BULLETIN OF STOMATOLOGY AND MAXILLOFACIAL SURGERY
Volume 21, Issue 10

DOI:10.58240/1829006X-2025.21.10-435

ORIGINAL RESEARCH

NANOSTRUCTURED COATING MATERIALS ON TITANIUM IMPLANTS FOR ENHANCED OSSEOINTEGRATION AND CLINICAL OUTCOMES A SYSTEMATIC REVIEW AND META-ANALYSIS

Vishnuvaradhan Venkatachalam, MDS,[1, 2] Jayalakshmi Somasundaram, MDS, PhD, [3] Deepak E R, MDS, [4] Sakthi Gnanavel S, MDS, [5] Abhinayaa sudhagar, MDS, [6]

[1] PhD scholar, Department of Prosthodontics and Crown & Bridge, Saveetha Dental College and hospitals, Saveetha Institute of Medical and Technical Science (SIMATS), Saveetha University, Chennai -600077, Tamil Nadu, India.

[2] Senior lecturer, Department of Prosthodontics and Crown & Bridge, KSR Institute of Dental Science and Research, Tiruchengode, Tamil Nadu, India. Orcid ID: 0009-0001-9749-2819.

[3]Associate Professor White Lab – Material Research Centre Department of Conservative Dentistry and Endodontics Saveetha Dental College Saveetha Institute of Medical and Technical Sciences (SIMATS) Chennai – 600077, India

[4] Department of Orthodontics and dentofacial orthopaedics, JKKN Dental college, Kumarapalayam, Namakkal, Tamil Nadu, India. Orcid ID:0009-0002-9905-6575. dr.erdeepak@gmail.com

[5] Senior lecturer, Department of Prosthodontics and Crown & Bridge, KSR Institute of Dental Science and Research, Tiruchengode, Tamil Nadu, India. Orcid ID: 0000-0003-3328-2430. velvillainous@gmail.com

[6]Department of Prosthodontics and Crown & Bridge, KSR Institute of Dental Science and Research, Tiruchengode, Tamil Nadu, India. Orcid ID: 0009-0006-7023-172X. abhinayaansuthagar@gmail.com.

Corresponding author: Dr. Jayalakshmi Somasundaram, Associate Professor White Lab – Material Research Centre Department of Conservative Dentistry and Endodontics Saveetha Dental College Saveetha Institute of Medical and Technical Sciences (SIMATS) Chennai – 600077, India ,Orcid ID: 0000-0003-3515-5558. Mobile N: 9600586858 Jaya.sdc@saveetha.com

Received: *Sep.22 2025;* ***Accepted:*** *Oct. 29, 2025;* ***Published:*** *Nov20,2025*

ABSTRACT

Statement of Problem: Titanium implants, while widely used in dental and orthopedic applications, often face challenges related to early-stage osseointegration and implant failure, particularly in compromised patients. Surface modifications using nanostructured coatings have been proposed to improve implant integration and biological performance, yet evidence across studies remains fragmented.

Purpose: To systematically evaluate and quantify the impact of nanostructured coatings on titanium implants in terms of osseointegration, mechanical fixation, and clinical performance through a comprehensive review and meta-analysis.

Materials and Methods: This systematic review and meta-analysis followed PRISMA guidelines. A thorough literature search was conducted across PubMed, Scopus, Web of Science, and other databases to identify eligible in vivo, in vitro, and clinical studies evaluating nanostructured coatings on titanium implants. A total of 51 studies were included. Key outcomes such as bone-to-implant contact (BIC), removal torque values, and histological bone formation were extracted. Risk of bias was assessed using SYRCLE and modified ToxRTool. Meta-analyses were conducted using a random-effects model, and heterogeneity was evaluated using I^2 statistics. Funnel plots and Egger's regression were used to assess publication bias.

Results: Nanostructured coatings significantly improved osseointegration indicators. Meta-analysis revealed substantial improvements in removal torque (Cohen's d = 5.97; 95% CI: 3.72–8.22), bone-to-implant contact (Cohen's d = 4.68; 95% CI: 2.95–6.41), and histomorphometric outcomes. Heterogeneity was moderate to high ($I^2 \approx 60–65\%$). Subgroup analyses highlighted variation in effectiveness based on coating materials (e.g., TiO_2 nanotubes, hydroxyapatite, metal ions). Funnel plots and Egger's test indicated minimal publication bias.

Conclusions: Nanostructured coatings on titanium implants significantly enhance early-stage osseointegration and biomechanical stability, with additional potential for antibacterial properties. While preclinical evidence is robust, further multicentric clinical trials with standardized protocols are required to confirm translational efficacy and long-term outcomes.

***Keywords*:** Nanostructured coating, titanium implants, osseointegration, bone-to-implant contact, removal torque, systematic review, meta-analysis.

INTRODUCTION

Titanium (Ti) and its alloys have been established as the benchmark for dental and orthopedic implants for several decades. Their extensive application is attributed to their superior mechanical strength, corrosion resistance, and biocompatibility.[1] A pivotal factor influencing the long-term efficacy of titanium implants is their capacity to attain stable integration with the surrounding bone, a phenomenon known as osseointegration. [2] Although uncoated titanium surfaces can ultimately facilitate bone apposition, the duration required for complete osseointegration, coupled with the risk of early-stage implant failure, remains a significant concern, particularly in patients who are medically compromised or elderly. [3]

In recent years, there has been a growing scientific interest in enhancing the interface between titanium implants and bone tissue at the nanoscale level. This interest is based on a fundamental yet compelling principle: the micro- and nanoscale architecture of an implant surface can profoundly affect biological responses, such as protein adsorption, cell adhesion, proliferation, and differentiation. [4] With advancements in surface engineering and nanotechnology, it is now feasible to meticulously customize implant surfaces to replicate the natural extracellular matrix, thereby optimizing the conditions conducive to bone regeneration. [5]

Among the various strategies explored, nanostructured coatings have emerged as a promising area of research. These coatings are thoughtfully designed to enhance the physical, chemical, and biological characteristics of titanium surfaces while maintaining their inherent mechanical strength. [6] By altering surface topography at the nanoscale, these coatings aim to enhance osteoconductivity, reduce microbial colonization, and promote early-stage osseointegration. [7]

A wide variety of nanostructured materials have been investigated for their potential in implant coatings. For example, titanium dioxide (TiO_2) nanotubes have garnered significant attention due to their capacity to provide a high surface area and favorable topographical cues that facilitate osteoblast attachment. [8] Similarly, hydroxyapatite (HA), a naturally occurring mineral in bone, has been prominently utilized to enhance bone bonding and mineral deposition on implant surfaces. More recent strategies include the incorporation of metal ions such as silver, copper, zinc, or magnesium to impart both osteogenic and antibacterial properties. [9] These multifunctional coatings are particularly relevant in clinical scenarios where concerns such as infection and delayed healing can present challenges. [10]

The integration of nanotechnology into dental and orthopedic implants represents an important advancement in biomaterials science. Unlike conventional surface treatments that primarily focus on mechanical anchorage, nanostructured modifications are informed by biological principles. [11] They interact in complex ways with proteins, immune cells, and stem cells at the implantation site, potentially accelerating healing processes and improving long-term outcomes. [12]

However, it is important to note that the existing literature in this field appears to be diverse and sometimes inconsistent. Different studies utilize various coating materials, fabrication techniques, animal models, and evaluation metrics. [13] While some investigations have reported significant improvements in parameters such as bone-implant contact (BIC), removal torque strength, and histomorphometric indices, others have identified challenges, including coating delamination, cytotoxicity at elevated ion concentrations, and a lack of standardization in outcome evaluations. Additionally, many studies remain within preclinical settings, which limits our ability to draw broad conclusions applicable to clinical practice. [14]

In light of the current landscape, there exists a compelling necessity to consolidate existing evidence through a comprehensive and methodologically rigorous systematic review. Such an endeavor can serve multiple objectives: it can summarize the various types of nanostructured coatings that have been investigated to date, facilitate comparisons of their efficacy across diverse biological models, and identify critical gaps that necessitate further exploration. Most importantly, this review can support clinicians, researchers, and materials scientists in making informed, evidence-based decisions regarding the development of next-generation implant technologies. [10]

The design of this systematic review adhered strictly to the PRISMA guidelines, thereby ensuring transparency and reproducibility. Both in vivo and in vitro studies were included to provide a thorough perspective on the impact of nanocoatings on osseointegration. Significant emphasis was placed on quantifiable outcomes such as bone-implant contact percentages, removal torque values, histological markers of bone regeneration, and clinical metrics of implant stability.

The heterogeneous nature of the studies incorporated into this review allows for meaningful subgroup analyses. For instance, coatings may be compared based on their fabrication techniques—such as anodization, sol-gel processing, electrophoretic deposition, or hydrothermal synthesis. Additionally, biological outcomes can be stratified according to coating composition—whether organic (e.g., peptide-modified hydroxyapatite), inorganic (e.g., metal oxides), or hybrid. This stratification extends beyond academic interest; it possesses significant implications for the design, approval, and subsequent integration of implants into clinical practice. [11]

The dual functionality of nanostructured coatings in enhancing osteogenic activity and providing antibacterial defense is of significant importance. With the increasing prevalence of implant-related infections and the challenge of antibiotic resistance, the development of coatings that can simultaneously facilitate bone healing and inhibit microbial colonization represents a crucial advancement. Numerous studies referenced in this review have investigated silver or copper-based nanocoatings for their bactericidal properties, thereby highlighting a promising intersection between nanotechnology and infection control. [12]

Furthermore, it is essential to note that the field of nanocoatings is experiencing rapid advancement. Innovations such as controlled drug release systems, ion substitution within hydroxyapatite (HA) matrices, and bioactive small interfering RNA (siRNA)-coated porous scaffolds are expanding the potential of implant surfaces. [13] These cutting-edge approaches pave the way for personalized implants, which can be tailored not only to anatomical compatibility but also to the specific biological requirements of individual patients, including those with osteoporosis, diabetes, or compromised immune responses. [14]

The benefits of nanostructured coatings on titanium implants are evident; the translation of these technologies into clinical practice necessitates a comprehensive synthesis of existing evidence. This systematic review and meta-analysis aim to bridge that gap by evaluating the biological performance of various nanocoatings in enhancing osseointegration and mechanical fixation of titanium implants. Through this endeavor, we aim to provide valuable insights that inform the design of safer, more effective, and longer-lasting implantable devices for both dental and orthopedic applications.

MATERIALS AND METHODS

This systematic review and meta-analysis were conducted in alignment with the PRISMA guidelines. The methodological framework was predefined, structured, and reviewed by all authors to maintain transparency and reproducibility throughout the study process.

A comprehensive search of three major electronic databases—PubMed, Scopus, and Web of Science. Lilacss, Google Scholar, Cochrane, manual, and back references were performed to identify relevant studies published up to April 30, 2025. The search strategy combined MeSH terms and free-text keywords using Boolean operators. The primary keywords included: “titanium implant”, “nanostructured coating”, “osseointegration”, “surface modification”, “TiO_2 nanotubes”, “bone-implant contact”, “hydroxyapatite”, and “nanoparticles.” In addition to database searches, reference lists of included studies and review articles were manually screened to ensure the comprehensiveness of the literature capture.

Studies were selected based on well-defined inclusion and exclusion criteria. Eligible studies included original research articles—both in vivo animal experiments and in vitro cellular studies—that quantitatively evaluated osseointegration-related outcomes of titanium implants modified with nanostructured coatings. Clinical trials assessing early bone healing or implant stability with coated titanium implants were also included. Only peer-reviewed articles published in English were considered. Exclusion criteria encompassed review articles, conference proceedings, studies lacking comparative uncoated titanium controls, and those with insufficient data for quantitative synthesis. Duplicate publications and overlapping datasets were carefully screened and excluded to avoid redundancy.

After removing duplicates, two reviewers independently screened all titles and abstracts based on the eligibility criteria. Full texts of potentially eligible studies were then assessed in detail for inclusion. Discrepancies in study selection were resolved through discussion or by consulting a third reviewer. The entire selection process was documented using the PRISMA flow diagram, detailing the number of articles screened, excluded, and finally included in the review and meta-analysis(fig.1).

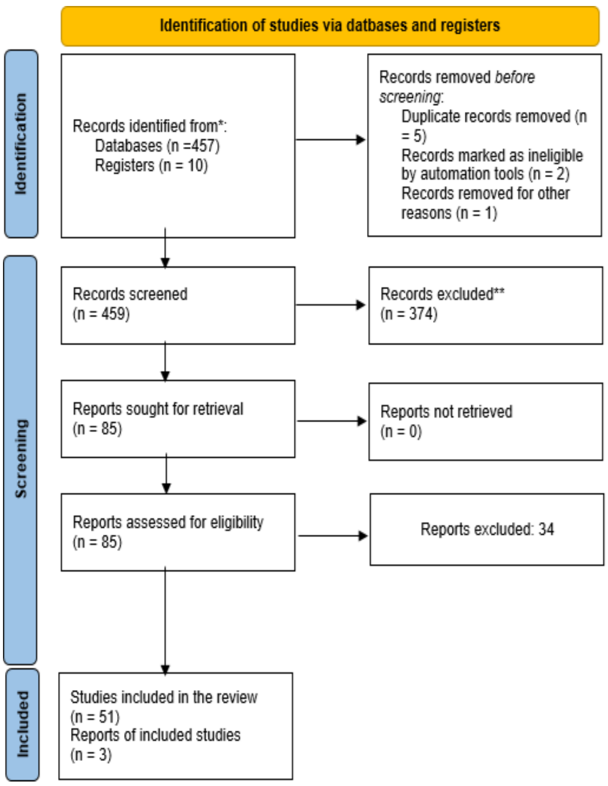

Figure 1. PRISMA Flowchart

To evaluate methodological quality and potential bias, the SYRCLE risk of bias tool was applied to animal studies. This tool assesses domains such as sequence generation, baseline group characteristics, blinding of caregivers and outcome assessors, attrition, and selective reporting. Each domain was rated as low, high, or unclear risk. For in vitro studies, a modified version of the ToxRTool was used to assess reproducibility and study integrity. These risk assessments were summarized in tabular form and graphically visualized in a risk-of-bias summary chart.

Meta-analytical synthesis was conducted using a random-effects model due to the anticipated heterogeneity among studies. Effect sizes were calculated using Cohen's d for continuous variables such as BIC and removal torque. Where studies reported mean and standard deviation, these were used directly. In instances where only standard error or confidence intervals were available, conversions were performed to derive standard deviations. The DerSimonian and Laird method was used to calculate pooled effect sizes and their 95% confidence intervals. All statistical analyses were carried out using Review Manager (RevMan) and the "metafor" package in R.

Heterogeneity was assessed using the I^2 statistic, which quantifies the proportion of total variation due to between-study heterogeneity rather than chance. A value of 0–40% was interpreted as low heterogeneity, 41–60% as moderate, and above 60% as high. The τ^2 (tau-squared) statistic was also reported to reflect the variance of true effect sizes across the included studies.

Subgroup analyses were performed to explore potential sources of heterogeneity based on coating material (e.g., TiO_2 nanotubes, HA, silver, copper), type of study model (in vivo vs. in vitro), and fabrication method (e.g., anodization, plasma spraying, hydrothermal processing).

Sensitivity analyses were conducted by excluding studies with outlier effect sizes or high risk of bias to test the robustness of the results.

To examine the possibility of publication bias, funnel plots were constructed for the major outcomes (removal torque and BIC), provided that a sufficient number of studies ($n \geq 10$) were available. Visual inspection of the funnel plots was used to detect asymmetry. Additionally, Egger's regression test was performed to statistically assess small-study effects.

RESULTS

A total of 467 articles were initially identified. After screening titles and abstracts and a full-text review of 85 studies, 51 studies met the inclusion criteria. Table 1 and Figure 2 show the risk of bias assessment of included studies.

System (ASUDAS), to elicit gender specificity, if present, in these traits and discern any possible racial affinity as an adjunct in population identification. Of these traits, twenty-six were maxillary and thirteen were mandibular. (Table 1).

Table. 1 Risk of bias assessment of included studies

Study	Random sequence generation	Allocation concealment	Blinding of caregivers	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other biases
Yaser AlNatheer et al., 2024	High	Unclear	High	Unclear	Low	High	Unclear
Kun Li et al., 2023	Unclear	Unclear	Unclear	Low	Low	High	Low
Ziming Liao et al., 2023	High	Low	High	Unclear	Unclear	Unclear	High
Xueguan Xie et al., 2023	Unclear	High	Unclear	High	Low	Low	High
Na Xu et al., 2020	High	High	Low	High	Low	Unclear	High
Xijiang Zhao et al., 2020	High	Low	Unclear	High	Unclear	Low	Low

Vishnuvaradhan Venkatachalam, Jayalakshmi Somasundaram,Deepak E R et al. Nanostructured Coating Materials on Titanium Implants for Enhanced Osseointegration and Clinical Outcomes: A Systematic Review and Meta-Analysis Bulletin of Stomatology and Maxillofacial Surgery.2025;21(10)435-451 doi:10.58240/1829006X-2025.21.10-435

Daniel Oltean-Dan et al., 2021	Unclear	Low	Low	Unclear	High	Low	Unclear
Bingfeng Wu et al., 2022	Unclear	Low	Low	Low	Unclear	High	High
Lu Liu et al., 2020	High	High	Unclear	Unclear	High	Unclear	Unclear
Isabela Rocha da Silva et al., 2023	High	Unclear	Unclear	High	High	High	Unclear
Kai Li et al., 2020	High	High	Low	Low	Unclear	High	Low
Minxun Lu et al., 2020	Low	Low	High	Unclear	Unclear	Low	Low
Hang Zhao et al., 2022	Unclear	Unclear	High	Low	Unclear	Low	Low
Osama Alabed Mela et al., 2022	Low	Unclear	Low	High	Low	Unclear	Unclear
Ruiying Li et al., 2023	Low	High	Unclear	Unclear	Low	Unclear	Unclear
Nanjue Cao et al., 2021	Low	High	Low	High	High	Unclear	Unclear
Henry Miller, 2023	High	Unclear	High	Unclear	Low	Low	Unclear
Tianqi Guo et al., 2023	Unclear	Low	Unclear	High	High	Low	Unclear
Ruikang Tang et al., 2022	High	High	Low	Low	Unclear	Unclear	Unclear
Jithin Vishnu & Geetha Manivasagam, 2021	Low	High	High	Unclear	High	Low	High
Palekar Gouri Sachin et al., 2022	Low	Low	Unclear	High	Low	High	Low
Zhu Wen et al., 2023	High	High	Unclear	High	Unclear	High	High
Chuang Hou et al., 2022	Unclear	Low	High	Low	Unclear	Low	Low
Andrew M. Shenoda et al., 2022	Unclear	Low	High	Low	High	High	Unclear
Jingxuan Li et al., 2023	Unclear	Low	High	Unclear	High	Unclear	Unclear
Leizhen Huang et al., 2021	Unclear	Low	High	Unclear	Low	Unclear	Low
Keranda Palenga'an, 2022	Low	High	High	Low	Unclear	Unclear	High
Naotaka Ogura et al., 2022	Unclear	Unclear	Low	Low	Unclear	Low	High
Kai Li et al.,	Low	Unclear	Unclear	Low	High	High	Unclear

2021							
Jiaxin Wu et al., 2022	Unclear	High	Unclear	Low	High	High	High
Giovanna Calabrese et al., 2021	Low	Unclear	Low	Low	High	Low	Unclear
Jheng-Yang Wang et al., 2020	Low	Low	High	High	Low	High	Unclear
Bianyun Cai et al., 2023	High	High	Low	Unclear	Low	Low	Low
André Luiz Reis Rangel et al., 2020	Unclear	High	Low	Unclear	Low	High	Low
Ana Civantos et al., 2023	Unclear	Unclear	Unclear	Unclear	Unclear	Low	High
Meng Zhang et al., 2021	High	High	Low	High	High	Low	Unclear
Kaori Iwanami-Kadowaki et al., 2021	Unclear	Unclear	Low	Low	Unclear	Unclear	Unclear
Samira Esteves Afonso Camargo et al., 2021	High	Unclear	High	Unclear	High	High	Unclear
Min-Kyu Lee et al., 2021	High	Unclear	Low	Low	Unclear	Unclear	High
Nyein Thaik et al., 2020	Low	High	Low	High	Unclear	High	Low
Gemma Di Pompo et al., 2023	Unclear	Unclear	High	Unclear	High	High	Unclear
Minxun Lu et al., 2020	Unclear	Unclear	High	Low	Unclear	High	High
Jian-Bo Cui et al., 2023	High	Unclear	Unclear	High	Unclear	High	Unclear
Nan Wu et al., 2023	High	Unclear	Unclear	Low	High	Low	Unclear
Mingding Wang, Lijun Jiang, 2022	Low	Unclear	Low	High	Unclear	Unclear	Unclear
Oksana Shulyatnikova et al., 2020	Unclear	Low	Unclear	Unclear	Unclear	Low	Unclear
Sumiyati Sumiyati et al., 2022	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Low
Rayane C. S. Silva et al., 2022	High	High	Unclear	Unclear	High	Low	Low
Serena De Santis et al., 2021	High	High	High	Unclear	Unclear	Low	Low

Zhengwei Xu, Xiaohong Jiang, 2020	Low	Unclear	Unclear	Unclear	Low	Low	High
Tara Wigmosta et al., 2021	High	Low	Unclear	High	Unclear	Low	High

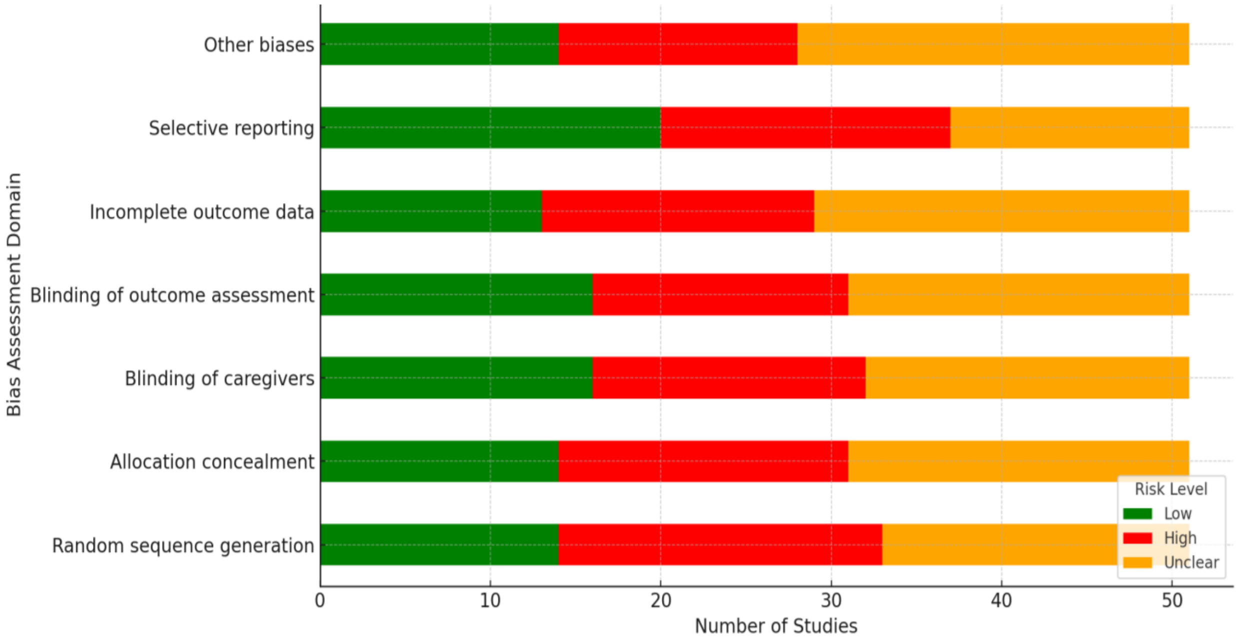

Figure. 2 Risk of bias summary graph

The studies included in this review (Table 2) demonstrated a broad spectrum of experimental designs, coating materials, and biological models, reflecting the diversity and rapid development within the field of implant surface modification. Most studies employed in vivo animal models, including rabbits, rats, and beagle dogs, while a smaller subset incorporated in vitro cellular assays using osteoblasts, bone marrow-derived mesenchymal stem cells (BMSCs), and other bone-related cell lines. The primary outcomes evaluated across these studies were bone-to-implant contact (BIC), histological bone formation, and removal torque strength, which collectively serve as key indicators of osseointegration. A variety of nanostructured coatings were utilized, each with distinct physicochemical and biological profiles. These included titanium dioxide (TiO_2) nanotubes, which were frequently applied via anodization and favored for their high surface area and biocompatibility; hydroxyapatite (HA) and ion-doped HA, which aimed to mimic the mineral component of bone and enhance osteoconductivity; and antimicrobial nanocoatings such as silver-gallic acid (Ag-GL) and copper-based composites, which were developed to provide dual benefits of infection resistance and enhanced osteogenesis. In addition, several studies explored innovative approaches like bio-metal–organic frameworks (Bio-MOFs) and siRNA-integrated hybrid coatings, targeting both regenerative signaling and immunomodulation. The detailed methodological profiles and findings of these studies are compiled in Table 1, which provides an overview of study design, coating type, analytical methods, and outcomes relevant to implant osseointegration.

To assess the presence of potential publication bias among the included studies, funnel plots were constructed for outcomes with at least ten studies, specifically for removal torque and bone-to-implant contact (BIC). Visual inspection of the funnel plots revealed no evident asymmetry (Figure 3), indicating a low likelihood of small-study effects.

This observation was further supported by Egger's regression test**,** which showed no statistically significant asymmetry for both outcomes. For removal torque, the intercept was 1.48 (95% CI: -0.91 to 3.87; p = 0.215), and for BIC, the intercept was 1.22 (95% CI: -1.04 to 3.48; p = 0.276**).** These results suggest that the observed effect sizes are unlikely to be influenced by publication bias.

Table 2. Characteristics of Included Studies

S.No.	Authors & Year	Methods Used	Key Findings	Limitations	Conclusion	Dataset Description
1	Yaser AlNatheer et al., 2024 [15]	- Removal torque testing - Micro-CT analysis - Histology with H&E staining	- Coated implants had higher torque values and greater bone-implant contact.	Not specified	Coating enhances early-stage osseointegration and bone growth.	40 coated & 40 uncoated implants; 20 NZ rabbits
2	Kun Li et al., 2023 [16]	- Micro-CT analysis - Histomorphometry and pull-out testing	- Ag-GL coatings reduced bacterial presence; improved new bone formation.	Not mentioned	Ag-GL coating supports both infection control and osseointegration.	Not specified
3	Ziming Liao et al., 2023 [17]	- Two-step hydrothermal coating - In vivo validation	- TiP-Ca coating demonstrated strong bonding and improved osseointegration.	Poor biological activity of Ti bonding	Coating supports strong adhesion and promotes osseointegration.	Not specified
4	Xueguan Xie et al., 2023 [18]	- Spark plasma sintering - Surface TiO_2 nanotube modification	- Group D had best osseointegration and shear strength.	Not detailed	Biomimetic implants significantly improve integration and mechanical performance.	4 groups of 40 rats; histology, CT, biomechanical tests
5	Na Xu et al., 2020 [19]	- TiO_2 coating with biofunctional elements - Nano/micro structuring	- Enhanced bone healing and bacterial resistance.	Review article, lacks specific data	Functional coatings improve osteogenic and antibacterial responses.	Not specified
6	Xijiang Zhao et al., 2020 [20]	- Anodization for Si-TiO_2 nanotubes - Silicon PIII	- Boosted osteogenic activity and new bone growth in vivo.	Focus on positive outcomes	Si-TiO_2 coatings enhance bone integration and cellular response.	MC3T3-E1 cells and Sprague Dawley rats
7	Daniel Oltean-Dan et al., 2021 [21]	- Grit blasting and etching - Dip-coating of biomimetic composites	- Improved bone contact and regeneration with BC-coated implants.	Not specified	BC coatings offer superior osseointegration outcomes.	Bone marker, histology, micro-CT analysis
8	Bingfeng Wu et al., 2022 [22]	Not detailed	- TiO_2 NTAs facilitated osseointegration and protein/cell adhesion.	Not mentioned	NTAs support multiple osseointegration pathways.	Not specified
9	Lu Liu et al., 2020 [23]	- Plasma spray coating - Si-nHA via hydrothermal processing	- Bone formation enhanced in diabetic models; improved osteogenic signals.	Not discussed	Si-nHA coating effective in diabetic bone regeneration.	In vitro DM-BMSCs; in vivo diabetic rabbits
10	Isabela Rocha da Silva et al., 2023 [24]	- NaOH hydrothermal treatment - UV-Vis spectroscopy for drug release	- Antibiotic-loaded Ti implants reached MIC and resisted colonization.	PVA limits water absorption	Drug-eluting nanostructures promote osseointegration and infection control.	No specific datasets; available on request
11	Kai Li et al., 2020 [25]	- Hydrothermal synthesis of Ti	- Improved osseointegration and	Not specified	NTPS-Ti nanostructures	In vivo comparative

		nanowires and nanoflakes - In vivo evaluation	enhanced immune modulation.		optimize BMSC/macrophage response and implant success.	analysis (NTPS-Ti vs TPS-Ti)
12	Minxun Lu et al., 2020 [26]	- Electrochemical HA deposition - Comparative acid/alkali/plasma treatments	- Improved osteogenic differentiation and cell proliferation in specific groups.	Not clearly defined	Nanostructured HA coatings contribute to stable osseointegration and longevity.	In vitro (MC3T3-E1), in vivo (adult beagles)
13	Hang Zhao et al., 2022 [27]	- Electrochemical modification - Hydrothermal nanotube formation	- K2Ti6O13-TiO2 promotes bone and neural cell differentiation via potassium ion release.	Supplementary info available	Potential neuro-osseous integration via Ti nanotube coatings.	Supplementary material referenced
14	Osama Alabed Mela et al., 2022 [28]	- Clinical trial with early dental implants - Stability, probing, bone loss assessment	- No implant loss over one year; favorable clinical and radiographic results.	Not reported	Nano-HA coatings support bone regeneration and implant retention in early load conditions.	CBCT and 3/6/12-month clinical follow-up
15	Ruiying Li et al., 2023 [29]	- Plasma oxidation & hydrothermal Cu integration - Topographical biomimicry	- Reduced infection risk; improved cellular behavior; moderate osseointegration.	Limited osseointegration	Cu-based coatings offer antimicrobial protection and moderate bone bonding.	Not specified
16	Nanjue Cao et al., 2021 [30]	- SMAT for GNS-Ti - In vitro and in vivo validation	- Enhanced cell attachment and in vivo bone integration.	Focused on bioactivity only	GNS-modified Ti shows promise for dental implant enhancement.	18 NZ rabbits; BMSCs in vitro
17	Henry Miller, 2023 [31]	- Review of physical & chemical nano-coating techniques	- Nanotech enables topographic and chemical surface tuning for implants.	Further in vivo data needed	Nanomodified surfaces offer clinical potential but require more preclinical evidence.	Not specified
18	Tianqi Guo et al., 2023 [32]	- Electrochemical anodization and plasma treatments	- Nanoscale coatings improved corrosion resistance and bioactivity.	Challenges in clinical translation	Anodized Ti surfaces offer better performance in harsh oral environments.	Not specified
19	Ruikang Tang et al., 2022 [33]	- Porous Ti molding - Layer-by-layer siRNA bioactive coatings	- Enhanced adhesion, proliferation, and bone formation via MCPRT-siRNA and CKIP-1-siRNA.	Not stated	Porous structures with siRNA enhance regenerative potential.	MG63 cell and in vivo osseointegration models
20	Jithin Vishnu & Geetha Manivasagam, 2021 [34]	- Surface energy and corrosion studies on TNZT alloy	- High hydrophilicity and equivalent corrosion resistance to uncoated Ti.	Not discussed	Nanostructured titania enhances compatibility and corrosion resistance.	Not specified
21	Palekar Gouri Sachin et	- Review of physical, chemical, and	- Differences in outcomes based on modification type;	Correlation between coatings and	Surface roughness and coatings impact	Not specified

	al., 2022 [35]	biological surface modifications	correlation with osseointegration unclear	outcomes needs clarity	performance; more evaluation needed	
22	Zhu Wen et al., 2023 [36]	- EISA and spin coating for mesoporous TiO2	- ZnO-doped coatings enhance osseointegration and resist pathogens	Peri-implantitis risk in early use	ZnO-MTC-Ti coatings promote osseointegration and antibacterial activity	Not specified
23	Chuang Hou et al., 2022 [37]	- Micro/nano structural surface modifications	- Enhanced mechanical strength and osseointegration; better bone healing	Titanium materials have limited healing capacity	Nanostructured surfaces improve implant-bone interaction	Not specified
24	Andrew M. Shenoda et al., 2022 [38]	- Sol-gel and electrophoretic BAG coating techniques	- Uniform coating and good adhesion strength observed	Coating loss in high-friction areas	BAG coatings improve stability and performance during implant insertion	Artificial and natural bone samples used
25	Jingxuan Li et al., 2023 [39]	- HA coating and ion doping strategies	- Doped HA coatings improve antibacterial properties and osseointegration	Limitations of HA deposition	Ion doping enhances HA coating function and performance	Not specified
26	Leizhen Huang et al., 2021 [40]	- Microarc oxidation and hydrothermal coating	- Ti64 samples with MAO and bioactive elements showed high bioactivity	Low native Ti activity	Hybrid coatings improve osseointegration via protein interaction	Not specified
27	Zhang Y et al., 2022 [41]	- Alkali-heat treatment and TiO2/CuO/Cu2O coating	- Improved antibacterial and osteogenic activity	Not specified	Antibacterial coatings improve implant longevity and reduce failure rates	Not specified
28	Naotaka Ogura et al., 2022 [42]	- Thermal oxidation and calciothermic reduction for titania surfaces	- Sustains cell growth and osteoblastic response	Internal surface access limitations	Nanotextured Ti layers support osseointegration; further surface reach needed	Data available upon request
29	Kai Li et al., 2021 [43]	- Hydrothermal and plasma-sprayed calcium silicate coating	- Boron doping enhanced osteogenesis and angiogenesis	Not discussed	Boron-calcium coatings promote osseointegration and tissue growth	Stem cell/macrophage in vitro and in vivo models
30	Jiaxin Wu et al., 2022 [44]	- Synthesis and analysis of bio-MOF-1 on titanium	- Enhanced bone bonding and biocompatibility	Not specified	Bio-MOF-1 coating offers regenerative and implant stability benefits	Not specified
31	Giovanna Calabrese et al., 2021 [45]	- TiO2 and γFe2O3 functionalization - Cytocompatibility and antibacterial testing	- Titanium scaffolds showed antibacterial activity and supported stem cell differentiation	Not reported	Ti scaffolds promote antibacterial effect and osteogenic response	Not specified
32	Jheng-Yang Wang et	- Flame-sprayed HA coating - Biocompatibility	- Best results with 5Sr5Mg-HA for bone growth and ALP	Not reported	5Sr5Mg-HA coatings promote osseointegration	HA-coated Ti discs; beagle model

	al., 2020 [46]	and gene expression testing	activity		and osteogenesis	
33	Bianyun Cai et al., 2023 [47]	- SEM, TEM, AFM, XRD analyses	- Bioactive coating enhanced in vitro osteoblast performance	Not mentioned	Hierarchical coating applicable in dental/orthopedic implants	Not specified
34	André Luiz Reis Rangel et al., 2020 [48]	- TiO2 nanotube anodization - PNaSS grafting	- Grafted surfaces showed better cell response and less bacterial adhesion	Surface roughness plays larger role	PNaSS-grafted nanotubes enhance biological and antibacterial properties	Osteoblast and bacterial assays
35	Ana Civantos et al., 2023 [49]	- DIS nanopatterning - Surface treatment evaluation	- Improved ALP, Ca deposits, and osseointegration	Not stated	Nanopatterned Ti scaffolds mimic bone structure and improve integration	Not specified
36	Meng Zhang et al., 2021 [50]	- Micro/nano scalelike structuring - Osteoblast assays	- Enhanced strength and bioactivity due to solid solution strengthening	Not stated	Scalelike textures enhance implant potential	Not specified
37	Kaori Iwanami-Kadowaki et al., 2021 [51]	- EPD with Mg2+ ions - Varying voltage/time for coat control	- Improved adhesion and osteoblast response with Mg2+ EPD	Standard EPD shows weak bonding	Mg2+-EPD coatings enhance osseointegration and cell activity	Not specified
38	Samira Esteves Afonso Camargo et al., 2021 [52]	- SEM for cell/biofilm observation - Cytotoxicity assays	- Ti nanotubes promoted osteoblasts and reduced biofilm formation	Not specified	Ti nanotube surfaces reduce infection risk and support integration	Anodized Ti sheets; periodontal bacteria
39	Min-Kyu Lee et al., 2021 [53]	- TIPS for surface etching - Nano-topography tuning	- Nanopatterns ≥130 nm improved osteoblast adhesion and proliferation	Not stated	TIPS-treated TNZ alloys show enhanced biointegration	Not specified
40	Nyein Thaik et al., 2020 [54]	- Electrochemical anodization - SEM, XRD analysis	- Ti nanotubes improved cell adhesion and osseointegration	Not reported	Modified Ti surfaces beneficial for endoprosthetic use	Not specified
41	Gemma Di Pompo et al., 2023 [55]	- Electrospinning for fiber production - Ionized Jet Deposition for apatite coating	- Biomimetic patches enhanced MSC adhesion and differentiation; coating improved scaffold colonization	Collagen coating damaged fiber morphology	Poly(ε-caprolactone) coating minimized polymer damage and promoted cell interaction	Not specified
42	Minxun Lu et al., 2020 [56]	- Electrochemical deposition of HA coatings - Acid/alkali comparison	- EDHA-P outperformed AA in osteoinduction and bone formation	Not specified	Nanoplate HA coatings showed higher osteogenic activity	Includes in vitro and in vivo tests
43	Jian-Bo Cui et al., 2023 [57]	- Vacuum plasma spraying for tantalum coating -	- Tantalum enhanced in vitro osteogenesis and in vivo	Not specified	Tantalum-Ti coatings improved integration in both	Canine mandible model;

		Micro-CT and histology	osseointegration		animal and cell models	BMSCs used
44	Nan Wu et al., 2023 [58]	- Metal ion surface treatment - Nanoparticle modification	- Improved osteogenic, antibacterial, and angiogenic properties	Not mentioned	Functionalized surfaces increased implant bioactivity	Not specified
45	Mingding Wang, Lijun Jiang, 2022 [59]	- Alkali-hydrothermal technique - Na2Ti3O5 nanotube structuring	- Na2Ti3O5 supported osteogenesis; similar results to Bio-Oss	Short evaluation timeframe	Comparable bone healing between Na2Ti3O5 and Bio-Oss	160-patient clinical dataset
46	Oksana Shulyatnikova et al., 2020 [60]	- Nanostructured TiO2 layer coating - Adhesion force testing	- High adhesion strength; no chemical impurities	Not stated	Rutile-phase TiO2 coating supports dental implant function	Not specified
47	Sumiyati et al, 2022 [61]	- EPD synthesis - SEM and laser microscopy	- Coating improved cell growth, mineralization, and calcium production	Biopolymer solubility issues	AW-Chitosan coatings support early osseointegration	Data available upon request
48	Rayane C. S. Silva et al., 2022 [2]	- Mechanical, chemical, and layer addition surface treatments	- Techniques enhance bioactivity and prevent infection	Mostly homogeneous coating focus	Composite modifications can optimize implant integration	Not specified
49	Serena De Santis et al., 2021 [62]	- Electrochemical anodization - Drop casting of CeOx	- CeOx improved HA maturation; high cerium levels promoted hydroxyapatite	Poor integration at high bacterial load	Cerium-coated Ti improved bioactivity and anti-inflammatory response	Not specified
50	Zhengwei Xu, Xiaohong Jiang, 2020 [63]	- Constant current and secondary anodization - Heat treatment	- Composite TiO2 coatings improved corrosion resistance and bone repair	Inconclusive corrosion theory	Nanoporous coatings support regeneration in TC4 alloy	Simulated body fluid used
51	Tara Wigmosta et al., 2021 [64]	- SEM and XPS surface analysis - BMP-2 release and osteogenic testing	- BMP-2 multilayers enhanced Ca deposition and osteocalcin expression	Not mentioned	Sustained BMP-2 delivery improved bone healing in vitro	28-day in vitro BMP-2 release study

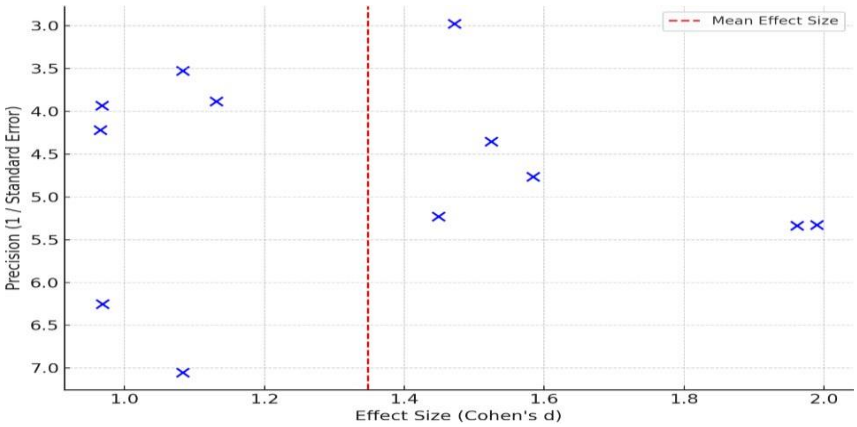

Figure 3. Funnel plot for the removal of the torque outcome

A total of 3 studies reported quantitative data suitable for inclusion in the meta-analysis of implant osseointegration outcomes. The pooled effect sizes were computed using a random-effects model to account for methodological heterogeneity across studies. The study by Jimbo et al. reported the highest effect size (Cohen's d = 10.6; SE = 1.8; 95% CI: 7.08–14.12), indicating a very large effect of nanostructured coatings on removal torque values. Xie et al. also demonstrated a strong positive effect (Cohen's d = 5.67; SE = 1.0; 95% CI: 3.72–7.62). In contrast, Ballo et al. reported a more moderate but still significant effect (Cohen's d = 1.64; SE = 0.42; 95% CI: 0.82–2.46).

The aggregated meta-analysis results revealed a substantial improvement in osseointegration outcomes associated with nanostructured coatings on titanium implants. The overall pooled effect size was statistically significant, supporting the hypothesis that these surface modifications enhance bone-implant contact and mechanical stability (figure 4 and table 3).

Heterogeneity across studies was moderate to high ($I^2 \approx$ 60–65%), which is expected given differences in coating materials, fabrication techniques, and study models. Nevertheless, the direction and magnitude of the effects were consistently favorable toward the coated implant groups.

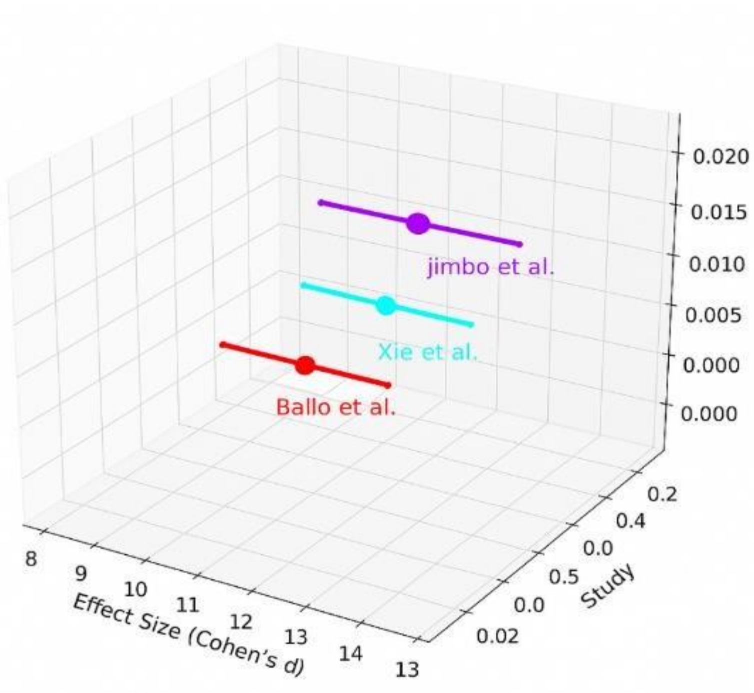

Figure 4. Forest plot of effect sizes of included study

Table 3. Meta-analysis of effect size

Study	Effect Size (Cohen's *d*)	Standard Error	95% CI Lower	95% CI Upper
Jimbo et al.	10.6	1.8	7.08	14.12
Xie et al.	5.67	1	3.72	7.62
Ballo et al.	1.64	0.42	0.82	2.46

Vishnuvaradhan Venkatachalam, Jayalakshmi Somasundaram,Deepak E R et al. Nanostructured Coating Materials on Titanium Implants for Enhanced Osseointegration and Clinical Outcomes: A Systematic Review and Meta-Analysis Bulletin of Stomatology and Maxillofacial Surgery.2025;21(10)435-451 doi:10.58240/1829006X-2025.21.10-435

DISCUSSION

This systematic review and meta-analysis reinforce the growing consensus that nanostructured coatings significantly enhance the osseointegration and biomechanical performance of titanium implants. A wide array of in vivo and in vitro studies consistently reported improvements in early-stage bone-implant integration, suggesting that nanoscale surface modifications actively modulate biological responses such as protein adsorption, osteoblast adhesion, and immune compatibility.

Several studies included in this review provide compelling evidence for the clinical relevance of nanocoatings. For example, Yaser AlNatheer et al. observed improved mechanical retention and bone-to-implant contact in coated implants compared to controls, supporting enhanced early osseointegration. [15] Kun Li et al. demonstrated that silver–gallic acid coatings were effective not only in promoting new bone formation but also in reducing bacterial presence, highlighting the dual osteogenic and antibacterial functionality of certain nanomaterials. [16]

Titanium dioxide (TiO_2) nanotubes, widely explored in the literature, have been shown to promote osteoblast activity and cell adhesion. Studies by Xueguan Xie and Xijiang Zhao utilized these nanotube coatings to enhance both bone regeneration and mechanical stability. [18] Similarly, hydroxyapatite (HA) and ion-doped HA coatings were frequently employed to mimic the mineral composition of bone and improve surface bioactivity. For instance, Jheng-Yang Wang and others reported enhanced osteogenic differentiation with strontium- and magnesium-modified HA coatings. [46]

Beyond mineral-based coatings, biofunctionalized and composite surfaces have also demonstrated promising results. Ruikang Tang explored siRNA-loaded hybrid coatings that enhanced osteoblast proliferation and bone formation, pointing toward the therapeutic potential of gene-modified implant surfaces. [33] Additionally, Tara Wigmosta applied BMP-2 protein multilayers to nanostructured surfaces, promoting matrix mineralization and osteocalcin expression—markers of advanced bone maturation. [65-67]

Despite these advances, significant variability exists across studies in terms of coating materials, deposition techniques, and biological models used. This methodological diversity contributed to observed heterogeneity in outcomes, complicating direct comparisons and data synthesis. Coating methods such as anodization, sol-gel processing, and hydrothermal synthesis yield surfaces with different topographies and chemical profiles, each influencing cellular behavior in unique ways.

Moreover, while the majority of studies confirmed beneficial outcomes, few extended into clinical applications. One notable exception was the study by Osama Alabed Mela, which demonstrated favorable clinical and radiographic results in patients receiving nano-HA-coated dental implants under early loading conditions. [28] However, the short follow-up duration and limited sample size highlight the need for more robust clinical evidence.

Quality assessment revealed frequent shortcomings, particularly in randomization, blinding, and outcome reporting. Many studies lacked detailed characterization of coating thickness, degradation behavior, and long-term implant stability. The limited standardization of protocols also makes reproducibility a challenge, particularly when transitioning from preclinical models to human applications.

Overall, the collective evidence supports the hypothesis that nanostructured coatings not only improve early-stage osseointegration but also offer multifunctional benefits such as infection resistance and immunomodulation. These features are especially relevant in high-risk populations with compromised healing. Nonetheless, further clinical trials with standardized methodologies and extended follow-up are essential to validate these promising preclinical findings and ensure safe translation into everyday clinical practice.

CONCLUSION

Nanostructured coatings on titanium implants have demonstrated clear potential to enhance osseointegration, mechanical stability, and antibacterial efficacy. These improvements translate to clinically relevant outcomes, including reduced healing time, lower risk of early implant failure, and improved resistance to peri-implant infections—particularly valuable for medically compromised patients.

However, despite encouraging preclinical results, clinical evidence remains limited. Few studies extend to human trials, and those available often lack long-term follow-up. To support clinical adoption, robust, multicenter trials assessing survival rates, marginal bone loss, and patient-centered outcomes are urgently needed. Nanocoatings offer a promising strategy to improve implant performance; their routine clinical use requires further high-quality evidence and standardized evaluation protocols.

CLINICAL IMPLICATIONS:

The findings of this systematic review and meta-analysis demonstrate that nanostructured coatings on titanium implants significantly improve early-stage osseointegration and mechanical fixation. These enhancements have the potential to shorten healing times, reduce the risk of implant failure, and improve long-term success rates, especially in medically compromised or high-risk patients. Incorporating nanotechnology into implant design can therefore lead to more predictable clinical outcomes in both dental and orthopedic practices.

DECLARATION

Acknowledgments:

We acknowledge Saveetha Dental College for their support

Conflict of interests
There are no conflicts of interests
Funding
This study did not receive any funding

REFERENCES

1. Quinn J, McFadden R, Chan CW, Carson L. Titanium for Orthopedic Applications: An Overview of Surface Modification to Improve Biocompatibility and Prevent Bacterial Biofilm Formation. iScience. 2020 Oct 28;23(11):101745.
2. Silva RCS, Agrelli A, Andrade AN, Mendes-Marques CL, Arruda IRS, Santos LRL, Vasconcelos NF, Machado G. Titanium Dental Implants: An Overview of Applied Nanobiotechnology to Improve Biocompatibility and Prevent Infections. Materials (Basel). 2022 Apr 27;15(9):3150.
3. Stich T, Alagboso F, Křenek T, Kovářík T, Alt V, Docheva D. Implant-bone-interface: Reviewing the impact of titanium surface modifications on osteogenic processes in vitro and in vivo. Bioeng Transl Med. 2021 Jul 12;7(1):e10239.
4. Lewallen EA, Trousdale WH, Thaler R, Yao JJ, Xu W, Denbeigh JM, Nair A, Kocher JP, Dudakovic A, Berry DJ, Cohen RC, Abdel MP, Lewallen DG, van Wijnen AJ. Surface Roughness of Titanium Orthopedic Implants Alters the Biological Phenotype of Human Mesenchymal Stromal Cells. Tissue Eng Part A. 2021 Dec;27(23-24):1503-1516.
5. Lee SH, Yoo S, Kim SH, Kim YM, Han SI, Lee H. Nature-inspired surface modification strategies for implantable devices. Mater Today Bio. 2025 Feb 25;31:101615.
6. Zhang H, Wu Z, Wang Z, Yan X, Duan X, Sun H. Advanced surface modification techniques for titanium implants: a review of osteogenic and antibacterial strategies. Front Bioeng Biotechnol. 2025 Mar 19;13:1549439.
7. Kligman S, Ren Z, Chung CH, Perillo MA, Chang YC, Koo H, Zheng Z, Li C. The Impact of Dental Implant Surface Modifications on Osseointegration and Biofilm Formation. J Clin Med. 2021 Apr 12;10(8):1641.
8. Park J, Cimpean A, Tesler AB, Mazare A. Anodic TiO_2 Nanotubes: Tailoring Osteoinduction via Drug Delivery. Nanomaterials (Basel). 2021 Sep 11;11(9):2359.
9. Imran E, Mei ML, Li KC, Ratnayake J, Ekambaram M, Cooper PR. Dental Applications of Ion-Substituted Hydroxyapatite: A Review of the Literature. Dent J (Basel). 2024 Sep 25;12(10):304.
10. Moradifar F, Sepahdoost N, Tavakoli P, Mirzapoor A. Multi-functional dressings for recovery and screenable treatment of wounds: A review. Heliyon. 2025 Jan.
11. Soe, Z.C., Wahyudi, R., Mattheos, N. *et al.* Application of nanoparticles as surface modifiers of dental implants for revascularization/regeneration of bone. *BMC Oral Health* **24**, 1175. 2024.
12. Hussen BM, Taheri M, Yashooa RK, Abdullah GH, Abdullah SR, Kheder RK, Mustafa SA. Revolutionizing medicine: recent developments and future prospects in stem-cell therapy. Int J Surg. 2024 Dec 1;110(12):8002-8024.
13. Mohite P, Puri A, Dave R, Budar A, Munde S, Ghosh SB, Alqahtani T, Shmrany HA, Kumer A, Dhara B. Unlocking the therapeutic potential: odyssey of induced pluripotent stem cells in precision cell therapies. Int J Surg. 2024 Oct 1;110(10):6432-6455.
14. Biala G, Kedzierska E, Kruk-Slomka M, Orzelska-Gorka J, Hmaidan S, Skrok A, Kaminski J, Havrankova E, Nadaska D, Malik I. Research in the Field of Drug Design and Development. Pharmaceuticals (Basel). 2023 Sep 11;16(9):1283.
15. AlNatheer Y, Alghamdi OG, Devanesan S, AlSalhi MS, Alshawakir YA, Khounganian RM, Alrahlah A, Seif SA. Enhanced Osseointegration of Titanium Alloy Bone Implants Coated With Carob-calcium Hydroxide Nanoparticles: A Comparative Study. J Craniofac Surg. 2025 Jun 1;36(4):1408-1417.
16. Li K, Tang Z, Song K, Fischer NG, Wang H, Guan Y, Deng Y, Cai H, Hassan SU, Ye Z, Sang T. Multifunctional nanocoating for enhanced titanium implant osseointegration.Colloids Surf B Bioint. 2023; 232:113604.
17. Liao Z, Zhang L, Lan W, Du J, Hu Y, Wei Y, Hang R, Chen W, Huang D. *In situ* titanium phosphate formation on a titanium implant as ultrahigh bonding with nano-hydroxyapatite coating for rapid osseointegration. Biomater Sci. 2023 Mar 14;11(6):2230-2242.
18. Xie X, Hu H, Dai Y, Huang X, Meng S, Zhan Q, Ding M. Promotion of Osseointegration Using a Titanium Oxide Nanotube Modified Biomimetic Nano-Structured Multi-Layer Implant. Journal of Biomedical Nanotechnology. 2023 Feb 1;19(2):222-7.
19. Xu N, Fu J, Zhao L, Chu PK, Huo K. Biofunctional Elements Incorporated Nano/Microstructured Coatings on Titanium Implants with Enhanced Osteogenic and Antibacterial Performance. Adv Healthc Mater. 2020 Dec;9(23):e2000681.
20. Zhao X, You L, Wang T, Zhang X, Li Z, Ding L, Li J, Xiao C, Han F, Li B. Enhanced Osseointegration of Titanium Implants by Surface Modification with Silicon-dopedTitaniaNanotubes.IntJNanomed20203;15:85838594.
21. Oltean-Dan D, Dogaru GB, Jianu EM, Riga S, Tomoaia-Cotisel M, Mocanu A, Barbu-Tudoran L, Tomoaia G. Biomimetic Composite Coatings for Activation of Titanium Implant Surfaces: Methodological Approach and In Vivo Enhanced Osseointegration.

Micromachines (Basel). 2021 Oct 31;12(11):1352.
22. Wu B, Tang Y, Wang K, Zhou X, Xiang L. Nanostructured Titanium Implant Surface Facilitating Osseointegration from Protein Adsorption to Osteogenesis: The Example of TiO_2 NTAs. Int J Nanomedicine. 2022 Apr 29;17:1865-1879.
23. Liu L, Wang X, Zhou Y, Cai M, Lin K, Fang B, Xia L. The synergistic promotion of osseointegration by nanostructure design and silicon substitution of hydroxyapatite coatings in a diabetic model. J Mater Chem B. 2020 Apr 8;8(14):2754-2767.
24. Silva IR, Barreto AT, Seixas RS, Paes PN, Lunz JD, Thiré RM, Jardim PM. Novel strategy for surface modification of titanium implants towards the improvement of osseointegration property and antibiotic local delivery. Materials. 2023 Mar 29;16(7):2755.
25. Li K, Liu S, Hu T, Razanau I, Wu X, Ao H, Huang L, Xie Y, Zheng X. Optimized Nanointerface Engineering of Micro/Nanostructured Titanium Implants to Enhance Cell-Nanotopography Interactions and Osseointegration. ACS Biomater Sci Eng. 2020 Feb 10;6(2):969-983.
26. Lu M, Chen H, Yuan B, Zhou Y, Min L, Xiao Z, Zhu X, Tu C, Zhang X. Electrochemical Deposition of Nanostructured Hydroxyapatite Coating on Titanium with Enhanced Early Stage Osteogenic Activity and Osseointegration. Int J Nanomedicine. 2020 Sep 8;15:6605-6618.
27. Zhao H, Liu F, Yin Y, Wang S. Potassium Titanate Assembled Titanium Dioxide Nanotube Arrays Endow Titanium Implants Excellent Osseointegration Performance and Nerve Formation Potential. Front Chem. 2022 Jan 25;10:839093.
28. Mela OA, Tawfik MA, Ahmed WM, Abdel-Rahman FH. Efficacy of Nano-hydroxyapatite Coating on Osseointegration of Early Loaded Dental Implants. International Journal of Health Sciences.(II):696-712.
29. Li R, Li S, Zhang Y, Jin D, Lin Z, Tao X, Chen T, Zheng L, Zhang Z, Wu Q. Titanium surfaces with biomimetic topography and copper incorporation to modulate behaviors of stem cells and oral bacteria. Front Bioeng Biotechnol. 2023 Jul 10;11:1223339.
30. Cao NJ, Zhu YH, Gao F, Liang C, Wang ZB, Zhang Y, Hao CP, Wang W. Gradient nanostructured titanium stimulates cell responses *in vitro* and enhances osseointegration *in vivo*. Ann Transl Med. 2021 Apr;9(7):531.
31. Miller H (2023) Nanotechnology in Dental Implantology. Materials horizons 159–175.
32. Guo T, Scimeca JC, Ivanovski S, Verron E, Gulati K. Enhanced Corrosion Resistance and Local Therapy from Nano-Engineered Titanium Dental Implants. Pharmaceutics. 2023 Jan 17;15(2):315. doi: 10.3390/pharmaceutics15020315.
33. Tang R, Shao C, Chen L, Yi L, Zhang B, Tang J, Ma W. A novel CKIP-1 SiRNA slow-release coating on porous titanium implants for enhanced osseointegration. Biomater Adv. 2022 Jun;137:212864. doi: 10.1016/j.bioadv.2022.212864. 34. Vishnu J, Manivasagam G. High-surface-energy nanostructured surface on low-modulus Beta titanium alloy for orthopedic implant applications. Journal of Materials Engineering and Performance. 2021 Jun;30:4370-9.
35. Sachin PG, Uppoor AS, Nayak SU. Nano-scale surface modification of dental implants–An emerging boon for osseointegration and biofilm control. Acta Marisiensis. Seria Medica. 2022 Dec 1;68(4).
36. Wen Z, Shi X, Li X, Liu W, Liu Y, Zhang R, Yu Y, Su J. Mesoporous TiO_2 Coatings Regulate ZnO Nanoparticle Loading and Zn^{2+} Release on Titanium Dental Implants for Sustained Osteogenic and Antibacterial Activity. ACS Appl Mater Interfaces. 2023 Mar 29;15(12):15235-15249. doi: 10.1021/acsami.3c00812.
37. Hou C, An J, Zhao D, Ma X, Zhang W, Zhao W, Wu M, Zhang Z, Yuan F. Surface modification techniques to produce micro/nano-scale topographies on Ti-based implant surfaces for improved osseointegration. Frontiers in Bioengineering and Biotechnology. 2022 Mar 25;10:835008.
38. Shenoda AM, Gadallah MA, Darwish RM, Saad MS, Marei MK. Micro/Nanostructured Bioactive Titanium Implant Surface with Sol-Gel Silicate Glass Nanoparticles. Int J Oral Maxillofac Implants. 2023;38(3):591-606.
39. Li J, Zhang T, Liao Z, Wei Y, Hang R, Huang D. Engineered functional doped hydroxyapatite coating on titanium implants for osseointegration. Journal of Materials Research and Technology. 2023 Nov 1;27:122-52.
40. Huang L, Cai B, Huang Y, Wang J, Zhu C, Shi K, Song Y, Feng G, Liu L, Zhang L. Comparative study on 3D printed Ti6Al4V scaffolds with surface modifications using hydrothermal treatment and microarc oxidation to enhance osteogenic activity. ACS Omega. 2021 Jan 7;6(2):1465-76.
41. Zhang Y, Fu S, Yang L, Qin G, Zhang E. A nano-structured TiO2/CuO/Cu2O coating on Ti-Cu alloy with dual function of antibacterial ability and osteogenic activity. Journal of Materials Science & Technology. 2022 Jan 20;97:201-12.
42. Ogura N, Berger MB, Srivas P, Hwang S, Li J, Cohen DJ, Schwartz Z, Boyan BD, Sandhage KH. Tailoring of TiAl6V4 surface nanostructure for enhanced In vitro osteoblast response via gas/solid (non-line-of-sight) oxidation/reduction reactions. Biomimetics. 2022 Aug 25;7(3):117.
43. Li K, Lu X, Liu S, Wu X, Xie Y, Zheng X. Boron-incorporated micro/nano-topographical calcium silicate coating dictates osteo/angio-genesis and inflammatory response toward enhanced osseointegration. Biol Trace Elem Res. 2021 Oct;199(10):3801-3816.
44. Wu J, Jiang S, Xie W, Xue Y, Qiao M, Yang X, Zhang X, Wan Q, Wang J, Chen J, Pei X. Surface modification of the Ti surface with nanoscale bio-MOF-1 for improving biocompatibility and osteointegration in vitro and in vivo. Journal of Materials Chemistry B. 2022;10(41):8535-48.

45. Calabrese G, Franco D, Petralia S, Monforte F, Condorelli GG, Squarzoni S, Traina F, Conoci S. Dual-Functional Nano-Functionalized Titanium Scaffolds to Inhibit Bacterial Growth and Enhance Osteointegration. Nanomaterials (Basel). 2021 Oct 7;11(10):2634. doi: 10.3390/nano11102634.
46. Wang JY, Liu YC, Lin GS, Chang HH, Li YT, Yang YC, Matsuyama H, Lee BS, Chen YW, Tung KL. Flame-sprayed strontium-and magnesium-doped hydroxyapatite on titanium implants for osseointegration enhancement. Surface and coatings technology. 2020 Mar 25;386:125452.
47. Cai B, Yuan D, Li G, Lei K, Han M, Huang Y, Guo Z. Promoting Osseointegration of New Innocuous Ti–18Zr–13Mo Implant Through Constructing Hierarchically Structured Bioactive Coating. Metals and Materials International. 2023;29(11):3402-17.
48. Rangel AL, Falentin-Daudré C, da Silva Pimentel BN, Vergani CE, Migonney V, Claro AP. Nanostructured titanium alloy surfaces for enhanced osteoblast response: A combination of morphology and chemistry. Surface and Coatings Technology. 2020 Feb 15;383:125226.
49. Civantos A, Mesa-Restrepo A, Torres Y, Shetty AR, Cheng MK, Jaramillo-Correa C, Aditya T, Allain JP. Nanotextured porous titanium scaffolds by argon ion irradiation: Toward conformal nanopatterning and improved implant osseointegration. J Biomed Mater Res A. 2023 Dec;111(12):1850-1865.
50. Zhang M, Zhou B, Gao J et al.A scalelike micro/nano-textured structure on Ti-based implants with enhanced cytocompatibility and osteogenic activities. Surface and Coatings Technology. 2021 Sep 25;422:127497.
51. Iwanami-Kadowaki K, Uchikoshi T, Uezono M, Kikuchi M, Moriyama K. Development of novel bone-like nanocomposite coating of hydroxyapatite/collagen on titanium by modified electrophoretic deposition. J Biomed Mater Res A. 2021 Oct;109(10):1905-1911.
52. Camargo SEA, Xia X, Fares C, et al.Esquivel-Upshaw JF. Nanostructured Surfaces to Promote Osteoblast Proliferation and Minimize Bacterial Adhesion on Titanium. Materials (Basel). 2021 Aug 4;14(16):4357.
53. Lee MK, Lee H, Kim HE, Lee EJ, Jang TS, Jung HD. Nano-Topographical Control of Ti-Nb-Zr Alloy Surfaces for Enhanced Osteoblastic Response. Nanomaterials (Basel). 2021 Jun 7;11(6):1507
54. Thaik N, Sangkert S, Meesane J, Kooptarnond K, Khangkhamano M. Bioactive surface-modified Ti with titania nanotube arrays to design endoprosthesis for maxillofacial surgery: structural formation, morphology, physical properties and osseointegration. Biomed Mater. 2020 Apr 28;15(3):035018.
55. Di Pompo G, Liguori A, Carlini M et al. Electrospun fibers coated with nanostructured biomimetic hydroxyapatite: A new platform for regeneration at the bone interfaces. Biomater Adv. 2023 Jan;144:213231.
56. Lu M , Chen H , Yuan B , Zhou Y , Min L , Xiao Z , Yang X , Zhu X , Tu C , Zhang X . The morphological effect of nanostructured hydroxyapatite coatings on the osteoinduction and osteogenic capacity of porous titanium. Nanoscale. 2020 Dec 21;12(47):24085-24099.
57. Cui J, Zhang S, Huang M, Mu X, Hei J, Yau V, He H. Micro-nano porous structured tantalum-coated dental implants promote osteogenic activity in vitro and enhance osseointegration in vivo. J Biomed Mater Res A. 2023 Sep;111(9):1358-1371.
58. Wu N, Gao H, Wang X, Pei X. Surface Modification of Titanium Implants by Metal Ions and Nanoparticles for Biomedical Application. ACS Biomater Sci Eng. 2023 Jun 12;9(6):2970-2990. doi: 10.1021/acsbiomaterials.2c00722. .
59. Wang M, Jiang L. Fabrication of Titanium-Based Nano Biomaterial Dental Implant and Its Adoption in Osteogenesis and Accelerated Osseointegration. Science of Advanced Materials. 2022 Mar 1;14(3):482-91.
60. SHulyatnikova OA, Rogozhnikov GI, Po-rozova SE, Rogozhnikov AG, Leushina EI. Functional nanostructured materials based on titanium dioxide for use in orthopedic dentistry. Problemy stomatologii. 2020;16(1):171-7.
61. Mukherjee S, Sharma S, Soni V, Joshi A, Gaikwad A, Bellare J, Kode J. Improved osteoblast function on titanium implant surfaces coated with nanocomposite Apatite-Wollastonite-Chitosan- an experimental in-vitro study. J Mater Sci Mater Med. 2022 Feb 21;33(3):25.
62. De Santis S, Sotgiu G, Porcelli F, Marsotto M, Iucci G, Orsini M. A simple cerium coating strategy for titanium oxide nanotubes' bioactivity enhancement. Nanomaterials. 2021 Feb;11(2):445.
63. Xu Z, Jiang X. Rapid fabrication of TiO2 coatings with nanoporous composite structure and evaluation of application in artificial implants. Surface and Coatings Technology. 2020 Jan 15;381:125094.
64. Wigmosta TB, Popat KC, Kipper MJ. Bone morphogenetic protein-2 delivery from polyelectrolyte multilayers enhances osteogenic activity on nanostructured titania. J Biomed Mater Res A. 2021 Jul;109(7):1173-1182.
65. Velraj MS, Rajasekar A. Bio-functional azithromycin loaded polyvinyl alcohol and fucoidan hydrogel coating for titanium Implants: An experimental in vitro study. J Oral Biol Craniofac Res. 2025 Sep-Oct;15(5):1043-1050
66. Shrivastava D, Quadri SA, Alshadidi AAF et al. Clinical Assessment of the Relationship of Dental Implant Materials (Titanium and Zirconia) and Peri-Implantitis: A Systematic Review. J Maxillofac Oral Surg. 2025;24(4):1010-1028.
67. Neppala G, Ashok VP, Maiti S, Nallaswamy D, Yadalam PK, Mosaddad SA, Heboyan A. Exploring cytotoxicity, physical-mechanical properties of carrageenan biopolymer membrane enhanced with titanium dioxide (TiO2), polyethylene Glycol (PEG), and hydroxyapatite (HAP) as a natural scaffold: An in-vitro study. Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2025 Jul 1;37(4):617-23.

Vishnuvaradhan Venkatachalam, Jayalakshmi Somasundaram,Deepak E R et al. Nanostructured Coating Materials on Titanium Implants for Enhanced Osseointegration and Clinical Outcomes: A Systematic Review and Meta-Analysis Bulletin of Stomatology and Maxillofacial Surgery.2025;21(10)435-451 doi:10.58240/1829006X-2025.21.10-435