

Review

Biomimetic Coatings in Implant Dentistry: A Quick Update

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Abstract: Biomimetic dental implants are regarded as one of the recent clinical advancements in implant surface modification. Coatings with varying thicknesses and roughness may affect the dental implant surface's chemical inertness, cell adhesion, and antibacterial characteristics. Different surface coatings and mechanical surface changes have been studied to improve osseointegration and decrease peri-implantitis. The surface medication increases surface energy, leading to enhanced cell proliferation and growth factors, and, consequently, to a rise in the osseointegration process. This review provides a comprehensive update on the numerous biomimetic coatings used to improve the surface characteristics of dental implants and their applications in two main categories: coating to improve osseointegration, including the hydroxyapatite layer and nanocomposites, growth factors (BMPs, PDGF, FGF), and extracellular matrix (collagen, elastin, fibronectin, chondroitin sulfate, hyaluronan, and other proteoglycans), and coatings for anti-bacterial performance, covering drug-coated dental implants (antibiotic, statin, and bisphosphonate), antimicrobial peptide coating (GL13K and human beta defensins), polysaccharide antibacterial coatings (natural chitosan and its coupling agents) and metal elements (silver, zinc, and copper).

Keywords: dental implants; coatings; surface modifications; antibacterial; osseointegration



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1. Introduction

Nowadays, one of the most popular treatment choices for partially and completely edentulous arches is dental implants [1]. The intervention with implants promised greater outcomes than the treatment with traditional dentures, with an emphasis on alveolar bone preservation, esthetics, and prosthesis durability [2]. Osseointegration is essential to dental implant success, because it requires direct contact and interface between the peri-implant tissues and the implant surface in the absence of connective-tissue-layer involvement [3]. Osseointegration is also crucial for the success of bone grafts. The implant material's biocompatibility, the surface and design characteristics of the implant, both macroscopic and microscopic, the quantity and quality of bone, an unhindered healing phase, the loading circumstances, and the implant finish are all important factors in achieving successful osseointegration of the implant [4,5].

Failure of dental implants can occur for a variety of causes. These include issues relating to implants, clinicians, and patients; also, infections and foreign-body responses may contribute to the quick loss of alveolar bone [6]. The loss of alveolar bone, which is typically accompanied by the deposition of microbial plaque and bacterial infections known as peri-implantitis, is the most frequent cause of implant failure [7,8].

For dental implants to be clinically effective in the long term, osseointegration and the contact between the implant material and the bone are essential [9]. There is considerable evidence that improving osseointegration is strongly associated with the durability and prolonged clinical success of dental implants, as demonstrated in the research study [10]. A variety of surface coatings [11] and mechanical surface changes [12] have been studied to see whether they can improve osseointegration and bone formation. Surface medication leads to enhanced cell proliferation and growth factors, which results in an increase in the osseointegration process [13]. According to studies, the surface area of the implant increases with increased surface roughness, which leads to higher cell proliferation and cell growth [14]. Because of these surface modifications, the biocompatibility of the implant material is greatly improved, as is the adsorption of protein and cells [15]. This results in faster osseointegration and also a shorter period of healing, which is desirable for both clinicians and patients, and thereby improves the patient’s quality of life [5,9]. Hence, biomimetic coating is the process of dental-implant surface modification mainly targeting increasing osseointegration and reducing microbial biofilm formation. The aim of this narrative review is to provide a succinct update on the numerous biomimetic coatings that are used to improve the surface characteristics of dental implants, as well as their applications. Figure 1 shows the overview of this review.

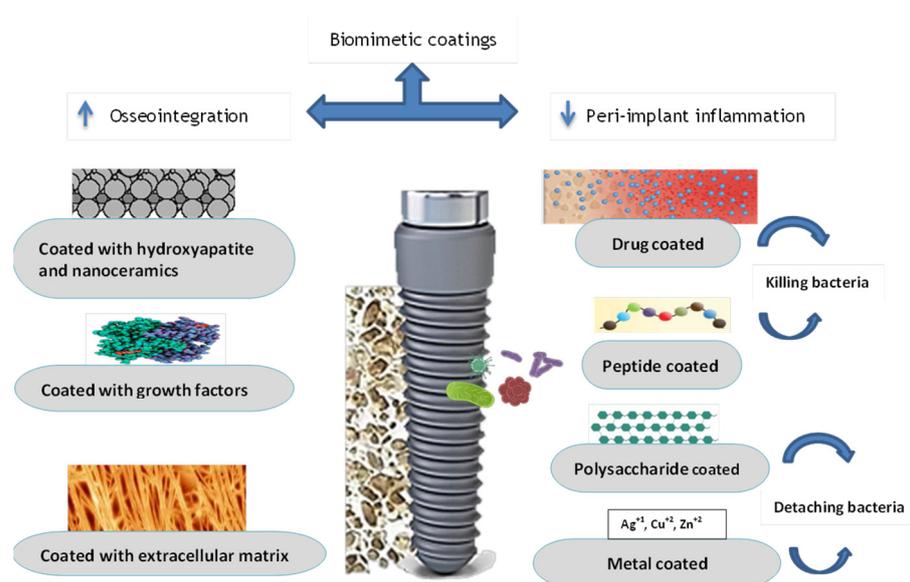


Figure 1. Overview of the review.

2. Implant Surface Modifications

Metals are not new in dentistry. However, metals are materials with no biological activity, which contributes to their limited attractiveness as biomaterials [16]. During the last three decades, remarkable technological breakthroughs in ceramics and polymers have permitted their usage in medical devices. Due to their superior biofunctional properties, ceramics and polymers have replaced many metal-based devices [17]. Due to their strength, durability, and lifespan, metals still account for over 70% of implant devices in the medical and dental industries [18]. Ceramics and polymers cannot replace metallic biomaterials. Metals cannot have biofunctions added to them during production procedures such as heat treatment, casting, melting, or forging [19].

The surface modification (Table 1) has an impact on the material’s surface shape, structure, and composition, while keeping its core mechanical properties. Metals with biofunctional characteristics have also been required recently [20]. Dental implants must be compatible with hard and soft tissue for osseointegration and bone development, and antibacterial characteristics to prevent biofilm formation. These biofunctional properties oppose protein adsorption and cell adhesion [21]. A metallic implant reacts with living

tissues right away when it is placed into a human body. Put differently, the biofunction of a metallic substance is determined and characterized by its early reaction. Surface biofunction can be enhanced by surface alteration. For these reasons, many methods of metal surface modification are being researched and tested (Figure 2) [22–24]

Table 1. Different methods of surface modifications.

Physical Surface Modifications (Subtractive)	Chemical Surface Modifications (Additive)	Biological Surface Modifications (Biomimetic)
Plasma spraying Low-pressure plasma spraying High-velocity oxy-fuel spraying Sputter deposition Magnetron sputtering Ion beam-assisted sputtering Pulsed laser deposition	Sol-gel deposition Electrophoretic deposition Electrochemical deposition Acid etching Anodization Peroxidation Alkaline treatment Fluoride treatment Vacuum treatment Plasma coating	Extracellular matrix Peptides Growth factors (BMPs, PDGF, and FGF) Drugs (antibiotic, statin, and bisphosphonate)

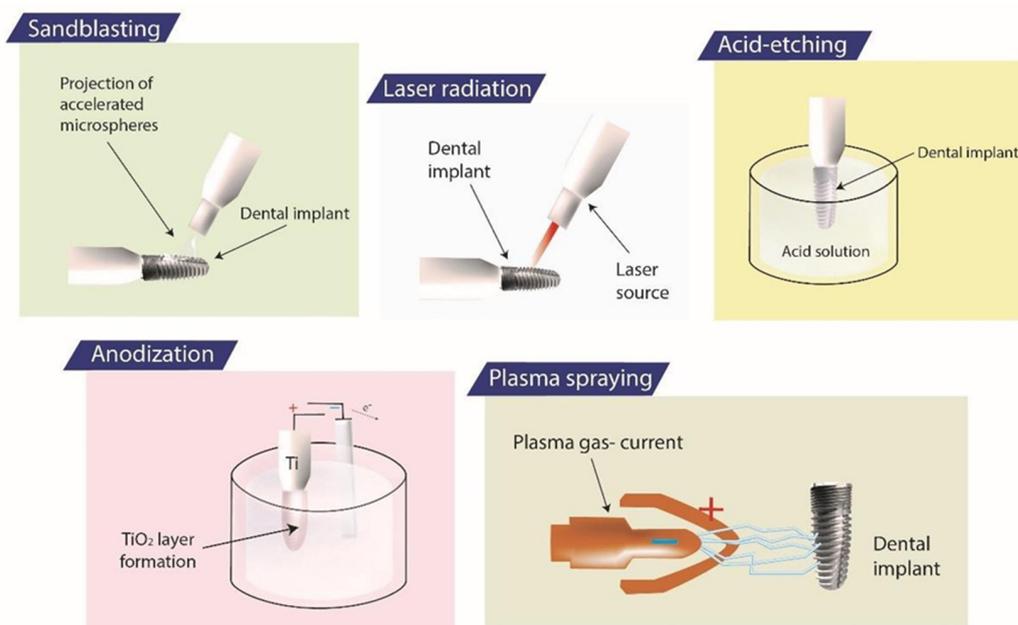


Figure 2. Different techniques of dental-implant surface modifications. Reprinted from Ref. [24].

3. Biomimetic Coating

Implant dentistry progress encourages the advancement in improving implants’ mechanical and biological properties. Aside from altered processes that cause the implant surface to distort plastically, certain supplementary technologies can produce surface depositions known as coatings [25]. The most essential way to improve clinical effectiveness is to update implant-coating technology. Various surface-coating combinations have been used to increase implant biocompatibility, bioactivity, and antibacterial potential [21]. Biomimetic dental implants are regarded as one of the most recent clinical advancements in implant surface modification. Otto Schmitt used the term “biomimetics” for the first time in the 1950s [26]. The structure, synthesis, and operation of biologically created materials, as well as biological systems and processes, are all included in biomimetics, which is the artificial emulation of natural processes to create similar products [27–29].

The ideal characteristics of biomimetic agents are discussed as the following: the ability to generate proper cell differentiation for promoting new bone formation, easy synthesis or manufacturing, with no extraction from allografts to reduce the danger of infectious–contagious disease transmission, resorbability in response to osteogenic activity, eliminating issues with implant loss owing to coating delamination, not generating immunological responses in the host, chemical stability until the implant is inserted into the surgical socket, and finally, a good cost-to-benefit ratio [29–31]. Table 2 shows the key properties of biomimetic coatings and Figure 3 illustrates the trend in publications related to biomimetic dental implants, according to PubMed.

Table 2. Key properties of biomimetic coatings.

Properties of Bioactive Coatings	Studies	Findings
Bioactivity and osseointegration	Mackovic et al., 2012 [32]	With their extremely quick kinetics for bone-like hydroxyapatite mineralization and non-toxic effects on osteoblast cells, nanoscaled bioactive glass particles are a potentially useful material for bone-tissue engineering.
	Li et al., 2018 [33]	Carbonated hydroxyapatite (CHA) bioceramic coating with synergistic surface chemistry and topography alteration has a bright future as an implant coating, to promote optimal osseointegration.
Cellular response	Yu and Wei, 2013 [34]	Cell adhesion on distinct biomaterial surfaces is directly influenced by substrate surface qualities, which in turn influence cell proliferation and differentiation.
Ion dissolution and osteogenesis	Wu et al., 2020 [35]	Researchers used biological coating and surface topography modification to make biomimetic titanium implants with good-quality osteogenic potential.
Mechanical performance	Sebdani and Fathi, 2011 [36]	The elastic modulus, hardness, and fracture toughness of produced composite coatings increased as forsterite concentrations rose.
	Erol-Tygun et al., 2013 [37]	Modified bioglasses (such as nanoparticles) may increase the mechanical characteristics of these materials (hardness, elastic modulus, and tensile strength).

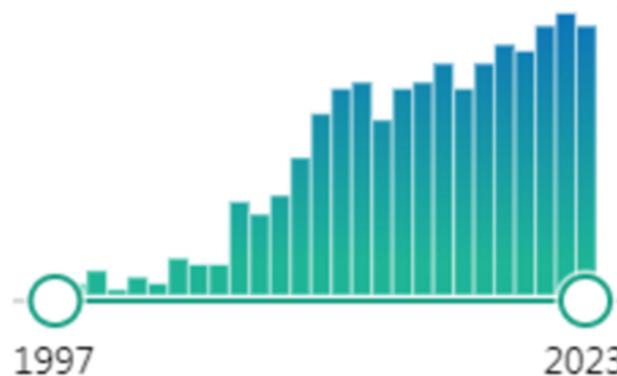


Figure 3. Trend in publications related to biomimetic dental implants, according to PubMed.

3.1. Coating to Improve Osseointegration

Although advances in surface topography have resulted in improved osseointegration, a wide range of inorganic and organic coatings are being researched, to increase the tissue integration of dental implants [38]. The mechanical performance of strong biometals and the bone-bonding potential of bioactive materials can be combined when bioactive materials are coated on them. The surface features of dental implants, such as chemical inertness, cell adhesion, and antibacterial properties, can be impacted by coatings that differ in thickness and roughness [21,39]. The following section mostly discusses current advancements in dental implants coated with bioactive materials. Figure 4 shows the stages of osseointegration around dental implants [40].

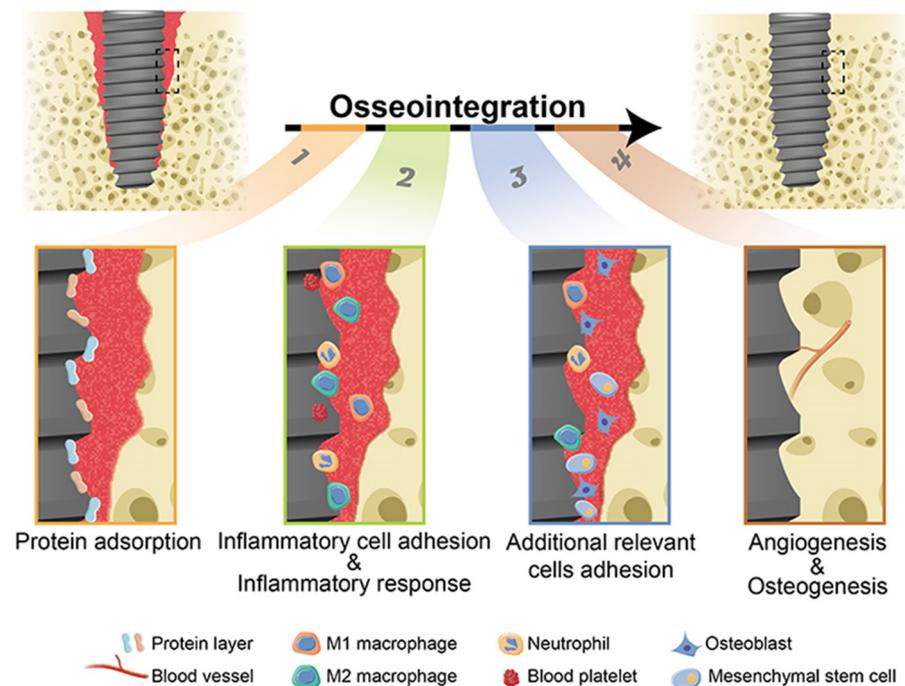


Figure 4. Stages of osseointegration around dental implants. Reprinted from Ref. [40].

3.1.1. Hydroxyapatite Layer and Nanocomposites

Of the several methods, one of the most popular is coating implants with hydroxyapatite (HA) [41]. HA is a biologically stable type of calcium phosphate that mineralizes to strengthen the organic matrix without causing inflammation or immunogenicity [42]. It is composed of naturally occurring ions from physiological settings, and has good osteoconductive and osteointegration properties. Several ion-substituted hybrid anchors paved the path for implant architecture featuring diverse biological activities. Ion-substituted HA coatings have been demonstrated to significantly enhance cell attachment, despite the possibility that they will negatively affect the growth and differentiation of cells attached to the coating surface [43,44].

Moreover, the bioactivity and osteoconductivity of the titanium substrate can be enhanced by the HA layer. By using a micro-arc oxidation process to create a porous hydroxyapatite-coated titanium alloy surface, it will be possible to enhance the mechanical properties and promote bone formation by increasing the interface contact rate and bone-to-implant contact [45]. Recently, implant surface qualities have been enhanced by the use of nano-hydroxyapatite, which can be combined with collagen, bioglass, or titanium dioxide, to create a composite that mimics the bio-environment of natural bones [46]. The specific surface area and adsorption capacity of nano-sized particles are greatly increased. The nano-hydroxyapatite coating provides better bone bonding with dental implants over time, when compared to a standard dual acid-etched surface. Because HA coatings can immobilize growth factors and proteins through non-covalent interactions, hybrid coatings that hasten the healing of bones have been created [21].

In conclusion, since HA's chemical and crystallographic structures are remarkably comparable to those of human bone, virtually all biocompatibility issues are resolved, making its application particularly promising. Nevertheless, HA has certain drawbacks, including fracture toughness, low tensile strength, and brittleness. However, when created as a coating for practical use, HA's benefits can be fully utilized.

Table 3 contains a selection of a list of recent publications on nanoceramics used as coating materials.

Table 3. Surface coating of implants using nanoceramics.

Studies	Methodology	Findings
Ripamonti et al., 2012 [47]	Plasma sprayed with crystalline hydroxyapatite	The findings in nonhuman primates suggest that geometrically built plasma-sprayed titanium implants are intrinsically osteogenic, with the concavities creating an ideal microenvironment for inducing bone development.
Alghamdi et al., 2013 [11]	Calcium phosphate (CaP) coating sprayed by radio frequency magnetrons	In both healthy and osteoporotic situations, dental implants modified with a thin layer of calcium pseudophosphate (CaP) coating efficiently enhance osseointegration.
Jing et al., 2015 [45]	HA coating by micro-arc oxidation approach	Bone ingrowth and the strength of the bone–implant interface will be significantly improved by this coating process.
Carradò et al., 2017 [48]	Sodium titanate/hydroxyapatite nanoporous bilayer	Osteointegration and osteoconduction <i>in vivo</i> are enhanced by a nanoporous hydroxyapatite/sodium titanate bilayer. It avoids delamination during screwing and may strengthen the durability of HA-coated dental implants without adhesive failures.
Lukaszewska-Kuska et al., 2018 [49]	HA coating using a direct electrochemical method	Potential advantage in chemical and physical properties that promote osseointegration.
Hu et al., 2018 [50]	Nanostructured HA coating on Ti-6Al-4V implants	Ti-6Al-4V implants covered with nanostructured HA may enhance osteointegration in diabetes animals by increasing angiogenesis and osteogenesis and addressing pathological bone loss.
Fang et al., 2019 [51]	Nanocrystalline hydroxyapatites with SDF-1	Biomimetic HA microsphere can promote alveolar bone repair.
Eawsakul et al., 2020 [52]	Double layers of gold nanoparticles	The coating possessed homogeneity and good biocompatibility, promoted osteoblast cell proliferation and had good stability.
Yu et al., 2021 [53]	Polydopamine nanoparticles functionalized with hydroxyapatite (HA/nPDAs) coated in three dimensions on implant surfaces	The coating's ability to prevent reactive oxygen species (ROS) and encourage osteogenesis in both normal and high ROS environments (like diabetes, periodontitis, and osteoporosis) showed great promise for enhancing implant osteointegration, particularly in situations where high ROS levels are brought on by diseases.
Su et al., 2022 [54]	Composite multifunctional coating of polydopa-mine/hydroxyapatite/gelatin (PHG) prepared using gelatin and polydopa-mine/hydroxyapatite nano-particles	The proposed PHG coating may increase soft tissue sealing and bone bonding.
Alcudia et al., 2022 [55]	Porous silver nanoparticle/polycaprolactone/polyvinyl alcohol coatings	This coatings exhibited excellent adherence and a honeycomb-like surface structure that could facilitate vascularization of the implant and improve osseointegration.
Mokobia et al., 2023 [56]	ZnO-NPs-Coated implants	Implant fixation was improved by ZnO-NPs coating on metal surfaces because it promoted osteogenesis and soft tissue integration. Furthermore, to achieve a strong biological attachment for implants, osteoconductive nanoparticles formed a chemical relationship with bone. There is little doubt that implants with ZnO-NPs placed to their surfaces exhibit superior clinical outcomes due to a decreased risk of infection.

3.1.2. Growth Factors

Numerous growth factors are produced by platelets and macrophages, which are present during the first phase of osseointegration and help to initiate the second phase [57]. To speed up this process, coating materials containing Transforming Growth Factor (TGF), Platelet-Derived Growth Factor (PDGF), and Fibroblast Growth Factor (FGF) have been employed [20,58].

The signal protein known as vascular endothelial growth factor, or VEGF, is involved in both vasculogenesis and angiogenesis. It has been demonstrated that VEGF increases alkaline phosphatase (ALP) activity, activates genes and protein expression related to vasculogenesis, and increases primary rat osteoblast proliferation in vitro. In the related in vivo experiment, coating the implant with VEGF significantly increases the activation of osteoblasts and endothelial cells [59,60]. When compared to SiHA or VEGF-coated groups, respectively, the silicon substituted hydroxyapatite (SiHA)-coated scaffolds combined with VEGF had a synergistic effect on enhanced ossification, larger bone trabeculae, and greater angiogenesis degree in a sheep model [61].

Growth factors known as bone morphogenetic proteins (BMPs) are crucial for the development of cartilage and bone. BMPs have the ability to regulate osteogenic cells and promote bone mesenchymal stem cell (MSC) development [62,63]. More encouraging findings are achieved when BMPs are used, since they have a strong biological potential for osteoinduction. BMPs (BMP-2, BMP-4, and BMP-7) are members of the superfamily of Transforming Growth Factors (TGF) [64]. When compared to anodized implants, titanium implants containing BMP-2 had better bone-to-implant contact, more new bone development, and a higher density of surrounding bone than acid-etched implants [65,66]. BMP-7 has shown promise as a bone regeneration stimulant throughout the years. Research has demonstrated that administering a comparatively modest concentration of BMP-7 locally can enhance osseointegration through the development of a particular delivery mechanism including a titanium surface covered with poly-ethyl acrylate [67,68].

To conclude, growth factors have been shown to improve bone regeneration and osseointegration. The initial findings reported in the literature appear encouraging, even if further clinical research is needed to confirm the long-term benefits of growth factors as dental implant surface coatings. Table 4 shows a selected list of recent articles on the surface implant coating with growth factors.

Table 4. Surface implant coating with growth factors.

Studies	Methodology	Outcomes
Lee et al., 2010 [69]	Titanium implants covered with a biodegradable polymer and basic fibroblast growth factor (bFGF).	The study’s findings suggest that electro spraying poly lactic-co-glycolic acid (PLGA) and beta-fibroblast growth factor (bFGF) onto a titanium implant may promote bone formation adjacent to the implant’s surface.
Kim et al., 2013 [66]	Anodized implants covered in a mixture of human BMP-2 recombinant and human VEGFs.	Encourage the growth of vertical alveolar bone, yet it is unknown how rhBMP-2 and rhVEGF work together.
Schliephake et al., 2015 [70]	Oligodeoxynucleotides (ODNs) were anchored to the surface of sandblasted acid-etched (SAE) titanium screw implants and were hybridized with complementary strands of ODN conjugated to rhVEGF165	Accelerate the bone-implant contact of titanium implants that have been sandblasted and etched to a certain point. The growth factor appears to have a limited effect on the tissue right next to the surface of the implant.
Guang et al., 2017 [59]	Coating the implant with VEGF in vivo	Experiments could help osteoblasts and endothelial cells grow.

Table 4. Cont.

Studies	Methodology	Outcomes
Yang et al., 2017 [71]	Titanium disc and screw types coated with human bone morphogenetic protein-2 (hBMP-2) and human growth and differentiation factor-5 (hGDF-5) to allow for the controlled release of the growth factors.	Enhance the clinical characteristics of implants for use in dentistry and orthopedics.
Al-Jarsha et al., 2018 [68]	Poly-ethyl acrylate (PEA)-coated titanium discs were adsorbed with human bone morphogenetic protein 7 (BMP-7).	Cell adhesion, proliferation, mineralization, and the production of osteogenic markers (osteopontin and osteocalcin) demonstrated that, in the absence of PEA coatings, the system was more effective in promoting osteodifferentiation of mesenchymal cells than combinations of titanium and BMP-7.
Keceli et al., 2020 [72]	PDGF and BMP-6 are loaded into the titanium implant after anodization.	There is a considerable probability that the early osseointegration phase will be prolonged as a result of a more favorable factor release and its role in the mineralization, proliferation, and related gene expression in osteoblastic cells.
Eawsakul et al., 2021 [52]	Creating BMP-2 immobilization on titanium that has been altered using the layer-by-layer method (LBL).	Enhanced osteoblast cell proliferation and exhibited an increase in stability.
Palermo et al., 2022 [60]	Using concentrated growth factor (CGF) permeated dental implants.	Improved osseointegration and post-surgical problems.
Maekawa et al., 2022 [73]	The first study to use BMP gene delivery combined with chemical vapor deposition (CVD) technology on titanium to encourage in vivo bone-to-implant contact and repair.	Enhances alkaline phosphatase activity and osteoblast cell development in vitro; enhances alveolar bone regeneration and bone-to-implant contact in a manner akin to high exogenous BMP-7 dosages in vivo. This new method of targeted gene distribution on implant surfaces provides an alternative to alveolar bone rebuilding.

3.1.3. Extra Cellular Matrix

Another method to increase dental implant biocompatibility is by accumulating extracellular matrix (ECM) proteins on implant surfaces, which control cell-matrix adhesion [74]. Fibroblast growth factors stimulate fibroblasts to secrete extracellular matrix (ECM) proteins like hyaluronan, collagen, chondroitin sulfate, fibronectin, and elastin during the proliferative stage of osseointegration [57]. By rearranging intracellular microfilaments and microtubules, these extracellular matrix proteins seem to be essential for the early stages of bone healing. They also help cells adhere and spread, and via the action of cell surface integrins and fibronectin arginine–glycine–asparagine motifs, they guide osteoprogenitor cell migration to the implant surface [75,76]. However, using such a unique protein has three significant limitations: the high cost of synthesis, the molecule’s antigenicity and instability, and the macromolecule’s steric hindrance in focal adhesion [77,78].

There is enough evidence from the literature on the usefulness and contribution of ECMs as coating materials to the osseointegration process. However, in order to allow the use of early loading techniques and ensure implant success in patients with damaged bone tissue, future research should look into the developments in dental implant surface design including ECMs. These developments are critical to improve the healing process and enhancing bone formation. Table 5 contains a selection of recent articles on the surface coating with ECM.

Table 5. Surface coating with ECM.

Studies	Methodology	Findings
Morra et al., 2010 [79]	Collagen's biochemical surface alteration in reaction to acid-etched titanium surfaces.	Results suggest that surface topography (morphological) and surface linkage of bioactive chemicals (biochemical) signals might work in concert to produce multifunctional implant surfaces.
Alghamdi et al., 2013 [80]	Comparison of three types of implants: uncoated, nano-CaP-coated, and coated with type 1 collagen.	Results failed to demonstrate a consistent beneficial effect of the collagen covering on bone growth throughout a three-month period, following implantation.
Lee et al., 2014 [81]	The development of peri-implant bone in implant groups that were uncoated (UC) and coated with HA, collagen plus HA (CH), and collagen, HA, and bone morphogenetic protein-2 (BMP-2).	Compared to the other groups, the BIC and new bone formation were significantly higher in the CH group. There were no notable variations observed in the other groups.
Korn et al., 2014 [82]	Collagen was combined with sulfated hyaluronan (sHya) or chondroitin sulfate (CS) in the coatings.	Implant surface coatings made of the selected organic ECM components demonstrated some potential to affect in vivo osseointegration.
de Barros et al., 2015 [83]	The implant surfaces underwent sandblasting and acid etching, and a portion of them were also coated with chondroitin sulfate and collagen type II (collagen/CS).	The width of the peri-implant gap affects the formation of peri-implant bone. There was not enough newly formed bone to completely fill in all the gaps surrounding each surface. The coating had a beneficial effect on bone growth when it was close to the surface.
Raphel et al., 2016 [84]	Elastin-like protein (ELP) that undergoes chemical modification to allow for new photocrosslinking and solution processing techniques to create stable coatings on the surfaces of titanium-based orthopedic and dental implants.	ELP coatings facilitate early implant loading, and may lessen micromotion, which may lead to aseptic loosening and early implant failure. They are also resistant to surgical implantation and accelerate osseointegration.
Yin et al., 2019 [85]	TNS-MAP is the designation given to titanium that has been alkali-treated and has nanonetwork structures (TNSs) covered with mussel adhesive protein (MAP).	TNS-MAP, a novel biocomposite implant material, with potential applications in orthopedics and practical dentistry.
Wu et al., 2020 [35]	TiO ₂ nanotubes or sandblasting and acid etching the surface of titanium were used to modify it. Mineralized extracellular matrix (ECM) made from cultured bone-marrow mesenchymal stromal cells was then applied.	The results demonstrated a viable strategy for producing biomimetic titanium implants with good osteogenic capacity, by combining surface topographical alteration with biological coating.
Syam et al., 2021 [86]	Dip-coating titanium (IDCT-Ti) implants with tetrapeptide Gly-Arg-Gly-Asp (GRGD).	The topography, hemocompatibility, and wettability of the implant surface—all of which are linked to enhanced osteoblast-cell adherence to implant surfaces and osseointegration—were positively impacted.
Rappe et al., 2022 [87]	The metallic foams were treated with an inorganic alkali thermochemical process and grafted with a cell adhesive tripeptide (RGD), in order to create a bioactive surface.	Combining these two techniques may be beneficial in improving the stability and osteointegration of porous metallic implants.

3.2. The Antibacterial Performance of Coating

Implant-associated infections are a frequent postoperative outcome of implant rehabilitation, which can cause patient discontent, additional costs, and, potentially, implant failure. Microorganisms within implants are shielded from antibodies by biofilms adhering to the implant surface [88,89]. On the other hand, antibiotic overuse can potentially increase the spread of drug-resistant microorganisms [90]. In an effort to combat this, a large number of researchers have worked to create specialized implants with functional coatings that can either specifically target and kill the bacteria or prevent bacterial adherence and biofilm formation [91,92]. Figure 5 shows the bacterial interaction with naked implant surface, a bactericidal surface, and a bacteriostatic surface.

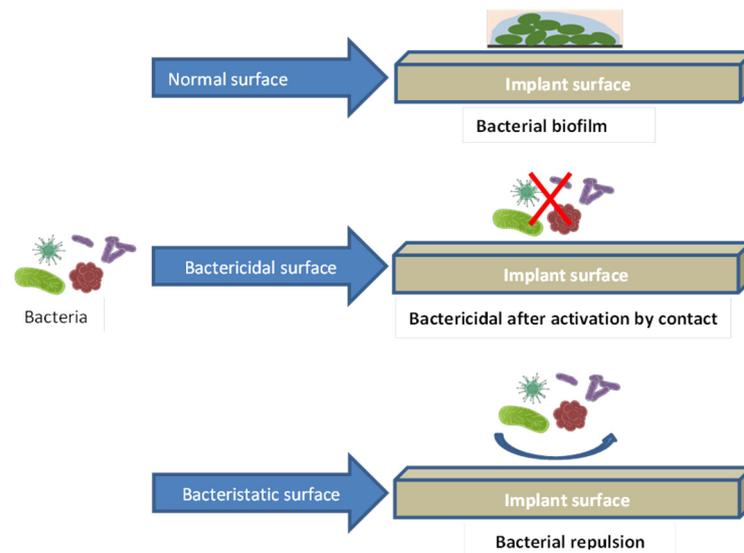


Figure 5. Bacterial interaction with naked implant surface, a bactericidal surface, and a bacteriostatic surface. The red × in the second diagram indicates bactericidal killing bacteria.

3.2.1. Drug-Coated Dental Implant

Antibiotics, Simvastatin, and bisphosphonate are examples of drug coating on the surface of dental implants [93]. Antimicrobial surfaces have been developed in dental implantology in two different ways, so far. Antimicrobials are actively released from type I surfaces to inhibit bacterial adherence and promote killing, whereas antimicrobials are permanently bound to type II surfaces, to prevent long-term bacterial adherence and promote killing [94,95]. Implants featuring a type I surface have proven effective in treating infections related to implants; however, their eluting activities may pose challenges, as the initial burst of antibiotics happens during the first week of implantation and then decreases exponentially over time, raising the possibility of generating bacteria resistant to antibiotics that will persist for a long time [96,97].

A number of bactericidal and bacteriostatic chemicals were permanently added to implant surfaces, in order to generate a type II surface that prevents the formation of biofilm around dental implants, in order to solve this restriction of the type I surface [88,98]. For instance, applying a bacteriostatic medication like tetracycline permanently on implant surfaces efficiently eliminated bacteria that may otherwise infect the implant surface, promoting cell proliferation and bone healing [99]. In a similar way, prolonged vancomycin coating of titanium implants inhibited *Streptococcus aureus* colonization, while speeding up bone repair. [100]. Vancomycin therefore works better than antibiotics that cling to germs permanently, such as gentamicin, which becomes ineffective when bacteria are re-exposed [98,101]. However, widespread use of vancomycin would exacerbate the worry about the spread of vancomycin-intermediate and vancomycin-resistant *Streptococcus aureus* (VISA) strains [102]. Bisphosphonates (alendronate, etidronate, tiludronate, and zoledronate) are medications that stimulate osteoblasts and bone production, while

blocking osteoclastic activity and bone resorption [103,104]. For the antibacterial activity, bisphosphonate-coated implants revealed a significant decrease in bacterial adhesion [105]. Simvastatin may promote bone growth and enhance bone-to-implant contact by upregulating the production of VEGF and BMP [106]. Porous titanium surfaces coated with simvastatin improved alkaline phosphatase activity, type I collagen synthesis, and osteocalcin release from pre-osteoblasts, in vitro [107]. In addition, Simvastatin-Hydroxyapatite coatings are reported to have good antibacterial performance [108].

To sum up, in order to provide targeted drug delivery and therapeutic activities, a variety of strategies have been used to induce prolonged drug release from dental implants, for a range of medications. Drug excretion from dental implants has been documented in a number of in vitro and in vivo animal models, and in experimental investigations; nevertheless, more clinical study is necessary before considering drug-eluting dental implants for clinical application.

3.2.2. Antimicrobial Peptide Coating

Innate host defense antimicrobial peptide coatings (AMPs), which are tiny cationic peptides, demonstrate a wide range of antibacterial activity against different pathogens, such as gram-positive and gram-negative bacteria, and they also lessen the development of bacterial resistance [109,110]. Applications for AMPs are numerous; however, one of the more notable uses is the covalent immobilization method used to biofunctionalize titanium to confer antibacterial properties [111]. To stop germs from growing on implant surfaces, a number of bactericidal peptides have been employed, such as GL13K and human beta defensins (HBDs) [112]. The salivary defense protein BPI fold-containing family A member 2 (BPIFA2) is the source of GL13K, a parotid secretory protein [113]. According to research by Holmberg et al., GL13K applied to implant surfaces has a bactericidal effect against *Porphyromonas gingivalis*, while preserving cytocompatibility and promoting sufficient proliferation of osteoblasts and gingival fibroblasts [114]. Likewise, HBDs showed broad-spectrum antibacterial action, and stimulated osteoblast and mesenchymal stem cell growth when applied to implant surfaces [115,116].

Peptide antibiotics are gaining traction as a viable implant coating material to lessen/prevent peri-implantitis and increase dental-implant success rates, because of their wide range of activity and less potential to cause bacterial resistance. It would facilitate their transition to clinical application if more evidence could be provided about the reliability of these peptides adsorbed onto implant surfaces and their resistance to buffers, pH changes and bodily fluids.

3.2.3. Polysaccharide Antibacterial Coating

Natura Chitosan is a neutral cationic polymer generated from the deacetylation of chitin [117]. Chitosan-immobilized implant surfaces have been shown to exhibit antibacterial characteristics [118,119]. Triethoxysilylpropyl succinic anhydride (TESPSA) functions as a coupling agent that has the potential to form a stable double-peptide bond with chitosan [120]. The TESPSA/chitosan coating demonstrated good adhesion resistance at titanium surfaces, according to Campos et al. [121]. In order to boost antibacterial activity, Palla-Rubio et al. incorporated silica–chitosan hybrid materials onto titanium implants. They found that a suitable concentration of 5–10% for encapsulated chitosan displayed antibacterial features [122]. The antibacterial properties of polyelectrolyte multilayers containing hyaluronic acid and chitosan were also appreciated against *S. aureus* [123]. Ag-conjugated chitosan nanoparticle coating on titanium surface shows promise in preventing growth of *S. mutans* and *P. gingivalis* and in reducing the formation of biofilms and bacterial adhesion [124,125]. Additionally, antimicrobials may be provided by using chitosan coatings in a biocompatible way, to prevent the growth of bacteria. On the titanium surface, chitosan coatings containing either 0.2% or 20% tetracycline digluconate were applied and tested for their ability to fend off infections such *Actinobacillus*, *Actinomycetemcomitans*, and *Staphylococcus epidermidis*. A total of 89 percent of tetracycline and 100 percent of

chlorhexidine were released by the coatings in 7 and 2 days, respectively; nevertheless, the chlorhexidine that was released posed a risk to human osteoblasts and fibroblasts [126].

In summary, considerable progress has been made in using polysaccharides as coatings with antibacterial properties. A wide variety of the most often utilized coating processes have been developed, each with varying possibilities for development. Future technological developments could focus on improving the structures and properties of polysaccharides as coatings, as well as creating commercially viable polysaccharide-based coatings for particular uses.

3.2.4. Antibacterial Properties of Metal-Element Components

Antibiotic resistance and a restricted antibacterial range are just two of the drawbacks associated with using antibiotic coatings on dental implants [127]. Silver, copper and zinc have also been used in coating of implants as an alternative, because of their antibacterial properties and the fact that they are available in nanoparticulate forms [128,129]. Silver’s multilayer antibacterial action is widely recognized, and assures a broad range of antibacterial activity, as well as long-term antibacterial activity [130]. Table 6 shows several elements that were used as coating that have a good antibacterial property.

Table 6. Surface coating with antimicrobial properties of metals.

Studies	Methodology	Findings
[131]	AgNPs with polydopamine (PDA) coating applied to titanium.	May successfully prevent the growth of microorganisms against <i>S. mutans</i> and <i>P. gingivalis</i> .
[132]	Spin-coating technology was used to manufacture a series of Zn-incorporated coatings on micro rough titanium (Micro-Ti) using the sol-gel process.	Encourages osseointegration and prevents gram-positive and gram-negative germs from adhering to surfaces.
[133]	A two-step hydrothermal process was used to create nanorod-array structured coatings with a controlled-release feature of zinc (Zn) based on the in situ conversion of ZnO to ZnO@ZnS. This method gave titanium surface cell selectivity.	Maintained a strong antimicrobial effect against <i>S. aureus</i> and <i>E. coli</i>
[134]	Zinc ions and fluoride integrated into calcium phosphate coatings.	Possess bactericidal effects, particularly efficient at preventing the proliferation, colonization, and adherence of <i>P. gingivalis</i> .
[135]	TiOB [®] (chemically oxidized titanium) coating containing ionic zinc.	Revealed that TiOB [®] functionalization with ionic zinc demonstrates bactericidal characteristics similar to a coating containing gentamicin.
[136]	Zinc oxide (ZnO) nanoparticles.	Displayed antimicrobial properties
[137]	Copper nanoparticles (CuNPs).	Can release copper ions, which are thought to have a dual function in aiding in the development of new bone and avoiding infection.
[138]	Calcium silicate coatings containing cerium oxide (CeO ₂ -CS).	Promoted osteoblast differentiation, demonstrated significant antibacterial efficacy against <i>E. faecalis</i> while maintaining acceptable biocompatibility.
[139]	Tantalum-based implant.	Coated surface performed significant antibacterial action against <i>F. nucleatum</i> and <i>P. gingivalis</i> .
[140]	Poly (lactic-co-glycolic acid)/Ag/ZnO nanorods coating.	Provided a strong antibacterial activity and high degree of cytocompatibility.
[141]	Using plasma electrolytic oxidation (PEO), selective laser melting (SLM) produced volume-porous Ti-Ta-Nb-Zr scaffolds with a surface biofunctionalized.	Provided robust osteogenic stimulation and antimicrobial activity, without causing cytotoxicity in mammalian cells.
[142]	Silver/strontium glass integrated polyelectrolyte multilayer coatings on 316L stainless steel.	Angiogenesis, osseointegration, and antibacterial activity were all improved by the PEM/AgSrMBG coating’s prolonged release of silver and strontium ions.
[143]	Titanium substrates were treated with phosphorus, calcium, and copper co-incorporated titanium oxide (TiO ₂) layers, using plasma electrolytic oxidation.	Bactericidal action against <i>E. coli</i> . The biological reaction to the phosphorus-, calcium-, and copper-containing layer has improved MG-63 osteoblastic cell integration, proliferation, and viability.
[144]	By using one-step micro-arc oxidation (MAO) technology, zinc and strontium were added to the surface coating of implants in different concentrations.	Bone marrow mesenchymal stem cells (BMSCs) can be effectively promoted to proliferate and differentiate when exposed to <i>S. aureus</i> and <i>P. gingivalis</i> ; exhibits good antibacterial activity against these bacteria, and greater proliferation is seen in the cells on the coating with a higher strontium level.

Antibacterial metal alloys exhibit strong and durable antibacterial capabilities, together with excellent mechanical properties, corrosion resistance, and all-round qualities that point to their possible future applications. Nonetheless, a few issues remain prior to the clinical application, such as the exact antibacterial mechanism and possible toxicity of some elements.

4. Conclusions

Biomolecules, such as bioactive chemicals and multifunctional molecules, can be attached to implant surfaces to enhance the osteogenic process around implants. This process includes inducing cell adhesion, providing an osteogenic stimulation, and potentially having antimicrobial properties.

To improve osseointegration, the use of hydroxyapatite and BMP in the coatings of implants appear to be the most promising methods. The treatment of implant surfaces with nano-hydroxyapatite, which can be combined with collagen, may create a composite mimicking the bio-environment of natural bones, and thus reduce inflammation and accelerate the healing of the peri-implant bone.

Growth factors such as VEGF, which is involved in angiogenesis, but especially BMPs, are crucial for increasing bone-implant contact and osteoinduction, allowing the development of new bone on the implant periphery.

The covering of implant surfaces with ECM proteins such as growth factors from fibroblasts appears essential at the early stages of bone healing, but presents significant limitations, such as their high synthesis cost, antigenicity and instability of the coating material.

Concerning the antibacterial performance, the addition of tetracycline or bisphosphonate to type II implant coatings to prevent bacterial adhesion and the formation of biofilms seems to be the method most often used.

Regarding AMPs to prevent germs from growing on implant surfaces, GL13K and HBDs showed broad-spectrum antibacterial action, while stimulating the growth of osteoblastic and mesenchymal stem cells.

Other antibacterial compounds, such as TEPSA, chitosan, or multilayer silver implant coatings have also reported good results, but should be developed particularly against the resistance or profiling of specific strains of the oral environment, such as *S.aureus*, *S. mutans* and *P. gingivalis*.

Therefore, long-term clinical studies are still necessary to assess the effectiveness of various coatings and ascertain the success rates of novel implant coatings, even in light of the encouraging results. In addition, more investigation is needed to ascertain whether standard implant surface treatments and coatings can yield dependable therapeutic outcomes, especially with regard to attaining osseointegration stability and preventing inflammation, mobility, infection and mechanical issues.

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References

1. Thanissorn, C.; Guo, J.; Jing Ying Chan, D.; Koyi, B.; Kujan, O.; Khzam, N.; Miranda, L.A. Success rates and complications associated with single immediate implants: A systematic review. *Dent. J.* **2022**, *10*, 31. [[CrossRef](#)] [[PubMed](#)]
2. Rosales-Leal, J.I.; Rodríguez-Valverde, M.A.; Mazzaglia, G.; Ramón-Torregrosa, P.J.; Díaz-Rodríguez, L.; García-Martínez, O.; Vallecillo-Capilla, M.; Ruiz, C.; Cabrerizo-Vilchez, M. Effect of roughness, wettability and morphology of engineered titanium surfaces on osteoblast-like cell adhesion. *Colloids Surf. A Physicochem. Eng. Asp.* **2010**, *365*, 222–229. [[CrossRef](#)]
3. Hudieb, M.; AlKhader, M.; Mortaja, S.; Abusamak, M.; Wakabayashi, N.; Kasugai, S. Impact of bone augmentation of facial bone defect around osseointegrated implant: A three dimensional finite element analysis. *Dent. J.* **2021**, *9*, 114. [[CrossRef](#)] [[PubMed](#)]

4. Shaikh, M.Q.; Nath, S.D.; Akilan, A.A.; Khanjar, S.; Balla, V.K.; Grant, G.T.; Atre, S.V. Investigation of patient-specific maxillofacial implant prototype development by metal fused filament fabrication (MF3) of Ti-6Al-4V. *Dent. J.* **2021**, *9*, 109. [[CrossRef](#)] [[PubMed](#)]
5. El-Banna, A.; Bissa, M.W.; Khurshid, Z.; Zohaib, S.; Asiri, F.Y.I.; Zafar, M.S. Surface modification techniques of dental implants. In *Dental Implants*; Elsevier: Amsterdam, The Netherlands, 2020; pp. 49–68.
6. Albrektsson, T.; Buser, D.; Sennerby, L. Crestal bone loss and oral implants. *Clin. Implant Dent. Relat. Res.* **2012**, *14*, 783–791. [[CrossRef](#)] [[PubMed](#)]
7. Shemtov-Yona, K.; Rittel, D. Fatigue of dental implants: Facts and fallacies. *Dent. J.* **2016**, *4*, 16. [[CrossRef](#)] [[PubMed](#)]
8. Nguyen-Hieu, T.; Borghetti, A.; Aboudharam, G. Peri-implantitis: From diagnosis to therapeutics. *J. Investig. Clin. Dent.* **2012**, *3*, 79–94. [[CrossRef](#)] [[PubMed](#)]
9. Jaquiéry, C.; Ilgenstein, B.; Jungo, M.; Rüeger, K.; Chenaux, S.; Papadimitropoulos, A.; Jäger, K. Clinical and radiological outcome of titanium implants in clinical practice: A 5 year, prospective, multicenter case series. *Dent. J.* **2014**, *2*, 106–117. [[CrossRef](#)]
10. Buser, D.; Sennerby, L.; De Bruyn, H. Modern implant dentistry based on osseointegration: 50 years of progress, current trends and open questions. *Periodontology 2000* **2017**, *73*, 7–21. [[CrossRef](#)]
11. Alghamdi, H.; Cuijpers, V.; Wolke, J.; Van den Beucken, J.; Jansen, J. Calcium-phosphate-coated oral implants promote osseointegration in osteoporosis. *J. Dent. Res.* **2013**, *92*, 982–988. [[CrossRef](#)]
12. Stadlinger, B.; Korn, P.; Tödtmann, N.; Eckelt, U.; Range, U.; Bürki, A.; Ferguson, S.; Kramer, I.; Kautz, A.; Schnabelrauch, M. Osseointegration of biochemically modified implants in an osteoporosis rodent model. *Eur. Cells Mater.* **2013**, *25*, 326–340; discussion 339. [[CrossRef](#)]
13. Tsujino, T.; Takahashi, A.; Watanabe, T.; Isobe, K.; Kitamura, Y.; Okuda, K.; Nakata, K.; Kawase, T. Platelet adhesion on commercially pure titanium plates in vitro II. Immunofluorescence visualization of PDGF-B, TGFβ1, and PPARγ released from activated adherent platelets. *Dent. J.* **2019**, *7*, 109. [[CrossRef](#)] [[PubMed](#)]
14. Sollazzo, V.; Pezzetti, F.; Scarano, A.; Piattelli, A.; Bignozzi, C.A.; Massari, L.; Brunelli, G.; Carinci, F. Zirconium oxide coating improves implant osseointegration in vivo. *Dent. Mater.* **2008**, *24*, 357–361. [[CrossRef](#)] [[PubMed](#)]
15. Abdullatif, F.A.; Al-Askar, M. Does Ultraviolet Radiation Exhibit Antimicrobial Effect against Oral Pathogens Attached on Various Dental Implant Surfaces? A Systematic Review. *Dent. J.* **2022**, *10*, 93. [[CrossRef](#)] [[PubMed](#)]
16. Chmielewski, M.; Piloni, A. Current Molecular, Cellular and Genetic Aspects of Peri-Implantitis Disease: A Narrative Review. *Dent. J.* **2023**, *11*, 134. [[CrossRef](#)] [[PubMed](#)]
17. Fakheran, O.; Fischer, K.R.; Schmidlin, P.R. Enamel Matrix Derivatives as an Adjunct to Alveolar Ridge Preservation—A Systematic Review. *Dent. J.* **2023**, *11*, 100. [[CrossRef](#)] [[PubMed](#)]
18. Rahmitasari, F.; Ishida, Y.; Kurahashi, K.; Matsuda, T.; Watanabe, M.; Ichikawa, T. PEEK with reinforced materials and modifications for dental implant applications. *Dent. J.* **2017**, *5*, 35. [[CrossRef](#)] [[PubMed](#)]
19. Tallarico, M.; Martinolli, M.; Kim, Y.-J.; Cocchi, F.; Meloni, S.M.; Alushi, A.; Xhanari, E. Accuracy of computer-assisted template-based implant placement using two different surgical templates designed with or without metallic sleeves: A randomized controlled trial. *Dent. J.* **2019**, *7*, 41. [[CrossRef](#)]
20. Kligman, S.; Ren, Z.; Chung, C.-H.; Perillo, M.A.; Chang, Y.-C.; Koo, H.; Zheng, Z.; Li, C. The impact of dental implant surface modifications on osseointegration and biofilm formation. *J. Clin. Med.* **2021**, *10*, 1641. [[CrossRef](#)]
21. Dong, H.; Liu, H.; Zhou, N.; Li, Q.; Yang, G.; Chen, L.; Mou, Y. Surface modified techniques and emerging functional coating of dental implants. *Coatings* **2020**, *10*, 1012. [[CrossRef](#)]
22. Stanford, C.M. Surface modification of biomedical and dental implants and the processes of inflammation, wound healing and bone formation. *Int. J. Mol. Sci.* **2010**, *11*, 354–369. [[CrossRef](#)] [[PubMed](#)]
23. Hanawa, T. Biofunctionalization of titanium for dental implant. *Jpn. Dent. Sci. Rev.* **2010**, *46*, 93–101. [[CrossRef](#)]
24. Accioni, F.; Vázquez, J.; Merinero, M.; Begines, B.; Alcludia, A. Latest trends in surface modification for dental implantology: Innovative developments and analytical applications. *Pharmaceutics* **2022**, *14*, 455. [[CrossRef](#)]
25. Rampado, R.; Caliceti, P.; Agostini, M. Latest advances in biomimetic cell membrane-coated and membrane-derived nanovectors for biomedical applications. *Nanomaterials* **2022**, *12*, 1543. [[CrossRef](#)] [[PubMed](#)]
26. Harkness, J.M. An idea man (the life of Otto Herbert Schmitt). *IEEE Eng. Med. Biol. Mag.* **2004**, *23*, 20–41. [[CrossRef](#)]
27. Zafar, M.S.; Amin, F.; Fareed, M.A.; Ghabbani, H.; Riaz, S.; Khurshid, Z.; Kumar, N. Biomimetic aspects of restorative dentistry biomaterials. *Biomimetics* **2020**, *5*, 34. [[CrossRef](#)] [[PubMed](#)]
28. Kottoor, J. Biomimetic endodontics: Barriers and strategies. *Health Sci.* **2013**, *2*, 7–12.
29. Shin, H.; Jo, S.; Mikos, A.G. Biomimetic materials for tissue engineering. *Biomaterials* **2003**, *24*, 4353–4364. [[CrossRef](#)]
30. Jakšić, Z.; Jakšić, O. Biomimetic nanomembranes: An overview. *Biomimetics* **2020**, *5*, 24. [[CrossRef](#)]
31. Gareev, K.G.; Grouzdev, D.S.; Koziaeva, V.V.; Sitkov, N.O.; Gao, H.; Zimina, T.M.; Shevtsov, M. Biomimetic nanomaterials: Diversity, technology, and biomedical applications. *Nanomaterials* **2022**, *12*, 2485. [[CrossRef](#)]
32. Mačković, M.; Hoppe, A.; Detsch, R.; Mohn, D.; Stark, W.J.; Spiecker, E.; Boccaccini, A. Bioactive glass (type 45S5) nanoparticles: In vitro reactivity on nanoscale and biocompatibility. *J. Nanoparticle Res.* **2012**, *14*, 1–22. [[CrossRef](#)]
33. Li, S.; Yu, W.; Zhang, W.; Zhang, G.; Yu, L.; Lu, E. Evaluation of highly carbonated hydroxyapatite bioceramic implant coatings with hierarchical micro-/nanorod topography optimized for osseointegration. *Int. J. Nanomed.* **2018**, *13*, 3643. [[CrossRef](#)] [[PubMed](#)]

34. Yu, X.; Wei, M. Cellular performance comparison of biomimetic calcium phosphate coating and alkaline-treated titanium surface. *BioMed Res. Int.* **2013**, *2013*, 832790. [[CrossRef](#)] [[PubMed](#)]
35. Wu, Y.; Tang, H.; Liu, L.; He, Q.; Zhao, L.; Huang, Z.; Yang, J.; Cao, C.; Chen, J.; Wang, A. Biomimetic titanium implant coated with extracellular matrix enhances and accelerates osteogenesis. *Nanomedicine* **2020**, *15*, 1779–1793. [[CrossRef](#)] [[PubMed](#)]
36. Sebdani, M.M.; Fathi, M. Novel hydroxyapatite–forsterite–bioglass nanocomposite coatings with improved mechanical properties. *J. Alloys Compd.* **2011**, *509*, 2273–2276. [[CrossRef](#)]
37. Erol-Taygun, M.; Zheng, K.; Boccaccini, A.R. Nanoscale bioactive glasses in medical applications. *Int. J. Appl. Glass Sci.* **2013**, *4*, 136–148. [[CrossRef](#)]
38. Cicciù, M.; Fiorillo, L.; Herford, A.S.; Crimi, S.; Bianchi, A.; D’Amico, C.; Laino, L.; Cervino, G. Bioactive titanium surfaces: Interactions of eukaryotic and prokaryotic cells of nano devices applied to dental practice. *Biomedicines* **2019**, *7*, 12. [[CrossRef](#)] [[PubMed](#)]
39. Alghamdi, H.S. Methods to improve osseointegration of dental implants in low quality (type-IV) bone: An overview. *J. Funct. Biomater.* **2018**, *9*, 7. [[CrossRef](#)] [[PubMed](#)]
40. Wu, B.; Tang, Y.; Wang, K.; Zhou, X.; Xiang, L. Nanostructured titanium implant surface facilitating osseointegration from protein adsorption to osteogenesis: The example of TiO₂ NTAs. *Int. J. Nanomed.* **2022**, *17*, 1865–1879. [[CrossRef](#)]
41. Dorcioman, G.; Grumezescu, V.; Stan, G.E.; Chifiriu, M.C.; Gradisteanu, G.P.; Miculescu, F.; Matei, E.; Popescu-Pelin, G.; Zgura, I.; Craciun, V. Hydroxyapatite Thin Films of Marine Origin as Sustainable Candidates for Dental Implants. *Pharmaceutics* **2023**, *15*, 1294. [[CrossRef](#)]
42. López-Valverde, N.; Flores-Fraile, J.; Ramírez, J.M.; Macedo de Sousa, B.; Herrero-Hernández, S.; López-Valverde, A. Bioactive surfaces vs. conventional surfaces in titanium dental implants: A comparative systematic review. *J. Clin. Med.* **2020**, *9*, 2047. [[CrossRef](#)]
43. Taymour, N.; Fahmy, A.E.; Gepreel, M.A.H.; Kandil, S.; El-Fattah, A.A. Improved Mechanical Properties and Bioactivity of Silicate Based Bioceramics Reinforced Poly (ether-ether-ketone) Nanocomposites for Prosthetic Dental Implantology. *Polymers* **2022**, *14*, 1632. [[CrossRef](#)] [[PubMed](#)]
44. Qadir, M.; Li, Y.; Wen, C. Ion-substituted calcium phosphate coatings by physical vapor deposition magnetron sputtering for biomedical applications: A review. *Acta Biomater.* **2019**, *89*, 14–32. [[CrossRef](#)] [[PubMed](#)]
45. Jing, W.; Zhang, M.; Jin, L.; Zhao, J.; Gao, Q.; Ren, M.; Fan, Q. Assessment of osteoinduction using a porous hydroxyapatite coating prepared by micro-arc oxidation on a new titanium alloy. *Int. J. Surg.* **2015**, *24*, 51–56. [[CrossRef](#)] [[PubMed](#)]
46. Choi, A.; Ben-Nissan, B.; Matinlinna, J.; Conway, R. Current perspectives: Calcium phosphate nanocoatings and nanocomposite coatings in dentistry. *J. Dent. Res.* **2013**, *92*, 853–859. [[CrossRef](#)] [[PubMed](#)]
47. Ripamonti, U.; Roden, L.C.; Renton, L.F. Osteoinductive hydroxyapatite-coated titanium implants. *Biomaterials* **2012**, *33*, 3813–3823. [[CrossRef](#)] [[PubMed](#)]
48. Carradò, A.; Perrin-Schmitt, F.; Le, Q.; Giraudel, M.; Fischer, C.; Koenig, G.; Jacomine, L.; Behr, L.; Chalom, A.; Fiette, L. Nanoporous hydroxyapatite/sodium titanate bilayer on titanium implants for improved osseointegration. *Dent. Mater.* **2017**, *33*, 321–332. [[CrossRef](#)] [[PubMed](#)]
49. Łukaszewska-Kuska, M.; Krawczyk, P.; Martyla, A.; Hędzielek, W.; Dorocka-Bobkowska, B. Hydroxyapatite coating on titanium endosseous implants for improved osseointegration: Physical and chemical considerations. *Adv. Clin. Exp. Med. Off. Organ Wroc. Med. Univ.* **2018**, *27*, 1055–1059. [[CrossRef](#)] [[PubMed](#)]
50. Hu, Z.; Wang, X.; Xia, W.; Wang, Z.; Zhang, P.; Xia, L.; Lin, K.; Zhu, M. Nano-structure designing promotion osseointegration of hydroxyapatite coated Ti–6Al–4V alloy implants in diabetic model. *J. Biomed. Nanotechnol.* **2019**, *15*, 1701–1713. [[CrossRef](#)]
51. Fang, C.-H.; Lin, Y.-W.; Lin, F.-H.; Sun, J.-S.; Chao, Y.-H.; Lin, H.-Y.; Chang, Z.-C. Biomimetic synthesis of nanocrystalline hydroxyapatite composites: Therapeutic potential and effects on bone regeneration. *Int. J. Mol. Sci.* **2019**, *20*, 6002. [[CrossRef](#)]
52. Eawsakul, K.; Tancharoen, S.; Nasongkla, N. Combination of dip coating of BMP-2 and spray coating of PLGA on dental implants for osseointegration. *J. Drug Deliv. Sci. Technol.* **2021**, *61*, 102296. [[CrossRef](#)]
53. Yu, Y.; Li, X.; Li, J.; Li, D.; Wang, Q.; Teng, W. Dopamine-assisted co-deposition of hydroxyapatite-functionalised nanoparticles of polydopamine on implant surfaces to promote osteogenesis in environments with high ROS levels. *Mater. Sci. Eng. C* **2021**, *131*, 112473. [[CrossRef](#)] [[PubMed](#)]
54. Su, T.; Zheng, A.; Cao, L.; Peng, L.; Wang, X.; Wang, J.; Xin, X.; Jiang, X. Adhesion-enhancing coating embedded with osteogenesis-promoting PDA/HA nanoparticles for peri-implant soft tissue sealing and osseointegration. *Bio-Des. Manuf.* **2022**, *5*, 233–248. [[CrossRef](#)]
55. Alcudia, A.; Begines, B.; Rodriguez-Lejarraga, P.; Greyer, V.; Godinho, V.C.F.; Pajuelo, E.; Torres, Y. Development of porous silver nanoparticle/polycaprolactone/polyvinyl alcohol coatings for prophylaxis in titanium interconnected samples for dental implants. *Colloid Interface Sci. Commun.* **2022**, *48*, 100621. [[CrossRef](#)]
56. Mokobia, K.E.; Ifijen, I.H.; Ikhuoria, E.U. ZnO-NPs-coated implants with osteogenic properties for enhanced osseointegration. In Proceedings of the TMS 2023 152nd Annual Meeting & Exhibition, San Diego, CA, USA, 19–23 March 2023; pp. 288–300.
57. Terheyden, H.; Lang, N.P.; Bierbaum, S.; Stadlinger, B. Osseointegration–communication of cells. *Clin. Oral Implant. Res.* **2012**, *23*, 1127–1135. [[CrossRef](#)] [[PubMed](#)]

58. Barbu, H.M.; Iancu, S.A.; Rapani, A.; Stacchi, C. Guided bone regeneration with concentrated growth factor enriched bone graft matrix (sticky bone) vs. bone-shell technique in horizontal ridge augmentation: A retrospective study. *J. Clin. Med.* **2021**, *10*, 3953. [[CrossRef](#)]
59. Guang, M.; Huang, B.; Yao, Y.; Zhang, L.; Yang, B.; Gong, P. Effects of vascular endothelial growth factor on osteoblasts around dental implants in vitro and in vivo. *J. Oral Sci.* **2017**, *59*, 215–223. [[CrossRef](#)]
60. Palermo, A.; Ferrante, F.; Stanca, E.; Damiano, F.; Gnoni, A.; Batani, T.; Carluccio, M.A.; Demitri, C.; Siculella, L. Release of VEGF from dental implant surface (IML[®] Implant) coated with Concentrated Growth Factors (CGF) and the Liquid Phase of CGF (LPCGF): In vitro results and future expectations. *Appl. Sci.* **2019**, *9*, 2114. [[CrossRef](#)]
61. Izquierdo-Barba, I.; Santos-Ruiz, L.; Becerra, J.; Feito, M.; Fernández-Villa, D.; Serrano, M.; Díaz-Güemes, I.; Fernández-Tomé, B.; Enciso, S.; Sánchez-Margallo, F. Synergistic effect of Si-hydroxyapatite coating and VEGF adsorption on Ti6Al4V-ELI scaffolds for bone regeneration in an osteoporotic bone environment. *Acta Biomater.* **2019**, *83*, 456–466. [[CrossRef](#)]
62. Sheikh, Z.; Javaid, M.A.; Hamdan, N.; Hashmi, R. Bone regeneration using bone morphogenetic proteins and various biomaterial carriers. *Materials* **2015**, *8*, 1778–1816. [[CrossRef](#)]
63. Katagiri, T.; Watabe, T. Bone morphogenetic proteins. *Cold Spring Harb. Perspect. Biol.* **2016**, *8*, a021899. [[CrossRef](#)] [[PubMed](#)]
64. Carreira, A.; Lojudice, F.H.; Halcsik, E.; Navarro, R.; Sogayar, M.C.; Granjeiro, J.M. Bone morphogenetic proteins: Facts, challenges, and future perspectives. *J. Dent. Res.* **2014**, *93*, 335–345. [[CrossRef](#)] [[PubMed](#)]
65. Ramazanoglu, M.; Lutz, R.; Ergun, C.; von Wilmsow, C.; Nkenke, E.; Schlegel, K.A. The effect of combined delivery of recombinant human bone morphogenetic protein-2 and recombinant human vascular endothelial growth factor 165 from biomimetic calcium-phosphate-coated implants on osseointegration. *Clin. Oral Implant. Res.* **2011**, *22*, 1433–1439. [[CrossRef](#)] [[PubMed](#)]
66. Kim, J.-E.; Kang, S.-S.; Choi, K.-H.; Shim, J.-S.; Jeong, C.-M.; Shin, S.-W.; Huh, J.-B. The effect of anodized implants coated with combined rhBMP-2 and recombinant human vascular endothelial growth factors on vertical bone regeneration in the marginal portion of the peri-implant. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol.* **2013**, *115*, e24–e31. [[CrossRef](#)] [[PubMed](#)]
67. Schierano, G.; Canuto, R.A.; Mauthe von Degerfeld, M.; Navone, R.; Peirone, B.; Preti, G.; Muzio, G. Role of rhBMP-7, fibronectin, and type I collagen in dental implant osseointegration process: An initial pilot study on minipig animals. *Materials* **2021**, *14*, 2185. [[CrossRef](#)] [[PubMed](#)]
68. Al-Jarsha, M.; Moulisová, V.; Leal-Egaña, A.; Connell, A.; Naudi, K.B.; Ayoub, A.F.; Dalby, M.J.; Salmerón-Sánchez, M. Engineered coatings for titanium implants to present ultralow doses of BMP-7. *ACS Biomater. Sci. Eng.* **2018**, *4*, 1812–1819. [[PubMed](#)]
69. Lee, S.Y.; Koak, J.Y.; Heo, S.J.; Kim, S.K.; Lee, S.J.; Nam, S.Y. Osseointegration of anodized titanium implants coated with poly (lactide-co-glycolide)/basic fibroblast growth factor by electrospray. *Int. J. Oral Maxillofac. Implant.* **2010**, *25*, 315–320.
70. Schliephake, H.; Rublack, J.; Aeckerle, N.; Förster, A.; Schwenzer, B.; Reichert, J.; Scharnweber, D. In vivo effect of immobilisation of bone morphogenetic protein 2 on titanium implants through nano-anchored oligonucleotides. *Eur. Cells Mater.* **2015**, *30*, 28–40. [[CrossRef](#)]
71. Yang, D.H.; Moon, S.W.; Lee, D.-W. Surface modification of titanium with BMP-2/GDF-5 by a heparin linker and its efficacy as a dental implant. *Int. J. Mol. Sci.* **2017**, *18*, 229. [[CrossRef](#)]
72. Keceli, H.G.; Akman, A.C.; Bayram, C.; Nohutcu, R.M. Tissue engineering applications and nanobiomaterials in periodontology and implant dentistry. In *Nanobiomaterials in Dentistry*; Elsevier: Amsterdam, The Netherlands, 2016; pp. 337–387.
73. Maekawa, S.; Cho, Y.D.; Kauffmann, F.; Yao, Y.; Sugai, J.V.; Zhong, X.; Schmiedeler, C.; Kinra, N.; Moy, A.; Larsson, L. BMP Gene-Immobilization to Dental Implants Enhances Bone Regeneration. *Adv. Mater. Interfaces* **2022**, *9*, 2200531. [[CrossRef](#)]
74. Adanir, N.; Khurshid, Z.; Ratnayake, J. The Regenerative Potential of Decellularized Dental Pulp Extracellular Matrix: A Systematic Review. *Materials* **2022**, *15*, 6386. [[CrossRef](#)] [[PubMed](#)]
75. Nakamura, N.; Ito, A.; Kimura, T.; Kishida, A. Extracellular matrix induces periodontal ligament reconstruction in vivo. *Int. J. Mol. Sci.* **2019**, *20*, 3277. [[CrossRef](#)] [[PubMed](#)]
76. Scotchford, C.A.; Ball, M.; Winkelmann, M.; Vörös, J.; Csucs, C.; Brunette, D.; Danuser, G.; Textor, M. Chemically patterned, metal-oxide-based surfaces produced by photolithographic techniques for studying protein-and cell-interactions. II: Protein adsorption and early cell interactions. *Biomaterials* **2003**, *24*, 1147–1158. [[CrossRef](#)] [[PubMed](#)]
77. Marconi, G.D.; Fonticoli, L.; Della Rocca, Y.; Oliva, S.; Rajan, T.S.; Trubiani, O.; Murmura, G.; Diomedede, F.; Pizzicannella, J. Enhanced Extracellular Matrix Deposition on Titanium Implant Surfaces: Cellular and Molecular Evidences. *Biomedicines* **2021**, *9*, 1710. [[CrossRef](#)] [[PubMed](#)]
78. Petrie, T.A.; Raynor, J.E.; Dumbauld, D.W.; Lee, T.T.; Jagtap, S.; Templeman, K.L.; Collard, D.M.; García, A.J. Multivalent integrin-specific ligands enhance tissue healing and biomaterial integration. *Sci. Transl. Med.* **2010**, *2*, 45ra60. [[CrossRef](#)] [[PubMed](#)]
79. Morra, M.; Cassinelli, C.; Cascardo, G.; Bollati, D.; Rodriguez y Baena, R. Multifunctional implant surfaces: Surface characterization and bone response to acid-etched Ti implants surface-modified by fibrillar collagen I. *J. Biomed. Mater. Res. Part A* **2010**, *94*, 271–279. [[CrossRef](#)] [[PubMed](#)]
80. Alghamdi, H.S.; van Oirschot, B.A.; Bosco, R.; van den Beucken, J.J.; Aldosari, A.A.F.; Anil, S.; Jansen, J.A. Biological response to titanium implants coated with nanocrystals calcium phosphate or type 1-collagen in a dog implantation model. *Surf. Modif. Endosseous Implant Mater.* **2015**, *2015*, 129.
81. Lee, S.-W.; Hahn, B.-D.; Kang, T.Y.; Lee, M.-J.; Choi, J.-Y.; Kim, M.-K.; Kim, S.-G. Hydroxyapatite and collagen combination-coated dental implants display better bone formation in the peri-implant area than the same combination plus bone morphogenetic

- protein-2-coated implants, hydroxyapatite only coated implants, and uncoated implants. *J. Oral Maxillofac. Surg.* **2014**, *72*, 53–60. [[CrossRef](#)]
82. Korn, P.; Schulz, M.; Hintze, V.; Range, U.; Mai, R.; Eckelt, U.; Schnabelrauch, M.; Möller, S.; Becher, J.; Scharnweber, D. Chondroitin sulfate and sulfated hyaluronan-containing collagen coatings of titanium implants influence peri-implant bone formation in a minipig model. *J. Biomed. Mater. Res. Part A* **2014**, *102*, 2334–2344. [[CrossRef](#)]
83. de Barros, R.R.; Novaes Jr, A.B.; Korn, P.; Queiroz, A.; de Almeida, A.L.; Hintze, V.; Scharnweber, D.; Bierbaum, S.; Stadlinger, B. Bone formation in a local defect around dental implants coated with extracellular matrix components. *Clin. Implant Dent. Relat. Res.* **2015**, *17*, 742–757. [[CrossRef](#)]
84. Raphel, J.; Karlsson, J.; Galli, S.; Wennerberg, A.; Lindsay, C.; Haugh, M.G.; Pajarinen, J.; Goodman, S.B.; Jimbo, R.; Andersson, M. Engineered protein coatings to improve the osseointegration of dental and orthopaedic implants. *Biomaterials* **2016**, *83*, 269–282. [[CrossRef](#)] [[PubMed](#)]
85. Yin, D.; Komasa, S.; Yoshimine, S.; Sekino, T.; Okazaki, J. Effect of mussel adhesive protein coating on osteogenesis in vitro and osteointegration in vivo to alkali-treated titanium with nanonetwork structures. *Int. J. Nanomed.* **2019**, *14*, 3831–3843. [[CrossRef](#)] [[PubMed](#)]
86. Syam, S.; Wu, C.-J.; Lan, W.-C.; Ou, K.-L.; Huang, B.-H.; Lin, Y.-Y.; Saito, T.; Tsai, H.-Y.; Chuo, Y.-C.; Yen, M.-L. The potential of a surface-modified titanium implant with tetrapeptide for osseointegration enhancement. *Appl. Sci.* **2021**, *11*, 2616. [[CrossRef](#)]
87. Rappe, K.S.; Ortiz-Hernandez, M.; Punset, M.; Molmeneu, M.; Barba, A.; Mas-Moruno, C.; Guillem-Marti, J.; Caparrós, C.; Rupérez, E.; Calero, J. On-growth and in-growth osseointegration enhancement in PM porous Ti-scaffolds by two different bioactivation strategies: Alkali thermochemical treatment and RGD peptide coating. *Int. J. Mol. Sci.* **2022**, *23*, 1750. [[CrossRef](#)] [[PubMed](#)]
88. Esteves, G.M.; Esteves, J.; Resende, M.; Mendes, L.; Azevedo, A.S. Antimicrobial and antibiofilm coating of dental implants—Past and new perspectives. *Antibiotics* **2022**, *11*, 235. [[CrossRef](#)] [[PubMed](#)]
89. Franci, G.; Falanga, A.; Galdiero, S.; Palomba, L.; Rai, M.; Morelli, G.; Galdiero, M. Silver nanoparticles as potential antibacterial agents. *Molecules* **2015**, *20*, 8856–8874. [[CrossRef](#)] [[PubMed](#)]
90. Murugaiyan, J.; Kumar, P.A.; Rao, G.S.; Iskandar, K.; Hawser, S.; Hays, J.P.; Mohsen, Y.; Adukkadukkam, S.; Awuah, W.A.; Jose, R.A.M. Progress in alternative strategies to combat antimicrobial resistance: Focus on antibiotics. *Antibiotics* **2022**, *11*, 200. [[CrossRef](#)] [[PubMed](#)]
91. Mandracci, P.; Mussano, F.; Rivolo, P.; Carossa, S. Surface treatments and functional coatings for biocompatibility improvement and bacterial adhesion reduction in dental implantology. *Coatings* **2016**, *6*, 7. [[CrossRef](#)]
92. Chouirfa, H.; Bouloussa, H.; Migonney, V.; Falentin-Daudré, C. Review of titanium surface modification techniques and coatings for antibacterial applications. *Acta Biomater.* **2019**, *83*, 37–54. [[CrossRef](#)]
93. Wychowański, P.; Starzyńska, A.; Adamska, P.; Ślupecka-Ziemilska, M.; Sobocki, B.K.; Chmielewska, A.; Wysocki, B.; Alterio, D.; Marvaso, G.; Jereczek-Fossa, B.A. Methods of topical administration of drugs and biological active substances for dental implants—A narrative review. *Antibiotics* **2021**, *10*, 919. [[CrossRef](#)]
94. Lopez-Valverde, N.; Macedo-de-Sousa, B.; Lopez-Valverde, A.; Ramirez, J.M. Effectiveness of antibacterial surfaces in osseointegration of titanium dental implants: A systematic review. *Antibiotics* **2021**, *10*, 360. [[CrossRef](#)]
95. Hickok, N.; Shapiro, I.; Chen, A. The impact of incorporating antimicrobials into implant surfaces. *J. Dent. Res.* **2018**, *97*, 14–22. [[CrossRef](#)]
96. Patil, C.; Agrawal, A.; Abullais, S.S.; Arora, S.; Khateeb, S.U.; Elagib, M.F.A. Effectiveness of Different Chemotherapeutic Agents for Decontamination of Infected Dental Implant Surface: A Systematic Review. *Antibiotics* **2022**, *11*, 593. [[CrossRef](#)] [[PubMed](#)]
97. Bormann, N.; Schwabe, P.; Smith, M.; Wildemann, B. Analysis of parameters influencing the release of antibiotics mixed with bone grafting material using a reliable mixing procedure. *Bone* **2014**, *59*, 162–172. [[CrossRef](#)] [[PubMed](#)]
98. Antoci Jr, V.; Adams, C.S.; Hickok, N.J.; Shapiro, I.M.; Parvizi, J. Antibiotics for local delivery systems cause skeletal cell toxicity in vitro. *Clin. Orthop. Relat. Res.* **2007**, *462*, 200–206. [[CrossRef](#)] [[PubMed](#)]
99. Davidson, H.; Poon, M.; Saunders, R.; Shapiro, I.M.; Hickok, N.J.; Adams, C.S. Tetracycline tethered to titanium inhibits colonization by G ram-negative bacteria. *J. Biomed. Mater. Res. Part B Appl. Biomater.* **2015**, *103*, 1381–1389. [[CrossRef](#)] [[PubMed](#)]
100. Stewart, S.; Barr, S.; Engles, J.; Hickok, N.J.; Shapiro, I.M.; Richardson, D.W.; Parvizi, J.; Schaer, T.P. Vancomycin-modified implant surface inhibits biofilm formation and supports bone-healing in an infected osteotomy model in sheep: A proof-of-concept study. *J. Bone Jt. Surg.* **2012**, *94*, 1406. [[CrossRef](#)] [[PubMed](#)]
101. Suchý, T.; Vištejnová, L.; Šupová, M.; Klein, P.; Bartoš, M.; Kolinko, Y.; Blassová, T.; Tonar, Z.; Pokorný, M.; Sucharda, Z. Vancomycin-loaded collagen/hydroxyapatite layers electrospun on 3D printed titanium implants prevent bone destruction associated with *S. epidermidis* infection and enhance osseointegration. *Biomedicines* **2021**, *9*, 531. [[CrossRef](#)] [[PubMed](#)]
102. McGuinness, W.A.; Malachowa, N.; DeLeo, F.R. Focus: Infectious diseases: Vancomycin resistance in *Staphylococcus aureus*. *Yale J. Biol. Med.* **2017**, *90*, 269.
103. Rebelo, C.G.; Fernandes, J.C.H.; Bernardo, N.; Couto, P.; Fernandes, G.V.O. Bisphosphonates and Their Influence on the Implant Failure: A Systematic Review. *Appl. Sci.* **2023**, *13*, 3496. [[CrossRef](#)]
104. Sreelakshmi, C.; Arunima, P.; Ambili, R.; Reeja Mol, M.; Arun, B. Biomimetic coatings for Dental Implant: An update. *J. Int. Soc. Prev. Community Dent.* **2021**, *13*, 37–46.

105. Parfenova, L.V.; Galimshina, Z.R.; Gil'fanova, G.U.; Alibaeva, E.I.; Danilko, K.V.; Pashkova, T.M.; Kartashova, O.L.; Farrakhov, R.G.; Mukaeva, V.R.; Parfenov, E.V. Hyaluronic acid bisphosphonates as antifouling antimicrobial coatings for PEO-modified titanium implants. *Surf. Interfaces* **2022**, *28*, 101678. [[CrossRef](#)]
106. Sendyk, D.I.; Deboni, M.C.Z.; Pannuti, C.M.; Naclério-Homem, M.d.G.; Wennerberg, A. The influence of statins on osseointegration: A systematic review of animal model studies. *J. Oral Rehabil.* **2016**, *43*, 873–882. [[CrossRef](#)] [[PubMed](#)]
107. Yang, F.; Zhao, S.-f.; Zhang, F.; He, F.-m.; Yang, G.-l. Simvastatin-loaded porous implant surfaces stimulate preosteoblasts differentiation: An in vitro study. *Oral Surg. Oral Med. Oral Pathol. Endodontology* **2011**, *111*, 551–556. [[CrossRef](#)]
108. Sun, T.; Huang, J.; Zhang, W.; Zheng, X.; Wang, H.; Liu, J.; Leng, H.; Yuan, W.; Song, C. Simvastatin-hydroxyapatite coatings prevent biofilm formation and improve bone formation in implant-associated infections. *Bioact. Mater.* **2023**, *21*, 44–56. [[CrossRef](#)] [[PubMed](#)]
109. Yasir, M.; Willcox, M.D.P.; Dutta, D. Action of antimicrobial peptides against bacterial biofilms. *Materials* **2018**, *11*, 2468. [[CrossRef](#)] [[PubMed](#)]
110. Gao, Q.; Feng, T.; Huang, D.; Liu, P.; Lin, P.; Wu, Y.; Ye, Z.; Ji, J.; Li, P.; Huang, W. Antibacterial and hydroxyapatite-forming coating for biomedical implants based on polypeptide-functionalized titania nanospikes. *Biomater. Sci.* **2020**, *8*, 278–289. [[CrossRef](#)] [[PubMed](#)]
111. Costa, F.; Carvalho, I.F.; Montelaro, R.C.; Gomes, P.; Martins, M.C.L. Covalent immobilization of antimicrobial peptides (AMPs) onto biomaterial surfaces. *Acta Biomater.* **2011**, *7*, 1431–1440. [[CrossRef](#)]
112. Ramburrun, P.; Pringle, N.A.; Dube, A.; Adam, R.Z.; D'Souza, S.; Aucamp, M. Recent advances in the development of antimicrobial and antifouling biocompatible materials for dental applications. *Materials* **2021**, *14*, 3167. [[CrossRef](#)]
113. Balhara, V.; Schmidt, R.; Gorr, S.-U.; DeWolf, C. Membrane selectivity and biophysical studies of the antimicrobial peptide GL13K. *Biochim. Biophys. Acta Biomembr.* **2013**, *1828*, 2193–2203. [[CrossRef](#)]
114. Holmberg, K.V.; Abdolhosseini, M.; Li, Y.; Chen, X.; Gorr, S.-U.; Aparicio, C. Bio-inspired stable antimicrobial peptide coatings for dental applications. *Acta Biomater.* **2013**, *9*, 8224–8231. [[CrossRef](#)]
115. Garaicoa, J.L.; Bates, A.M.; Avila-Ortiz, G.; Brogden, K.A. Antimicrobial prosthetic surfaces in the oral cavity—A perspective on creative approaches. *Microorganisms* **2020**, *8*, 1247. [[CrossRef](#)] [[PubMed](#)]
116. Warnke, P.H.; Voss, E.; Russo, P.A.; Stephens, S.; Kleine, M.; Terheyden, H.; Liu, Q. Antimicrobial peptide coating of dental implants: Biocompatibility assessment of recombinant human beta defensin-2 for human cells. *Int. J. Oral Maxillofac. Implant.* **2013**, *28*, 982–988. [[CrossRef](#)] [[PubMed](#)]
117. Taher, B.B.; Rasheed, T.A. The Impact of Adding Chitosan Nanoparticles on Biofilm Formation, Cytotoxicity, and Certain Physical and Mechanical Aspects of Directly Printed Orthodontic Clear Aligners. *Nanomaterials* **2023**, *13*, 2649. [[CrossRef](#)] [[PubMed](#)]
118. Husain, S.; Al-Samadani, K.H.; Najeib, S.; Zafar, M.S.; Khurshid, Z.; Zohaib, S.; Qasim, S.B. Chitosan biomaterials for current and potential dental applications. *Materials* **2017**, *10*, 602. [[CrossRef](#)] [[PubMed](#)]
119. Xu, A.; Zhou, L.; Deng, Y.; Chen, X.; Xiong, X.; Deng, F.; Wei, S. A carboxymethyl chitosan and peptide-decorated polyetheretherketone ternary biocomposite with enhanced antibacterial activity and osseointegration as orthopedic/dental implants. *J. Mater. Chem. B* **2016**, *4*, 1878–1890. [[CrossRef](#)] [[PubMed](#)]
120. Buxadera-Palomero, J.; Godoy-Gallardo, M.; Molmeneu, M.; Punset, M.; Gil, F.J. Antibacterial properties of triethoxysilylpropyl succinic anhydride silane (TESPSA) on titanium dental implants. *Polymers* **2020**, *12*, 773. [[CrossRef](#)] [[PubMed](#)]
121. Campos, D.M.; Toury, B.; D'almeida, M.; Attik, G.N.; Ferrand, A.; Renoud, P.; Grosgeat, B. Acidic pH resistance of grafted chitosan on dental implant. *Odontology* **2015**, *103*, 210–217. [[CrossRef](#)]
122. Palla-Rubio, B.; Araújo-Gomes, N.; Fernández-Gutiérrez, M.; Rojo, L.; Suay, J.; Gurruchaga, M.; Goñi, I. Synthesis and characterization of silica-chitosan hybrid materials as antibacterial coatings for titanium implants. *Carbohydr. Polym.* **2019**, *203*, 331–341. [[CrossRef](#)]
123. Valverde, A.; Pérez-Álvarez, L.; Ruiz-Rubio, L.; Olivenza, M.A.P.; Blanco, M.B.G.; Díaz-Fuentes, M.; Vilas-Vilela, J.L. Antibacterial hyaluronic acid/chitosan multilayers onto smooth and micropatterned titanium surfaces. *Carbohydr. Polym.* **2019**, *207*, 824–833. [[CrossRef](#)]
124. Divakar, D.D.; Jastaniyah, N.T.; Altamimi, H.G.; Alnakhli, Y.O.; Alkheraif, A.A.; Haleem, S. Enhanced antimicrobial activity of naturally derived bioactive molecule chitosan conjugated silver nanoparticle against dental implant pathogens. *Int. J. Biol. Macromol.* **2018**, *108*, 790–797. [[CrossRef](#)]
125. Li, W.; Yang, Y.; Zhang, H.; Xu, Z.; Zhao, L.; Wang, J.; Qiu, Y.; Liu, B. Improvements on biological and antimicrobial properties of titanium modified by AgNPs-loaded chitosan-heparin polyelectrolyte multilayers. *J. Mater. Sci. Mater. Med.* **2019**, *30*, 52. [[CrossRef](#)] [[PubMed](#)]
126. Norowski, P.A.; Courtney, H.S.; Babu, J.; Haggard, W.O.; Bumgardner, J.D. Chitosan coatings deliver antimicrobials from titanium implants: A preliminary study. *Implant Dent.* **2011**, *20*, 56–67. [[CrossRef](#)] [[PubMed](#)]
127. Wang, Y.-C.; Lin, S.-H.; Chien, C.-S.; Kung, J.-C.; Shih, C.-J. In vitro bioactivity and antibacterial effects of a silver-containing mesoporous bioactive glass film on the surface of titanium implants. *Int. J. Mol. Sci.* **2022**, *23*, 9291. [[CrossRef](#)]
128. Shimabukuro, M. Antibacterial property and biocompatibility of silver, copper, and zinc in titanium dioxide layers incorporated by one-step micro-arc oxidation: A review. *Antibiotics* **2020**, *9*, 716. [[CrossRef](#)] [[PubMed](#)]
129. Kang, B.; Lan, D.; Liu, L.; Dang, R.; Yao, C.; Liu, P.; Ma, F.; Qi, S.; Chen, X. Antibacterial Activity and Bioactivity of Zn-Doped TiO₂ Coating for Implants. *Coatings* **2022**, *12*, 1264. [[CrossRef](#)]

130. Lampé, I.; Beke, D.; Biri, S.; Csarnovics, I.; Csik, A.; Dombrádi, Z.; Hajdu, P.; Hegedűs, V.; Rácz, R.; Varga, I. Investigation of silver nanoparticles on titanium surface created by ion implantation technology. *Int. J. Nanomed.* **2019**, *14*, 4709–4721. [[CrossRef](#)]
131. Choi, S.-H.; Jang, Y.-S.; Jang, J.-H.; Bae, T.-S.; Lee, S.-J.; Lee, M.-H. Enhanced antibacterial activity of titanium by surface modification with polydopamine and silver for dental implant application. *J. Appl. Biomater. Funct. Mater.* **2019**, *17*, 2280800019847067. [[CrossRef](#)]
132. Shen, X.; Hu, Y.; Xu, G.; Chen, W.; Xu, K.; Ran, Q.; Ma, P.; Zhang, Y.; Li, J.; Cai, K. Regulation of the biological functions of osteoblasts and bone formation by Zn-incorporated coating on microrough titanium. *ACS Appl. Mater. Interfaces* **2014**, *6*, 16426–16440. [[CrossRef](#)]
133. Luo, Q.; Cao, H.; Wang, L.; Ma, X.; Liu, X. ZnO@ ZnS nanorod-array coated titanium: Good to fibroblasts but bad to bacteria. *J. Colloid Interface Sci.* **2020**, *579*, 50–60. [[CrossRef](#)]
134. Kulkarni Aranya, A.; Pushalkar, S.; Zhao, M.; LeGeros, R.Z.; Zhang, Y.; Saxena, D. Antibacterial and bioactive coatings on titanium implant surfaces. *J. Biomed. Mater. Res. Part A* **2017**, *105*, 2218–2227. [[CrossRef](#)] [[PubMed](#)]
135. Kranz, S.; Guellmar, A.; Voelpel, A.; Lesser, T.; Tonndorf-Martini, S.; Schmidt, J.; Schrader, C.; Faucon, M.; Finger, U.; Pfister, W. Bactericidal and biocompatible properties of plasma chemical oxidized titanium (TiOB[®]) with antimicrobial surface functionalization. *Materials* **2019**, *12*, 866. [[CrossRef](#)]
136. Mahamuni-Badiger, P.P.; Patil, P.M.; Badiger, M.V.; Patel, P.R.; Thorat-Gadgil, B.S.; Pandit, A.; Bohara, R.A. Biofilm formation to inhibition: Role of zinc oxide-based nanoparticles. *Mater. Sci. Eng. C* **2020**, *108*, 110319. [[CrossRef](#)] [[PubMed](#)]
137. Wang, W.B.; Clapper, J.C. Antibacterial Activity of Electrospun Polyacrylonitrile Copper Nanoparticle Nanofibers on Antibiotic Resistant Pathogens and Methicillin Resistant Staphylococcus aureus (MRSA). *Nanomaterials* **2022**, *12*, 2139. [[CrossRef](#)] [[PubMed](#)]
138. Qi, S.; Wu, J.; Xu, Y.; Zhang, Y.; Wang, R.; Li, K.; Xu, Y. Chemical stability and antimicrobial activity of plasma-sprayed cerium oxide-incorporated calcium silicate coating in dental implants. *Implant Dent.* **2019**, *28*, 564–570. [[CrossRef](#)]
139. Zhang, X.-M.; Li, Y.; Gu, Y.-X.; Zhang, C.-N.; Lai, H.-C.; Shi, J.-Y. Ta-coated titanium surface with superior bacteriostasis and osseointegration. *Int. J. Nanomed.* **2019**, *14*, 8693–8706. [[CrossRef](#)] [[PubMed](#)]
140. Xiang, Y.; Li, J.; Liu, X.; Cui, Z.; Yang, X.; Yeung, K.; Pan, H.; Wu, S. Construction of poly (lactic-co-glycolic acid)/ZnO nanorods/Ag nanoparticles hybrid coating on Ti implants for enhanced antibacterial activity and biocompatibility. *Mater. Sci. Eng. C* **2017**, *79*, 629–637. [[CrossRef](#)] [[PubMed](#)]
141. Wu, Z.; Luo, J.; Zhang, J.; Huang, H.; Xie, Z.; Xie, X. Silver-releasing micro-/nanoporous coating on additively manufactured macroporous Ti-Ta-Nb-Zr scaffolds with high osseointegration and antibacterial properties. *Coatings* **2021**, *11*, 716. [[CrossRef](#)]
142. Kuo, Y.-J.; Chen, C.-H.; Dash, P.; Lin, Y.-C.; Hsu, C.-W.; Shih, S.-J.; Chung, R.-J. Angiogenesis, osseointegration, and antibacterial applications of polyelectrolyte multilayer coatings incorporated with silver/strontium containing mesoporous bioactive glass on 316L stainless steel. *Front. Bioeng. Biotechnol.* **2022**, *10*, 818137. [[CrossRef](#)]
143. Jamali, R.; Bordbar-Khiabani, A.; Yarmand, B.; Mozafari, M.; Kolahi, A. Effects of co-incorporated ternary elements on biocorrosion stability, antibacterial efficacy, and cytotoxicity of plasma electrolytic oxidized titanium for implant dentistry. *Mater. Chem. Phys.* **2022**, *276*, 125436. [[CrossRef](#)]
144. Liu, L.; Ma, F.; Liu, P.; Qi, S.; Li, W.; Zhang, K.; Chen, X. Preparation and antibacterial properties of ZnSr-doped micro-arc oxidation coatings on titanium. *Surf. Coat. Technol.* **2023**, *462*, 129469. [[CrossRef](#)]

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