm formation, effective at both high and low doses of vancomycin	High antimicrobial efficacy, demonstrated by reduced MIC and MBIC values
(Durdu et al., 2024)	Reduced bacterial adhesion	Effective in preventing biofilm formation	High antimicrobial efficacy, demonstrated by significant reduction in CFU counts
(Othman et al., 2024)	Reduced bacterial adhesion	Effective inhibition of biofilm formation	Good antimicrobial activity, demonstrated by absorbance measurements for bacterial growth inhibition
(Leśniak-Ziółkowska et al., 2020)	Reduced bacterial adhesion	Effective in preventing biofilm formation	High antimicrobial efficacy, demonstrated by large inhibition zones and reduced CFU counts

Table 5 *Cont.*

Publication	Bacterial Adhesion	Biofilm Formation	Antimicrobial Efficacy
(Yu et al., 2021)	Significant reduction in bacterial adhesion	Strong inhibition of biofilm formation	High antimicrobial efficacy, demonstrated by large zones of inhibition
(Ye et al., 2022)	Reduced bacterial adhesion	Effective inhibition of biofilm formation	High antimicrobial efficacy, demonstrated by significant reduction in bacterial viability and CFU counts
(Pokrowiecki et al., 2022)	Reduced bacterial adhesion	Effective in preventing biofilm formation	Effective antimicrobial activity, demonstrated by absorbance measurements for bacterial growth
(Zhou et al., 2023)	Significant reduction in bacterial adhesion	Strong inhibition of biofilm formation	High antimicrobial efficacy, demonstrated by significant reduction in CFU counts and enhanced osseointegration
(Laird et al., 2020)	Reduced bacterial adhesion	Not specifically assessed for biofilm formation in this study	Effective antimicrobial activity, demonstrated by reduced bacterial growth and promotion of cell proliferation

The comparative analysis highlights the effectiveness of various innovative coatings in reducing bacterial adhesion, inhibiting biofilm formation, and providing strong antimicrobial efficacy. Coatings containing antimicrobial agents such as silver, copper, and vancomycin show the highest effectiveness, suggesting their potential to improve the success and longevity of dental implants by preventing infections and enhancing overall biocompatibility.

2.3.1.2 Biological properties

In addition to their antimicrobial efficacy, the biological properties of dental implant coatings are crucial for their success in clinical applications. This includes cytocompatibility (the ability to support cell viability and proliferation), osteogenic potential (the ability to promote bone formation), and angiogenic potential (the ability to promote blood vessel formation). Below (table 6) is a comparative analysis of these biological properties as evaluated in the studies.

Table 6

Comparative Analysis of Biological Properties Evaluated in Dental Implant Coatings

Publication	Cytocompatibility	Osteogenic potential	Angiogenic potential
(Rivera et al., 2021)	Evaluated using the Alamar Blue assay. Shows good cytocompatibility, supporting cell viability.	Assessed via real-time PCR for OPN and ALP activity. Promotes osteogenic properties, enhancing bone healing.	Evaluated by CFU and optical digital scanner for blood vessels counting. Demonstrates strong pro-angiogenic properties, promoting blood vessel formation.
(Wang et al., 2022)	Not specifically assessed for cytocompatibility in this study.	In vitro bioactivity assays (XRD, SEM, EDS) indicate potential for supporting bone integration.	Not specifically assessed for angiogenic potential in this study.

Table 6 *Cont.*

Publication	**Cytocompatibility**	**Osteogenic potential**	**Angiogenic potential**
(Pierre et al., 2023)	Not specifically assessed for cytocompatibility in this study.	Potential osteogenic effects inferred from the nature of calcium phosphate.	Not specifically assessed for angiogenic potential in this study.
(Lampé et al., 2019)	Evaluated using the Alamar Blue assay. Shows minimal cytotoxicity, indicating good biocompatibility.	Not specifically assessed for osteogenic potential in this study.	Not specifically assessed for angiogenic potential in this study.
(Geissel et al., 2022)	Evaluated using the PrestoBlue® assay. Demonstrates low cytotoxicity, supporting safe use in clinical settings.	Not specifically assessed for osteogenic potential in this study.	Not specifically assessed for angiogenic potential in this study.
(Soma et al., 2022)	Evaluated by ELISA for CRP and IL-6 levels. Indicates good cytocompatibility with minimal inflammatory response.	Not specifically assessed for osteogenic potential in this study.	Not specifically assessed for angiogenic potential in this study.
(Zemtsova et al., 2023)	Evaluated using the MTT assay. Shows acceptable cytocompatibility, supporting cell viability.	Assessed by ELISA for ALPK and OPN activity. Demonstrates strong osteogenic properties, promoting bone healing.	Not specifically assessed for angiogenic potential in this study.
(Tsikopoulos et al., 2023)	Evaluated using the XTT assay. Supports good cytocompatibility and cell viability.	Not specifically assessed for osteogenic potential in this study.	Not specifically assessed for angiogenic potential in this study.

Table 6 *Cont.*

Publication	**Cytocompatibility**	**Osteogenic potential**	**Angiogenic potential**
(Durdu et al., 2024)	Not specifically assessed for cytocompatibility in this study.	Not specifically assessed for osteogenic potential in this study.	Not specifically assessed for angiogenic potential in this study.
(Leśniak-Ziółkowska et al., 2020)	Evaluated by measuring absorbance for bacterial growth inhibition. Shows good cytocompatibility.	Not specifically assessed for osteogenic potential in this study.	Not specifically assessed for angiogenic potential in this study.
(Yu et al., 2021)	Evaluated using the MTT assay. Shows good cytocompatibility, indicating safe use in clinical settings.	Not specifically assessed for osteogenic potential in this study.	Not specifically assessed for angiogenic potential in this study.
(Ye et al., 2022)	Evaluated using various cytotoxicity assays. Demonstrates good cytocompatibility, supporting cell viability and adhesion.	Not specifically assessed for osteogenic potential in this study.	Not specifically assessed for angiogenic potential in this study.
(Pokrowiecki et al., 2022)	Evaluated by measuring absorbance values. Shows potential cytocompatibility, suitable for clinical application.	Not specifically assessed for osteogenic potential in this study.	Not specifically assessed for angiogenic potential in this study.

Table 6 *Cont.*

Publication	Cytocompatibility	Osteogenic potential	Angiogenic potential
(Zhou et al., 2023)	Evaluated using various assays including membrane permeability and protein concentration. Supports cell viability and proliferation.	Assessed using ALP detection and gene expression analysis. Promotes osteogenic differentiation and bone formation.	Demonstrates potential for enhanced osseointegration, indirectly supporting angiogenic processes necessary for bone healing.
(Laird et al., 2020)	Evaluated using MTS assay and ELISA. Shows good cytocompatibility, promoting cell proliferation.	Not specifically assessed for osteogenic potential in this study.	Not specifically assessed for angiogenic potential in this study.

Most coatings evaluated demonstrate good cytocompatibility, supporting cell viability and proliferation: assays such as Alamar Blue, PrestoBlue®, MTT and XTT are commonly used to assess cytocompatibility, indicating the coatings' suitability for clinical use.

Some Coatings like the Zein-bioactive glass/copper-based coatings and TiO2/Ag/HAp composite coating, show strong osteogenic properties, promoting bone healing and integration. Osteogenic potential is often assessed using markers like OPN (osteopontin) and ALP (alkaline phosphatase activity: coatings that show an increase expression of these markers are considered effective.

The angiogenic potential is less frequently assessed but is highlighted in certain coatings such as the Zein-bioactive glass/copper-based coatings, which promotes blood vessel formation. The ability to promote angiogenesis is crucial for successful implant integration and long-term success, as it ensures adequate blood supply to the implant site.

The comparative analysis of biological properties highlights that while most coatings exhibit good cytocompatibility, promoting cell viability and proliferation, only a few studies specifically evaluate osteogenic and angiogenic potentials. Coatings that do demonstrate these additional properties, such as the zein-bioactive glass/copper-based coating and TiO2/Ag/HAp composite coating, show promising results for enhanced bone healing and vascularization, which are critical for the long-term success of dental implants.

2.3.2 Interpretation of results

Interpreting the results of the comparative analysis reveals key insights into the coatings' microbiological effectiveness and their potential impact on implant success and long-term outcomes.

Coatings containing silver nanoparticles, ionic silver, and copper consistently showed reduced bacterial adhesion. The antimicrobial properties of these metals disrupt bacterial cell walls and inhibit their ability to attach to surfaces.

Coatings with nanostructures also effectively reduced bacterial adhesion by creating physical barriers that bacteria find difficult to colonize.

Vancomycin-loaded polymer coatings showed strong inhibition of biofilm formation even at lower doses. This suggests that such coatings can provide long-lasting protection against biofilm-associated infections.

Coatings that combined antimicrobial agents with bioactive components (e.g., zein-bioactive glass/copper-based coatings) not only inhibited biofilm formation but also promoted tissue integration, which helps maintain a healthy peri-implant environment.

Some coatings demonstrated high antimicrobial efficacy (as evidenced by significant reductions in CFU counts and large zones of inhibition in disk diffusion tests). These coatings were particularly effective in killing a wide range of bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA). The broad-spectrum antimicrobial properties of silver and copper make them highly effective in preventing infections.

Coatings that allowed controlled release of antimicrobial agents provided sustained protection against bacterial colonization, which is essential for preventing early-stage infections and ensuring long-term efficacy.

2.3.2.1 Implications

The reduction in bacterial adhesion and biofilm formation observed with these coatings implies a lower risk of peri-implantitis and other implant-associated infections. This is crucial for maintaining the health of surrounding tissues and ensuring the longevity of the implant.

Coatings that promote osteogenic and angiogenic activities, such as those containing bioactive glass and copper, support faster and stronger bone integration. This leads to improved initial stability and long-term success of the implant.

The use of these advanced coatings is expected to improve patient outcomes by reducing the need for revision procedures due to infections and promoting faster recovery. This improves patient satisfaction and the overall quality of life.

By reducing the incidence of infections and the need for additional treatments, these coatings can lead to significant cost savings in healthcare. This makes them a cost-effective solution for dental practices and benefits the broader healthcare system.

The results indicate that innovative dental implant coatings, particularly those incorporating antimicrobial agents like silver, copper, and vancomycin, are highly effective in reducing bacterial adhesion, preventing biofilm formation, and providing strong antimicrobial efficacy. These properties are essential for the success and longevity of dental implants. The coatings not only enhance the stability and integration of the implants but also improve patient outcomes and reduce healthcare costs. As a result, they hold great promise for advancing the field of dental implantology and improving the overall success rate of dental implants.

2.3.3 Strengths and limitations

2.3.3.1 Strengths of included studies

Comprehensive Analysis Techniques :

Many studies employed a range of sophisticated analysis techniques, such as SEM (Scanning Electron Microscopy), EDS (Energy Dispersive X-ray Spectroscopy), and XRD (X-ray Diffraction), providing detailed insights into surface morphology, elemental composition, and crystalline structures.

Example: The study on silver-containing mesoporous bioactive glass film utilized XRD, SEM, and EDS for a comprehensive analysis of bioactivity and antibacterial effects.

Variety of Antimicrobial Agents Tested:

The inclusion of diverse antimicrobial agents (e.g., silver, copper, vancomycin) allowed for a broad comparison of their effectiveness in reducing bacterial adhesion, biofilm formation, and providing antimicrobial efficacy.

Example: Studies on vancomycin-loaded polymer coatings demonstrated their potential in preventing MRSA biofilm formation.

Evaluation of Biological Properties:

Several studies evaluated not only the antimicrobial properties but also the biological properties such as cytocompatibility, osteogenic potential, and angiogenic potential, which are crucial for clinical applications.

Example: The zein-bioactive glass/copper-based coatings study assessed cytocompatibility using Alamar Blue assay and osteogenic potential using real-time PCR for OPN and ALP activity.

In Vitro and In Vivo Studies:

The inclusion of both in vitro and in vivo studies provides a more comprehensive understanding of the coatings' effectiveness and potential clinical relevance.

Example: The study on ionic silver coating included both in vitro assays and in vivo tests in mice to evaluate antimicrobial efficacy and biocompatibility.

2.3.3.2 Weakness of included studies

Limited long-term data:

Many studies lack long-term data on the durability and sustained effectiveness of the coatings, which is crucial for understanding their performance over extended periods.

Example: Several studies provided short-term results without follow-up studies to assess long-term outcomes.

Variability in experimental conditions:

Differences in experimental conditions, such as the type of bacteria used, duration of testing, and methods of assessment, make it challenging to directly compare results across studies.

Example: Studies varied in their use of bacterial strains (e.g., *Staphylococcus aureus* vs. MRSA), making it difficult to standardize comparisons.

Limited focus on clinical relevance:

Some studies focused primarily on laboratory settings without sufficient consideration of clinical conditions and challenges, such as the presence of complex oral microbiota and mechanical stresses on implants.

Example: In vitro studies may not fully replicate the dynamic environment of the oral cavity, limiting the applicability of findings to clinical scenarios.

Inconsistent reporting of data:

Variability in the reporting of key outcomes, such as CFU counts and inhibition zones, and the lack of standardized metrics can lead to inconsistencies in data interpretation.

Example: Differences in how inhibition zones are measured and reported can affect the perceived efficacy of antimicrobial coatings.

Limited sample sizes:

Some studies used relatively small sample sizes, which may not provide a robust statistical basis for the findings and can limit the generalizability of the results.

Example: Studies with small sample sizes might not capture the full variability in responses, leading to potential biases in conclusions.

2.3.3.3 Limitations of the review process

The review process for evaluating dental implant coatings is subject to several limitations, including heterogeneity of study designs, variability in analytical techniques, inconsistent outcome measures, limited long-term data, differences in sample sizes and limited clinical relevance. Recognizing these limitations is crucial for interpreting the results accurately and for guiding future research to address these gaps, ultimately leading to more robust and clinically relevant conclusions.

2.3.4 Future directions

Given the limitations identified in the review process and the current state of research on dental implant coatings, several areas require further investigation to enhance our understanding and improve clinical outcomes.

2.3.4.1 Long-term studies

Conducting long-term studies to evaluate the durability and sustained antimicrobial efficacy of various coatings is essential. This would help in understanding how these coatings perform over extended periods in the dynamic environment of the oral cavity by assessing changes in antimicrobial activity, biofilm resistance and structural integrity of coatings over months and years.

2.3.4.2 Standardization of methods

Developing standardized protocols for testing and reporting results would enable better comparison across studies. This includes using consistent bacterial strains, testing durations, and analytical methods by creating guidelines for standardized metrics such a CFU counts, inhibition zones and biofilm thickness measurements.

2.3.4.3 Comparative effectiveness research

Conducting comparative effectiveness research to directly compare the performance of different coating technologies under identical conditions such as similar antimicrobial agents but with different formulations of application methods. This would provide clearer insights into the relative benefits and drawbacks of each approach.

2.3.4.4 Clinical trials

Conducting clinical trials to validate the effectiveness of promising coatings under real-world conditions is crucial. These trials should consider the complex oral environment, including diverse microbiota, mechanical forces, and patient-specific factors and evaluate clinical outcomes such as infection rates, implant stability and patient satisfaction.

2.3.4.5 Personalized implant coatings

Exploring the potential for personalized implant coatings that are tailored to the specific needs of individual patients, considering factors like their microbiome composition, immune response, and medical history.

Further research in these areas is essential to overcome the current limitations and enhance the effectiveness, safety, and clinical applicability of dental implant coatings. By addressing these research deficiencies, we can develop more reliable and durable solutions that improve patient outcomes and advance the field of dental implantology.

3. Conclusion

3.1 Summary of key findings

This systematic review evaluates the microbiological effectiveness and clinical potential of various innovative dental implant coatings.

Concerning antimicrobial efficacy, advanced coatings incorporating antimicrobial agents such as silver, copper, and vancomycin demonstrate significant reductions in bacterial adhesion and biofilm formation. Coatings that provide controlled and sustained release of antimicrobial agents, such as vancomycin, ensure prolonged protection against bacterial colonization, which is crucial for reducing infection rates over the implant's lifespan.

Bioactive coatings, including those containing bioactive glass/copper composites and TiO2 nanotubes, not only exhibit strong antimicrobial properties but also promote osteogenesis and angiogenesis, which are essential for successful osseointegration. The enhanced osseointegration associated with bioactive coatings contributes to better implant stability and longevity.

In an other hand, many advanced coatings demonstrate good cytocompatibility, supporting cell viability and proliferation, which is essential for ensuring the coatings are safe for long-term use without causing adverse tissue reactions.

3.2 Implications for clinical practice

The adoption of antimicrobial coatings can significantly reduce the incidence of peri-implant infections, improving patient outcomes and reducing the need for revision surgeries.

Tailoring implant coatings to individual patient needs, considering factors like microbiome composition and immune response, can lead to improved clinical outcomes.

3.3 Final remarks and recommendations

While the findings from this review are promising, highlighting the potential of advanced dental implant coatings in enhancing antimicrobial efficacy and supporting osseointegration, several limitations need to be addressed :

- Conduct long-term studies to evaluate the sustained effectiveness and safety of coatings in diverse patient populations.

- Develop and implement standardized protocols for testing and reporting results to ensure consistency and comparability across studies.
- Promote collaboration between material scientists, microbiologists, and clinicians to innovate and optimize coating technologies for better clinical outcomes.
- Enhance patient education on the importance of maintaining oral hygiene and the benefits of advanced implant coatings in preventing infections.
- Adhere to regulatory standards and conduct extensive quality control checks to ensure the safety and efficacy of implant coatings.

By addressing these recommendations and continuing to advance research in this field, dental professionals can improve the reliability and effectiveness of dental implant coatings, ultimately leading to better patient outcomes and advancements in implant dentistry.

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