IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 25, Issue 7 Ser. 3 (July. 2026), PP 26-35
www.iosrjournals.org

Antimicrobial And Osteoinductive Nanocoatings In Titanium Dental Implants: A Narrative Review Of Advances From 2010 To 2026

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Abstract:
Background: *Osseointegration failure and peri-implant infection remain the two principal causes of long-term dental implant complications. Conventional titanium surfaces, although mechanically reliable, are biologically inert and do not intrinsically resist bacterial colonization, which predisposes to peri-implant mucositis and peri-implantitis. Since the early 2010s, nanotechnology has progressively been applied to titanium implant surfaces in an effort to overcome this limitation.*
Objective: *To trace the evolution of antimicrobial and osteoinductive nanoscale surface modification of titanium dental implants from its foundational studies (2010-2016) through intermediate multifunctional strategies (2016-2023) to the current state of the art (2024-2026).*
Methods: *A narrative review of PubMed-indexed studies published between 2010 and 2026, covering titanium dioxide nanotube arrays, early silver and metal-oxide nanoparticle coatings, chitosan and graphene-based nanocomposites, nanotube-mediated drug and growth-factor delivery, systematic-review evidence on soft-tissue integration, and the current generation of polydopamine, zwitterionic, photothermal, bioinspired, stimuli-responsive, and osteoinductive nanocomposite coatings, including hydroxyapatite-organic hybrids and fullerene C60.*
Results: *Thirty studies spanning 2012-2026 were synthesized. The field progressed from single-mechanism nanoparticle coatings with unresolved cytotoxicity concerns toward multifunctional, often stimuli-responsive nanocoatings that reduce bacterial colonization by one to two orders of magnitude while preserving or enhancing osteoblastic differentiation, including in compromised host environments such as diabetes.* ***Conclusion:*** *Nanocoatings that address infection control and bone integration simultaneously consistently outperform single-mechanism modifications developed in the early 2010s, although most data still derive from short-term animal models and clinical translation remains limited.*

Key Word: *dental implants; nanotechnology; antimicrobial coating; osseointegration; peri-implantitis; titanium surface modification; nanotube; silver nanoparticle.*

Date of Submission: 10-07-2026 Date of Acceptance: 20-07-2026

I. Introduction

Titanium and its alloys remain the gold-standard material for endosseous dental implants due to their mechanical strength, corrosion resistance, and capacity for osseointegration, a concept first described by Brånemark in the 1960s and clinically consolidated over the following decades. Nonetheless, the bioinertness of conventional machined, sandblasted, or acid-etched titanium surfaces provides no intrinsic antibacterial protection, and implant surfaces readily support biofilm formation once exposed to the oral microbiome [2]. Peri-implant mucositis and peri-implantitis, the inflammatory conditions arising from this colonization, are now recognized as leading causes of late implant failure, alongside insufficient or delayed osseointegration [3].

Beginning around 2010, the field of implant surface science shifted decisively from micro-scale roughness modification—such as the sandblasted, large-grit, acid-etched (SLA) surface—toward nanoscale engineering, following early evidence that nanotopography and nanoparticle functionalization could influence protein adsorption, osteoblast differentiation, and bacterial adhesion independently of micro-roughness [1]. This narrative review traces that evolution across three broad periods: (i) foundational nanotube and nanoparticle studies (2010-2016), (ii) intermediate multifunctional and drug-delivery strategies (2016-2023), and (iii) the current generation of stimuli-responsive and bioinspired nanocoatings (2024-2026), synthesizing 30 PubMed-indexed studies to provide periodontists, prosthodontists, and implant surgeons with a comprehensive, historically grounded overview of this field.

The clinical stakes of this evolution are considerable. Peri-implant disease prevalence estimates place peri-implant mucositis in approximately one in every two implants and peri-implantitis in nearly one in five implants over a ten-year period, figures that have remained largely unchanged despite improvements in surgical protocol and prosthetic design, suggesting that the implant surface itself—rather than surgical technique alone—has been an under-addressed variable until the nanotechnology era [3]. At the same time, the global dental implant market has grown steadily since 2010, creating commercial as well as clinical pressure to develop implant surfaces that reduce revision rates and extend implant longevity beyond the 10-15 year window typically reported in longitudinal cohort studies. It is against this backdrop that the sixteen-year research trajectory synthesized in this review should be read: not as a series of isolated laboratory curiosities, but as a cumulative and increasingly convergent response to a well-defined and persistent clinical problem.

II. Historical Foundations: Nanotube Arrays And Early Nanotopography (2010-2018)

Before nanoscale functionalization became feasible, implant surface science was dominated by micro-scale roughening techniques such as sandblasting, acid-etching, and plasma-spraying, which increased bone-to-implant contact primarily by enlarging surface area and mechanical interlock rather than by engaging cellular signaling pathways at the sub-micron scale. The transition to nanoscale engineering required new fabrication tools—principally anodization, hydrothermal synthesis, and sol-gel deposition—that could reproducibly generate features below 100 nm on a titanium substrate. The studies synthesized in this section represent the first generation of research to systematically test whether such nanoscale features could deliver biological benefits beyond what micro-roughness alone provided.

A. Titanium dioxide nanotube arrays: fabrication and osteogenic response

Anodized titanium dioxide (TiO2) nanotube arrays were among the earliest nanostructures systematically investigated for dental and orthopedic implants. Beltrán-Partida et al. synthesized amorphous TiO2 nanotubes on Ti6Al4V alloy by anodization and demonstrated that ultraviolet sterilization combined with super-oxidized water disinfection markedly decreased Staphylococcus aureus viability while improving—rather than disrupting—osteoblast adhesion, morphology, and filopodial development, establishing that nanotube surfaces could be safely sterilized without loss of their osteogenic advantage [14]. Li et al. subsequently fabricated TiO2 nanorod arrays on titanium substrates using hydrothermal and sintering methods and showed that human periodontal ligament stem cells cultured on these nanorough surfaces exhibited more stretched morphology, higher proliferation, and significantly upregulated alkaline phosphatase, Runx2, and osteopontin expression compared with polished titanium controls, directly linking nanotopography to periodontal stem-cell osteogenic commitment [13].

Building on this foundation, Lim et al. coated TiO2 nanotubes with hydroxyapatite via a sol-gel process and reported that the hybrid nanotube-hydroxyapatite surface enhanced hydrophilicity and increased bone-to-implant contact from 32.5% on control titanium to 43.8% in a rat tibia model after four weeks, an early demonstration that nanotube arrays could serve as a substrate for further bioactive functionalization rather than as a stand-alone antibacterial strategy [12].

B. Nanotubes as growth-factor and drug-delivery reservoirs

A second major line of foundational research exploited the high surface area and tubular geometry of anodized TiO2 nanotubes as reservoirs for local drug and growth-factor delivery. Sun et al. loaded TiO2 nanotube arrays with recombinant human bone morphogenetic protein-2 (rhBMP-2) and applied a poly(lactic-co-glycolic acid) (PLGA) membrane of optimized thickness (250 nm) to achieve controlled release over four weeks, which improved osteoblast adhesion, proliferation, and alkaline phosphatase activity relative to uncoated nanotube or titanium surfaces [11]. Tao et al. extended this concept by constructing a pH-responsive multilayer of alginate dialdehyde-gentamicin and chitosan over BMP2-loaded titania nanotubes, such that the acidic microenvironment characteristic of early bacterial infection triggered accelerated gentamicin and BMP2 release; this system achieved strong antibacterial activity against Escherichia coli and Staphylococcus aureus at both 6 and 72 hours while simultaneously promoting osteoblast differentiation, representing one of the earliest stimuli-responsive antimicrobial-osteogenic nanocoatings reported in the literature and a direct conceptual precursor to the pH-sensitive smart coatings developed a decade later [15].

III. Early Antimicrobial Nanoparticle Coatings (2012-2021)

As nanotube-based drug delivery matured, a parallel and ultimately larger body of research pursued a simpler strategy: embedding intrinsically antibacterial nanoparticles directly into or onto the implant surface. This approach required no drug reservoir and no controlled-release engineering, but introduced its own central tension, one that would define an entire decade of research—the same ionic and reactive-oxygen-species mechanisms that killed bacteria could, above a certain local concentration or release rate, also impair osteoblast viability and, in the case of silver, raise concerns about systemic nanoparticle translocation. The studies below trace how successive research groups progressively solved this tension through chemical chelation, controlled anchoring, and ultimately hybrid multi-component coatings.

A. Silver nanoparticles: mechanisms, efficacy, and cytotoxicity concerns

Silver nanoparticles (AgNPs) were the first nanoscale antimicrobial agent extensively investigated for titanium implant surfaces, owing to silver's broad-spectrum bactericidal activity through ionic release and reactive-oxygen-species generation. Zhang et al. incorporated AgNPs into a dopamine-modified alginate/chitosan polyelectrolyte multilayer on titanium alloy, exploiting the self-polymerization of dopamine to reduce silver cations in situ without added reductants; the resulting AgNP-polyelectrolyte coating inhibited both Escherichia coli and Staphylococcus aureus while enhancing fibroblast proliferation, though a slight reduction in L929 cell viability signaled the cytotoxicity trade-off that would recur throughout the following decade of silver-nanoparticle research [4]. Li et al. subsequently layered hydroxyapatite, AgNPs, and chitosan on titanium via a polydopamine-assisted layer-by-layer process, finding that a three-layer chitosan topcoat could control the Fickian release of silver ions, reducing cytotoxicity while sustaining antibacterial ratios above 60% against Escherichia coli and above 50% against Staphylococcus aureus, alongside high alkaline phosphatase activity at days 3 and 14 [5].

Tian et al. doped hydroxyapatite coatings with silver nanoparticles arranged in oriented block arrays, demonstrating strong bactericidal activity against both gram-negative and gram-positive organisms together with improved human bone marrow stromal cell attachment, proliferation, and osteoinductivity relative to uncoated Ti-6Al-4V, and proposed the block-array morphology as a general strategy for incorporating silver into hydroxyapatite coatings while limiting long-term cytotoxicity [6]. Lampé et al. took a physical rather than chemical approach, using Electron Cyclotron Resonance Ion Source implantation followed by physical vapor deposition to anchor 58 nm silver nanoparticles onto Grade 2 titanium; this ion-implanted layer achieved a statistically significant 64.6% antibacterial effect against Staphylococcus aureus while remaining non-cytotoxic in Alamar Blue assays, with the authors explicitly noting that safe anchorage of the nanoparticles—rather than the antibacterial mechanism itself—was the critical design parameter, given contemporaneous evidence that free silver nanoparticles could induce pathology in mammalian cells if released into systemic circulation [7]. Xie et al. addressed this anchorage problem directly by combining polydopamine, hydroxyapatite, AgNPs, and chitosan into a single hybrid coating with dual organic chelation, which reduced silver-ion release enough to achieve 89.5-92.0% anti-biofilm efficiency against Staphylococcus aureus, Staphylococcus epidermidis, and Escherichia coli while stimulating MC3T3-E1 osteogenic differentiation and confirming in vivo biosafety through histology and blood testing over a longitudinal follow-up—representing the maturation of silver-nanoparticle coating design from simple bactericidal layers toward controlled-release, cytotoxicity-managed multifunctional systems [9].

Clinical translation of silver nanocoatings began with Odatsu et al., who applied a microwave-assisted nanosilver coating to healing abutments and evaluated it in a split-mouth randomized clinical trial; the coating showed no cytotoxic effect on human gingival fibroblasts in vitro and significantly suppressed dental-plaque adhesion on the coated abutments in vivo, providing one of the first direct clinical-trial demonstrations that a silver nanocoating could reduce peri-implant plaque accumulation in human patients rather than only in laboratory or animal models [8].

C. Metal-oxide nanoparticles beyond silver

In parallel with silver-focused research, Vargas-Reus et al. conducted a foundational comparative study of six metal and metal-oxide nanoparticles—silver, cuprous oxide, cupric oxide, zinc oxide, titanium dioxide, and tungsten oxide, alone and as silver composites—against the anaerobic pathogens Prevotella intermedia, Porphyromonas gingivalis, Fusobacterium nucleatum, and Aggregatibacter actinomycetemcomitans implicated in peri-implantitis. Minimum inhibitory and bactericidal concentrations ranked silver as most potent, followed by silver-copper-oxide composites, with zinc oxide achieving complete bacterial killing within two to four hours in time-kill assays, establishing metal-oxide nanoparticles as a viable alternative or adjunct to silver for implant-surface antimicrobial functionalization as early as 2012 [1]. Nearly a decade later, Spirescu et al. reviewed the broader landscape of inorganic nanoparticles—gold, silver, copper, zinc oxide, titanium oxide, magnesium oxide, and iron oxide—for antimicrobial therapies, concluding that incorporation of these nanoparticles into composite films was increasingly being extended from wound dressings and catheter coatings toward implant surface functionalization more broadly, reflecting the field's consolidation around a shared set of inorganic nanobiocides by the early 2020s [10].

D. Comparative synthesis of early antimicrobial nanoparticle strategies

Read together, the nine years of silver- and metal-oxide-nanoparticle research summarized above reveal a clear design evolution rather than a series of unrelated experiments. The earliest studies (2012-2013) established feasibility and antimicrobial ranking among candidate nanomaterials but paid comparatively little attention to controlling nanoparticle release, and cytotoxicity was reported as an incidental finding rather than a design target. By 2016, research groups had begun deliberately engineering release control—first through polydopamine-assisted layer-by-layer chelation, then through oriented hydroxyapatite block arrays—treating the antimicrobial-osteogenic trade-off as the primary variable to be optimized rather than a side effect to be tolerated. By 2019, three independent groups converged on broadly similar solutions within the same year: ion-implantation for physical anchoring, dual organic chelation (polydopamine plus chitosan) for chemical containment, and pH-responsive multilayer triggering for temporal confinement of antimicrobial activity to periods of actual infection. This convergence across independent laboratories is itself informative, since it suggests that by the end of the 2010s the field had reached a shared understanding of which design parameters mattered most, even though a single optimal solution had not yet emerged. The clinical translation of only one of these strategies—the microwave-assisted nanosilver healing-abutment coating evaluated by Odatsu et al. in a human split-mouth trial [8]—by 2020 indicates that engineering consensus in the laboratory does not automatically confer regulatory or clinical priority, a gap that is examined further in Section XI.

IV. Graphene-Based Nanocoatings (2019-2022)

Graphene oxide (GO) emerged as a distinct nanomaterial platform for implant coatings in the late 2010s, valued for its high surface area, tunable functionalization, and intrinsic antibacterial activity attributed to membrane-disrupting sharp-edge interactions. Li et al. constructed ultrathin layer-by-layer films alternating graphene oxide with lysozyme, achieving strong sterilization of both Staphylococcus aureus and Escherichia coli alongside enhanced osteogenic differentiation, and characterized the nanoscale film growth using ellipsometry and atomic force microscopy [18]. The same group subsequently incorporated tannic acid into a graphene oxide-lysozyme multilayer, reporting a synergistic antibacterial and osteogenic effect on human dental pulp stem cells and explicitly framing the coating as relevant to the growing global dental implant market [17]. Guo et al. applied graphene oxide to sulfonated, porous poly-ether-ether-ketone (PEEK)—an increasingly used alternative implant substrate—and demonstrated strong antibacterial activity against common dental pathogens together with good MC3T3-E1 adhesion, proliferation, and osteogenic differentiation, indicating that graphene oxide functionalization is transferable across both metallic and polymeric implant substrates [16].

V. Clinical And Systematic-Review Evidence On Nanostructured Surfaces (2022)

As nanocoating strategies proliferated through the 2010s, the need for systematic synthesis of their in vivo performance became apparent. Van den Borre et al. conducted a systematic review of surface coatings on percutaneous titanium implants and their effect on keratinized soft-tissue integration, screening 4971 publications and including 12 that met eligibility criteria. The review found that nanostructured ceramic coatings reduced the inflammatory response in favor of hemidesmosome formation, that porous titanium coatings with pores below 250 μm failed to support dermal fibroblast attachment whereas pores above 700 μm allowed extensive vascularized soft-tissue infiltration, and that biomolecule coatings—such as fibroblast growth factor-2 entrapped in biomimetic apatite—could produce a close-to-natural soft-tissue seal; however, the authors emphasized that most included studies had short implantation periods and small sample sizes, and concluded that robust long-term in vivo data remained lacking even a decade after the first nanostructured coatings had been described [19]. This systematic review is an important historical marker: it demonstrates that as of 2022, the translational gap identified in early 2010s nanotube and nanoparticle studies had narrowed but not closed.

VI. Nanoscale Surface Topography And Cellular Response: The Current Generation (2026)

Beyond chemical coatings, the physical nanotopography of an implant surface continues to be independently investigated for its influence on soft- and hard-tissue integration. Building on the nanorod and nanotube topography work of the early 2010s, Angulo Salas et al. developed a dynamic flow-chamber model applying controlled shear stress to compare polished versus nanodiamond-coated titanium surfaces populated with primary human gingival fibroblasts and keratinocytes. Nanorough surfaces supported significantly more stable cell attachment under physiologically relevant shear stress (0.05-0.49 Pa), with the greatest differences observed at 0.36 Pa over 1-2 hours of dynamic culture, and also improved simulated wound-healing repopulation dynamics at the transmucosal abutment interface [24]. This finding directly extends the soft-tissue integration questions raised by the 2022 systematic review, now addressed with a more physiologically realistic dynamic-shear model.

Complementary work in laser-based nanotexturing has shown that femtosecond-laser-induced micro/nanostructures on alumina (Al2O3) surfaces can produce durable superhydrophilicity (contact angle <5°) persisting for more than 40 days, particularly in deeper (>17 μm) periodic groove geometries without post-process thermal annealing [26]. Because surface wettability directly affects protein adsorption and subsequent cell adhesion, such techniques—transferable in principle to titanium and zirconia—represent a purely physical, coating-free strategy for enhancing early osseointegration, distinct from but complementary to the chemical nanocoating strategies reviewed above.

VII. Antimicrobial Nanocoatings: The Current Generation (2024-2026)

A. Metal and metal-oxide nanoparticles

The metal and metal-oxide nanoparticle strategies pioneered by Vargas-Reus and others in the early 2010s remain an active research area. A 2024 review by Hosseini Hooshiar et al. summarized the shape-dependent bio-physio-chemical functionalization of silver, gold, zinc oxide, titanium oxide, copper, and iron-oxide nanoparticles and concluded that metal nanoparticles can be incorporated as implant-coating constituents or as drug-delivery carriers, with documented efficacy against multidrug-resistant oral pathogens implicated in peri-implant mucositis and peri-implantitis [3]. A broader 2024 literature review by Marasli et al. similarly highlighted titania nanotubes, graphene, and chitosan-based hybrid coatings as viable platforms for simultaneous antibacterial protection, immunomodulation, and corrosion resistance, effectively consolidating fifteen years of nanomaterial research into a single translational framework [2].

B. Polydopamine and zwitterionic nanocoatings

Polydopamine (PDA), the same mussel-inspired catechol polymer used as an anchoring layer in the hybrid silver coatings of the mid-2010s, has been refined into a standalone antimicrobial platform. Nambiar et al. compared titanium discs coated with PDA alone versus PDA combined with poly(MBAAm-co-SBMA) zwitterionic nanoparticles. The zwitterion-modified coating produced a one-log reduction in Streptococcus mutans colony counts (1.25×10^4 versus 1.4×10^5 CFU/mL) relative to PDA alone, with comparable cytocompatibility (52.5% versus 49.1% cell viability) and favorable, uniform globular nanoparticle morphology confirmed by field-emission scanning electron microscopy [23].

C. Photothermally activated nanostructures

Li et al. anchored gold nanostars (GNS) onto titanium via silanization to create a dual-functional, on-demand antibacterial surface. Under near-infrared (NIR) irradiation, the Ti-GNS surface exhibited temperature-dependent photothermal bactericidal activity against Staphylococcus aureus and Escherichia coli, while simultaneously enhancing osteogenic differentiation of bone-marrow stem cells and improving osseointegration in a rat femoral model, without compromising biocompatibility [21]. This on-demand activation strategy avoids the continuous ion release and associated cytotoxicity that limited many of the silver-nanoparticle systems developed a decade earlier, instead allowing clinician-triggered antibacterial episodes.

D. Bioinspired multifunctional coatings

Wang et al. synthesized a mussel-protein-conjugated poly(amidoamine) dendrimer (DA-PAMAM-NH2) coating combining intrinsic antibacterial and osteogenic bifunctionality. Unlike the unconjugated dendrimer, whose bifunctional activity diminished after four weeks of immersion in simulated body fluid, the mussel-protein-conjugated coating maintained both antimicrobial and osteogenic performance after the same immersion period, and this durability was confirmed in vivo in titanium-alloy implants [20]. Long-term coating stability of this kind directly answers the durability concerns first raised regarding silver-ion release control in the 2016-2019 hybrid coatings, now solved through covalent bioinspired anchoring rather than chitosan diffusion barriers.

VIII. Stimuli-Responsive (Smart) Coatings

The pH-responsive concept pioneered by Tao et al. in 2019—triggering antibiotic and growth-factor release from titania nanotubes in response to the acidic microenvironment of early infection [15]—has since been extended into fully engineered smart-coating systems. Pereira et al. developed a layer-by-layer coating combining tetracycline complexed with anionic β-cyclodextrin beneath a pH-sensitive poly(methacrylic acid) film. The coating controlled drug release, reduced surface roughness relative to untreated titanium, showed broad-spectrum antimicrobial activity against human-saliva-derived biofilms, and, in a rat subcutaneous model, reduced inflammation while increasing collagen deposition and CD206 expression—markers of an anti-inflammatory, tissue-repair phenotype—with no cytotoxicity observed up to six days [22]. Stimuli-responsive systems of this kind represent the maturation of a strategy first demonstrated at proof-of-concept level in 2019, now validated with saliva-derived clinical biofilms rather than laboratory monocultures.

IX. Osteoinductive Nanomaterials And Special Clinical Scenarios

A. Hydroxyapatite-organic hybrid nanocoatings

Srinivasan et al. produced hydroxyapatite (HAP) derived from caprine femur bone, sequentially modified with an imidazole derivative, sodium alginate, and polyacrylonitrile, then deposited onto plasma-treated titanium via electrophoretic deposition. The optimized hybrid coating (m-HAP-3) exhibited an extracellular-matrix-like surface morphology, improved mechanical integrity relative to unmodified HAP, enhanced corrosion resistance, and dose-dependent antibacterial activity, addressing the classic brittleness limitation that had constrained standalone hydroxyapatite coatings since the sol-gel HAP-nanotube work of the late 2010s [27].

B. Fullerene C60

Ghanipour et al. conducted a combinatorial review of fullerene C60 applications in dentistry. Across the literature identified, fullerene incorporation improved the mechanical properties of dental materials, reduced implant surface roughness and friction, prevented bacterial and fungal infection, increased biocompatibility, and promoted osteoblast differentiation and biomineralization through alkaline-phosphatase-like catalytic activity—suggesting a role for this carbon nanostructure as a multifunctional additive in implant surface engineering [25].

C. Modulation of the diabetic peri-implant microenvironment

Diabetic patients present a disproportionately elevated risk of peri-implantitis and impaired osseointegration due to hyperglycemia-driven oxidative stress and accumulation of advanced glycation end-products. Pan et al. developed a TiO2/ZnO bio-heterojunction nanoparticle coating on carbon-fiber-reinforced PEEK implants that dynamically modulates reactive oxygen species through activation of the Keap1/Nrf2 pathway, providing antibacterial, osteogenic, and antioxidant synergy. In a diabetic rat femoral defect model, the modified implants demonstrated biosafety, sustained antibacterial activity, and improved osseointegration over six weeks, illustrating how nanocoatings can be tailored to specific systemic risk profiles rather than designed as one-size-fits-all solutions [28].

D. Complementary structural and material innovations

Nanoscale surface engineering is increasingly combined with implant macro- and micro-architecture innovations rather than deployed in isolation. Nanofibrillar peptide-hyaluronic acid scaffolds integrated into 3D-printed porous titanium implants have nearly doubled inner bone volume in a rabbit calvarial critical-size defect model compared with inert controls, and histological analysis confirmed enhanced bone-implant integration, active periosteum, and reduced inflammation even within the porous implant core, a region that nanocoatings alone cannot easily reach [29]. Trabecular tantalum implants replicating cancellous bone architecture have similarly shown robust osseointegration when combined with platelet-rich fibrin-augmented allografts in reconstructed human maxillae, with histomicrographs confirming bone ongrowth and ingrowth at the interconnected porous trabecular region without metal debris or adverse tissue reaction after 52 weeks of healing [30]. Together, these architecture-level strategies suggest that the next generation of implant design is unlikely to rely on nanocoating chemistry alone, but rather on the deliberate combination of macro-porosity, micro-architecture, and nanoscale surface functionalization.

X. Chronological Summary Of Key Nanocoating Strategies (2012-2026)

Table 1 synthesizes the studies reviewed above in chronological order, summarizing the nanomaterial strategy, mechanism, and principal finding of each, to give the reader a single-page overview of how the field progressed from early single-mechanism nanoparticle coatings toward the multifunctional and stimuli-responsive systems of the current decade.

Table 1: Chronological overview of key nanocoating strategies for titanium dental implants (2012-2026)

Year	Author(s)	Nanomaterial / Strategy	Principal finding
2012	Vargas-Reus et al. [1]	Ag, ZnO, CuO, TiO2, WO3 nanoparticles	Ranked antimicrobial potency against peri-implantitis pathogens; Ag most potent
2013	Zhang et al. [4]	AgNP-dopamine-alginate/chitosan multilayer	In-situ silver reduction via dopamine; antibacterial with mild cytotoxicity trade-off
2015	Beltrán-Partida et al. [14]	TiO2 nanotubes + super-oxidized water	Disinfection decreased bacterial viability without disrupting osteoblast behavior
2016	Li et al. [5]; Tian et al. [6]	HA/Ag/chitosan hybrid; AgNP-doped HA arrays	Chitosan/HA chelation controlled silver release, preserving osteogenic activity
2017	Li et al. [13]	TiO2 nanorod arrays	Enhanced periodontal ligament stem cell adhesion and osteogenic marker expression
2018	Sun et al. [11]; Lim et al. [12]	PLGA/TiO2 nanotube-BMP2; HA-coated nanotubes	Sustained growth-factor release; increased bone-to-implant contact to 43.8%
2019	Tao et al. [15]; Xie et al. [9]; Lampé et al. [7]	pH-responsive BMP2/gentamicin nanotubes; hybrid Ag/HA/chitosan; ion-implanted AgNP	First pH-triggered antibacterial-osteogenic system; controlled silver anchoring
2019-2020	Li & Li et al. [17], [18]	Graphene oxide-lysozyme-tannic acid films	Synergistic antibacterial/osteogenic effect via layer-by-layer assembly
2020	Odatsu et al. [8]	Microwave-assisted nano-Ag abutment coating	First split-mouth randomized clinical trial confirming plaque suppression in humans
2021	Guo et al. [16]; Spirescu et al. [10]	Graphene oxide on PEEK; inorganic NP review	Antibacterial coating extended to polymeric (PEEK) implant substrates
2022	Van den Borre et al. [19]	Systematic review, 12 studies	Nanostructured ceramic coatings favor hemidesmosome formation; long-term data still lacking
2024	Marasli et al. [2]; Hosseini Hooshiar et al. [3]; Wang et al. [20]	Review syntheses; mussel-inspired PAMAM dendrimer	Consolidated 15 years of nanomaterial research; durable bifunctional coating
2025	Li et al. [21]; Pereira et al. [22]; Pan et al. [28]; Oroumieh et al. [30]	Gold nanostars; pH-sensitive smart coating; TiO2/ZnO bio-heterojunction; trabecular tantalum	On-demand photothermal activity; saliva-biofilm validated smart release; diabetic microenvironment modulation
2026	Nambiar et al. [23]; Angulo Salas et al. [24]; Ghanipour et al. [25]; Signorile et al. [26]; Srinivasan et al. [27]; Rattner et al. [29]	Polydopamine/zwitterionic NPs; nanodiamond topography; fullerene C60; femtosecond laser texturing; HAP-organic hybrid; 3D-printed peptide scaffold	Current-generation multifunctional and coating-free nanoscale strategies

Several patterns emerge from Table 1 that are not immediately obvious when the studies are read individually. First, the number of distinct nanomaterial classes under active investigation has broadened over time rather than converging on a single dominant strategy: whereas 2012-2016 research concentrated almost entirely on silver and other metal-oxide nanoparticles, by 2024-2026 the field simultaneously supports polydopamine chemistry, carbon-based nanostructures (graphene oxide, fullerene C60), photothermal metal nanostructures, and coating-free nanotopographic strategies, suggesting that no single nanomaterial has proven universally superior and that implant manufacturers are likely to select among these strategies based on substrate compatibility and manufacturing cost rather than a single agreed 'best' nanocoating. Second, the interval between proof-of-concept publication and any form of clinical or systematic-review validation has remained long throughout the period reviewed: the silver-nanoparticle strategies first reported in 2012-2013 did not reach a human randomized trial until 2020 [8], a translational lag of roughly seven to eight years, and none of the current-generation (2024-2026) strategies reviewed in Sections VI-IX have yet been evaluated in human patients. This recurring lag is the central empirical justification for the regulatory and manufacturing discussion in Section XI below.

XI. Manufacturing Scalability And Regulatory Pathways

The sixteen studies reviewed in Sections II-IV rely on markedly different fabrication techniques—anodization, hydrothermal synthesis, sol-gel deposition, physical vapor deposition, ion implantation, electrophoretic deposition, and layer-by-layer polyelectrolyte assembly—each with distinct capital-equipment requirements, batch-to-batch reproducibility profiles, and per-unit processing costs. Anodization and sol-gel deposition, used to fabricate the earliest TiO2 nanotube and hydroxyapatite-nanotube surfaces, are comparatively low-cost and scalable to existing implant manufacturing lines, which likely explains why nanotube-based surfaces were among the first nanoscale modifications to approach commercial availability. In contrast, femtosecond laser microprocessing and layer-by-layer assembly of multi-component coatings such as graphene oxide-lysozyme-tannic acid films or pH-responsive polymer multilayers require more specialized equipment and longer processing times per implant, which may limit their near-term scalability even where laboratory efficacy is superior.

Regulatory considerations compound this manufacturing heterogeneity. Nanoparticle-coated implants intended for the United States market are generally reviewed by the Food and Drug Administration under the 510(k) premarket notification pathway when substantial equivalence to a predicate device can be demonstrated,

but the agency has signaled increasing scrutiny of nanomaterial-specific safety data, particularly for coatings incorporating silver or other metal nanoparticles with documented potential for systemic translocation [7]. In the European Union, nanomaterial-containing medical devices are subject to additional scrutiny under the Medical Device Regulation (EU) 2017/745, which explicitly addresses devices incorporating nanomaterials with a risk classification tied to the potential for internal exposure. These regulatory frameworks, both largely developed or substantially revised after 2017, postdate most of the foundational nanocoating research reviewed in Sections II and III, meaning that many of the coatings validated in vitro and in animal models during the 2012-2019 period have not yet undergone the nanomaterial-specific regulatory evaluation that would be required for clinical marketing today. This regulatory lag—rather than a lack of biological promise—may explain why relatively few of the nanocoating strategies described in this review, aside from the nanosilver healing-abutment system evaluated by Odatsu et al. [8], have reached human clinical trials or commercial availability to date.

XII. Clinical Perspectives And Translational Limitations

Reviewing sixteen years of research, from the earliest anodized nanotube arrays of 2012 through the current generation of stimuli-responsive and bioinspired nanocoatings, reveals a consistent trajectory: single-mechanism nanoparticle coatings, however effective in vitro, have repeatedly encountered the same two obstacles—uncontrolled ion or drug release leading to cytotoxicity, and insufficient long-term coating stability. Each successive generation of research has targeted one or both of these obstacles: chitosan and dopamine chelation to control silver release (2013-2019), layer-by-layer assembly to tune drug pharmacokinetics (2018-2019), stimuli-responsive triggering to confine antimicrobial activity to periods of actual infection (2019, then matured 2025), and covalent bioinspired anchoring to extend coating durability beyond four weeks (2024).

Despite this progress, several translational barriers persist. First, most data—both historical and current—originate from short-term rodent models (typically 4-8 weeks), whereas clinical implant success is assessed over years to decades; the 2022 systematic review by Van den Borre et al. explicitly confirmed that robust long-term in vivo data remained lacking even after a decade of nanocoating research [19]. Second, nanotoxicological safety profiles, particularly for metal nanoparticles with potential for systemic dissemination, are still not standardized across studies, a concern first raised regarding free silver nanoparticles in 2019 [7] and not yet fully resolved. Third, manufacturing scalability and cost differ substantially between techniques such as anodization, femtosecond laser texturing, electrophoretic deposition, and layer-by-layer assembly, which will influence which technologies reach commercial dental implant systems first. Randomized clinical trials with long-term (≥5 year) follow-up—of which the split-mouth trial by Odatsu et al. remains one of very few examples in human patients [8]—alongside harmonized nanosafety testing protocols, represent the most pressing research priorities before these technologies can be recommended for routine clinical use.

XIII. Future Directions

Building on the trajectory synthesized in this review, three research priorities appear most likely to shape the next phase of nanocoating development for titanium dental implants. First, combinatorial designs that pair a stimuli-responsive antimicrobial layer with an osteoinductive nanocomposite—rather than treating infection control and bone integration as sequential design goals—represent a natural extension of the diabetic-microenvironment work by Pan et al. [28] to other systemically compromised populations, such as patients on antiresorptive therapy or with chronic kidney disease, who are increasingly receiving dental implants but remain underrepresented in the nanocoating literature reviewed here. Second, standardized, cross-study nanotoxicological reporting—covering nanoparticle release kinetics, systemic biodistribution, and long-term (>6 month) local tissue response—would allow the translational barriers identified in Section XII to be addressed comparatively rather than coating by coating, and would likely accelerate regulatory review under the frameworks discussed in Section XI. Third, the small number of existing human clinical trials, exemplified by the split-mouth nanosilver abutment trial of Odatsu et al. [8], should be expanded to other nanocoating classes—particularly the polydopamine-zwitterionic and photothermal gold-nanostar systems described in Section VII, which have so far only been validated in vitro and in rodent models despite showing some of the most favorable combined antibacterial-osteogenic profiles reviewed in this article.

A further consideration for future research is the heterogeneity of in vitro testing conditions across the studies reviewed here. Antibacterial efficacy has been assessed variably against Staphylococcus aureus, Escherichia coli, Streptococcus mutans, and anaerobic peri-implantitis-associated species such as Porphyromonas gingivalis and Fusobacterium nucleatum, often under aerobic rather than the anaerobic or microaerophilic conditions that characterize the subgingival and peri-implant niche in vivo. Similarly, osteogenic outcomes have been measured using a mixture of murine pre-osteoblast lines (MC3T3-E1), human bone marrow stromal cells, human periodontal ligament stem cells, and human dental pulp stem cells, each with different baseline differentiation kinetics, making direct cross-study comparison of reported percentage improvements in alkaline phosphatase activity or bone-to-implant contact difficult without a common reference standard. Establishing a

standardized in vitro and preclinical testing panel—spanning a defined anaerobic peri-implant pathogen set and a single reference osteogenic cell line—would substantially improve the comparability of future nanocoating studies and facilitate more direct evidence synthesis than has been possible in the present narrative review.

XIV. Conclusion

Since the first anodized titanium dioxide nanotube arrays were characterized for dental implant application in the early 2010s, nanotechnology has fundamentally reframed the antimicrobial-versus-osteogenic trade-off that historically limited titanium dental implant surface design. The field's sixteen-year trajectory—from early silver-nanoparticle coatings constrained by cytotoxicity, through graphene-based and chitosan-hydroxyapatite hybrid systems that improved biocompatibility, to the current generation of stimuli-responsive smart coatings, photothermally activated nanostructures, bioinspired multifunctional dendrimers, and osteoinductive nanocomposites such as hydroxyapatite-organic hybrids and fullerene C60—demonstrates that infection control and bone integration can be pursued together rather than as competing goals. As these technologies mature from in vitro and short-term animal models toward long-term clinical validation, building on the small number of existing human trials, they hold considerable promise for reducing implant failure rates, particularly among medically compromised patients such as those with diabetes.

References

[1]. Vargas-Reus MA, Memarzadeh K, Huang J, Ren GG, Allaker RP. Antimicrobial Activity Of Nanoparticulate Metal Oxides Against Peri-Implantitis Pathogens. Int J Antimicrob Agents. 2012;40(2):135-139. Doi:10.1016/J.Ijantimicag.2012.04.012

[2]. Marasli C, Katifelis H, Gazouli M, Lagopati N. Nano-Based Approaches In Surface Modifications Of Dental Implants: A Literature Review. Molecules. 2024;29(13):3061. Doi:10.3390/Molecules29133061

[3]. Hosseini Hooshiar M, Mozaffari A, Hamed Ahmed M, Abdul Kareem R, Jaber Zrzo A, Salah Mansoor A, H Athab Z, Parhizgar Z, Amini P. Potential Role Of Metal Nanoparticles In Treatment Of Peri-Implant Mucositis And Peri-Implantitis. Biomed Eng Online. 2024;23(1):101. Doi:10.1186/S12938-024-01294-0

[4]. Zhang X, Li Z, Yuan X, Cui Z, Bao H, Li X, Liu Y, Yang X. Cytotoxicity And Antibacterial Property Of Titanium Alloy Coated With Silver Nanoparticle-Containing Polyelectrolyte Multilayer. Mater Sci Eng C Mater Biol Appl. 2013;33(5):2816-2820. Doi:10.1016/J.Msec.2013.03.010

[5]. Li M, Liu X, Xu Z, Yeung KWK, Wu S. Dopamine Modified Organic-Inorganic Hybrid Coating For Antimicrobial And Osteogenesis. ACS Appl Mater Interfaces. 2016;8(49):33972-33981. Doi:10.1021/Acsami.6b09457

[6]. Tian B, Chen W, Yu D, Lei Y, Ke Q, Guo Y, Zhu Z. Fabrication Of Silver Nanoparticle-Doped Hydroxyapatite Coatings With Oriented Block Arrays For Enhancing Bactericidal Effect And Osteoinductivity. J Mech Behav Biomed Mater. 2016;61:345-359. Doi:10.1016/J.Jmbbm.2016.04.002

[7]. Lampé I, Beke D, Biri S, Csarnovics I, Csik A, Dombrádi Z, Hajdu P, Hegedűs V, Rácz R, Varga I, Hegedűs C. Investigation Of Silver Nanoparticles On Titanium Surface Created By Ion Implantation Technology. Int J Nanomedicine. 2019;14:4709-4721. Doi:10.2147/IJN.S197782

[8]. Odatsu T, Kuroshima S, Sato M, Takase K, Valanezhad A, Naito M, Sawase T. Antibacterial Properties Of Nano-Ag Coating On Healing Abutment: An In Vitro And Clinical Study. Antibiotics (Basel). 2020;9(6):347. Doi:10.3390/Antibiotics9060347

[9]. Xie K, Zhou Z, Guo Y, Wang L, Li G, Zhao S, Liu X, Li J, Jiang W, Wu S, Hao Y. Long-Term Prevention Of Bacterial Infection And Enhanced Osteoinductivity Of A Hybrid Coating With Selective Silver Toxicity. Adv Healthc Mater. 2019;8(5):E1801465. Doi:10.1002/Adhm.201801465

[10]. Spirescu VA, Chircov C, Grumezescu AM, Vasile BȘ, Andronescu E. Inorganic Nanoparticles And Composite Films For Antimicrobial Therapies. Int J Mol Sci. 2021;22(9):4595. Doi:10.3390/Ijms22094595

[11]. Sun S, Zhang Y, Zeng D, Zhang S, Zhang F, Yu W. PLGA Film/Titanium Nanotubes As A Sustained Growth Factor Releasing System For Dental Implants. J Mater Sci Mater Med. 2018;29(9):141. Doi:10.1007/S10856-018-6138-1

[12]. Lim HP, Park SW, Yun KD, Park C, Ji MK, Oh GJ, Lee JT, Lee K. Hydroxyapatite Coating On Tio2 Nanotube By Sol-Gel Method For Implant Applications. J Nanosci Nanotechnol. 2018;18(2):1403-1405. Doi:10.1166/Jnn.2018.14868

[13]. Li Z, Qiu J, Du LQ, Jia L, Liu H, Ge S. Tio2 Nanorod Arrays Modified Ti Substrates Promote The Adhesion, Proliferation And Osteogenic Differentiation Of Human Periodontal Ligament Stem Cells. Mater Sci Eng C Mater Biol Appl. 2017;76:684-691. Doi:10.1016/J.Msec.2017.03.148

[14]. Beltrán-Partida E, Valdez-Salas B, Escamilla A, Curiel M, Valdez-Salas E, Nedev N, Bastidas JM. Disinfection Of Titanium Dioxide Nanotubes Using Super-Oxidized Water Decrease Bacterial Viability Without Disrupting Osteoblast Behavior. Mater Sci Eng C Mater Biol Appl. 2016;60:239-245. Doi:10.1016/J.Msec.2015.11.042

[15]. Tao B, Deng Y, Song L, Ma W, Qian Y, Lin C, Yuan Z, Lu L, Chen M, Yang X, Cai K. BMP2-Loaded Titania Nanotubes Coating With Ph-Responsive Multilayers For Bacterial Infections Inhibition And Osteogenic Activity Improvement. Colloids Surf B Biointerfaces. 2019;177:242-252. Doi:10.1016/J.Colsurfb.2019.02.014

[16]. Guo C, Lu R, Wang X, Chen S. Antibacterial Activity, Bio-Compatibility And Osteogenic Differentiation Of Graphene Oxide Coating On 3D-Network Poly-Ether-Ether-Ketone For Orthopaedic Implants. J Mater Sci Mater Med. 2021;32(11):135. Doi:10.1007/S10856-021-06614-7

[17]. Li H, Gao C, Tang L, Wang C, Chen Q, Zheng Q, Yang S, Sheng S, Zan X. Lysozyme (Lys), Tannic Acid (TA), And Graphene Oxide (GO) Thin Coating For Antibacterial And Enhanced Osteogenesis. ACS Appl Bio Mater. 2020;3(1):673-684. Doi:10.1021/Acsabm.9b01017

[18]. Li M, Li H, Pan Q, Gao C, Wang Y, Yang S, Zan X, Guan Y. Graphene Oxide And Lysozyme Ultrathin Films With Strong Antibacterial And Enhanced Osteogenesis. Langmuir. 2019;35(20):6752-6761. Doi:10.1021/Acs.Langmuir.9b00035

[19]. Van Den Borre CE, Zigterman BGR, Mommaerts MY, Braem A. How Surface Coatings On Titanium Implants Affect Keratinized Tissue: A Systematic Review. J Biomed Mater Res B Appl Biomater. 2022;110(7):1713-1723. Doi:10.1002/Jbm.B.35025

[20]. Wang M, Li J, Geng M, Yang Z, Xi A, Yu Y, Liu B, Tay FR, Gou Y. Mussel-Inspired Bifunctional Coating For Long-Term Stability Of Oral Implants. Acta Biomater. 2024;188:138-156. Doi:10.1016/J.Actbio.2024.09.010

[21]. Li L, Wu J, Liu L, Zhang P, Zhang Y, Zhou Z, Gao X, Sun S. Photothermal Antibacterial Effect Of Gold Nanostars Coating On Titanium Implant And Its Osteogenic Performance. Int J Nanomedicine. 2025;20:5983-5999. Doi:10.2147/IJN.S519183
[22]. Pereira MMA, Piazza RD, Barbugli PA, Tagit O, Van Den Beucken JJJP, Das A, Biffe CA, Barão VAR, Da Cruz SBA, Ervolino E, Faverani LP, Ganzaroli VF, Zandim-Barcelos DL, Feres M, Retamal-Valdes B, Spolidorio DMP, Pavarina AC, Santana AP, Verza BS, Marques RFC, De Molon RS, De Avila ED. Targeted Infection Control And Tissue Integration Via Ph-Sensitive Smart Coatings On Implant Surfaces. ACS Appl Mater Interfaces. 2025;18(1):2584-2603. Doi:10.1021/Acsami.5c19344
[23]. Nambiar S, Nayak DG, Isloor AM, Suman E, Nayak S, Kabekkodu SP, Rao RU. Next-Generation Polydopamine Nanocoatings Advancing The Understanding Of Surface Properties And Antimicrobial Efficacy. Sci Rep. 2026;16(1):3715. Doi:10.1038/S41598-025-33787-W
[24]. Angulo Salas LN, Kaiser F, Harrandt V, Mehta K, Garcia-Zintzun AI, Havlica J, Opitz J, Wolf-Brandstetter C. Characterization Of Cell Adhesion Phenomena At The Dental Abutment/Soft Tissue Interface By Means Of A Dynamic Cell Culture Model. Biomater Adv. 2026;183:214765. Doi:10.1016/J.Bioadv.2026.214765
[25]. Ghanipour R, Zare-Zardini H, Eslami H. Fullerene C60 In Dental Materials: A Comprehensive Review Of Carbon Nanotechnology Applications And Future Prospects. J Mater Sci Mater Med. 2026;37(1):36. Doi:10.1007/S10856-026-07009-2
[26]. Signorile A, Papa L, Pontrandolfi M, Gaudiuso C, Volpe A, Ancona A, Mezzapesa FP. Long-Lasting Hydrophilicity Of Al2O3 Surfaces Via Femtosecond Laser Microprocessing. Micromachines. 2026;17(1):29. Doi:10.3390/Mi17010029
[27]. Srinivasan G, Manickam A, Murugan J, Sivakumar S, Mohan S, Wan Nik WMNB. Biowaste To Bioactive Hydroxyapatite-Organic Hybrid Coatings With ECM-Like Topography And Mechanical Integrity For Multifunctional Titanium Implant Coatings. ACS Omega. 2026;11(14):21753-21769. Doi:10.1021/Acsomega.5c10904
[28]. Pan L, Zheng A, Huang N, Zhang S, Peng L, Zheng F, Cao L, Wang X, Jiang X. Protean Bio-Heterojunction Nanoparticle Coating For Dynamically Modulating Diabetic Microenvironment. Biomaterials. 2025;329:123912. Doi:10.1016/J.Biomaterials.2025.123912
[29]. Rattner N, Perlis V, Golden E, Pokhojaev A, Sarig R, Binderman I, Halperin-Sternfeld M, Dadia S, Adler-Abramovich L. 3D-Printed Titanium Implants With Bioactive Peptide-Polysaccharide Scaffolds For Personalized Bone Reconstruction. Adv Healthc Mater. 2026;15(12):E05131. Doi:10.1002/Adhm.202505131
[30]. Oroumieh SI, Shah H, Nordlund A, Ignacio De Bellis Tulle L, Souza BM, Desai A, Nayak VV, Carlos Carvajal Herrera J, Witek L, Coelho PG. An Evaluation Of Osseointegration Outcomes Around Trabecular Metal Implants In Human Maxillaries Reconstructed With Allograft And Platelet-Rich Fibrin. Biomimetics. 2025;10(11):789. Doi:10.3390/Biomimetics10110789