Oral and Implantology

A Journal of Innovations and Advanced Techniques for Oral Health

Vol. 18 | No. 1 | 2026 | pp. 52-63 | eISSN 2035-2468

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Multifunctional graphene oxide coatings for dental implant surfaces

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Contributions statement: both authors contributed equally to this work

Abstract

Graphene oxide (GO) has emerged as a promising multifunctional surface modification for dental implants, addressing two persistent causes of implant failure: peri-implant infection and inadequate osseointegration. This review summarises current evidence on the antibacterial, soft tissue, osteogenic, and mechanical effects of GO-based coatings on titanium and polymeric implant substrates. GO exerts broad-spectrum antibacterial activity through a combination of membrane disruption, reactive oxygen species generation, electron-transfer interference, electrostatic interactions, and photothermal heating. Its efficacy can be further enhanced in composite systems incorporating ions such as silver, zinc, and copper, or biopolymers such as chitosan and collagen. At the tissue level, GO-modified surfaces improve protein adsorption, fibroblast and epithelial adhesion, and peri-implant soft-tissue sealing, while fostering osteogenic differentiation, mineralised matrix deposition, and increased bone-to-implant contact in vivo. Mechanically, GO fortifies ceramic, polymeric, and hybrid coatings, thereby improving hardness, toughness, corrosion resistance, and fatigue behavior. Recent manufacturing advancements, including electrophoretic deposition, micro-arc oxidation, and tailored covalent functionalisation, offer scalable methodologies for producing clinically applicable GO coatings. Nevertheless, significant challenges persist, such as variability in GO synthesis and immobilisation, incomplete knowledge of long-term cytotoxicity, immune modulation, and particle biostability, as well as the scarcity of large-animal and human clinical data. Future research should focus on standardised characterisation, long-term in vivo evaluations, and safety assessments aligned with regulatory standards, alongside the development of intelligent GO-based systems that facilitate local drug delivery, osteoimmunomodulation, and on-demand antimicrobial activation. Overall, the current evidence suggests that GO coatings possess the potential to support next-generation multifunctional dental implants with enhanced biological performance and improved long-term clinical outcomes.

Keywords: Dental Implants; Graphene; Osseointegration.

Article History

Received: December 28, 2025

Accepted: April 3, 2026

Published: June 15, 2026

DOI

https://doi.org/ 10.11138/oi.v18i1.204

Journal Info

eISSN 2035-2468

Peer Review: Double-blind

Published: quarterly

How to Cite

Rawan Al-Rajhi, Abubaker Qutieshat: Multifunctional graphene oxide coatings for dental implant surfaces. Oral and Implantology. 2026;18(1):52-63. doi:10.11138/oi.v18i1.204

Introduction

The success of dental implants predominantly hinges on minimizing bacterial infection and ensuring dependable osseointegration. Peri-implantitis, primarily caused by biofilm accumulation, continues to be a principal factor in implant failure, whereas inadequate osseointegration of the bone undermines stability and longevity. Graphene oxide (GO), a two-dimensional carbon nanomaterial, has gained prominence as an adaptable surface modifier for implants due to its extensive surface area, oxygen-enriched functional groups, and adjustable hydrophilicity. These properties enable it to facilitate both antibacterial activity and osteogenic differentiation, thereby addressing two critical clinical challenges simultaneously [1–3].

Titanium and its alloys persist as the standard in clinical applications due to their exceptional strength, corrosion resistance, and biocompatibility. However, their bio-inert surfaces do not actively promote osseous bonding and may facilitate bacterial adhesion and biofilm formation, thereby increasing the risk of peri-implant inflammation [4]. Surface engineering techniques—such as sandblasting/acid etching, anodization, micro-arc oxidation, plasma spraying, ion implantation, and biomolecule immobilization—alter surface roughness or chemistry to enhance osseointegration. Nonetheless, most of these techniques are single-function and do not provide a durable combination of osteogenic and antimicrobial properties [5].

Graphene oxide (GO) is considered a beneficial coating material due to its hydroxyl, carboxyl, and epoxy functional groups, which impart hydrophilicity, chemical reactivity, and a strong affinity for metal oxides and polymers. This facilitates protein adsorption, enhances mechanical strength, and confers intrinsic antibacterial properties and osteogenic signaling [6]. GO can be immobilized on titanium substrates via various methods such as covalent functionalization, electrophoretic deposition, ultrasonic spraying, layer-by-layer assembly, or integration into micro-arc oxidation oxide layers. Additionally, it can be combined with bioactive materials such as hydroxyapatite, chitosan, gelatin, bioactive glass, or metallic ions. Surfaces modified with GO are capable of reducing bacterial viability and early biofilm formation, while concurrently promoting osteoblast and stem cell adhesion, proliferation, and matrix mineralization in vitro, as well as peri-implant bone formation in vivo [7]. More broadly, graphene-based materials exhibit atomic-scale thickness, high electrical conductivity, mechanical strength, and versatile chemical properties; GO is particularly suitable for implant applications due to the oxygenated groups that enable stable immobilization and increased surface wettability, thereby augmenting protein adsorption and subsequent cell adhesion and spreading [8–10].

Antibacterial properties and mechanisms of GO coatings

The prevention of bacterial colonization is essential for the long-term success of implants. The oral cavity encompasses a diverse array of Gram-positive and Gram-negative species that adhere to implant surfaces, form biofilms, and induce peri-implant inflammation. Once established, biofilms present considerable challenges to eradication due to the extracellular matrix that shelter bacteria and augment their resistance to antimicrobial agents and host immune responses. Therefore, research predominantly concentrates on implant coatings that inhibit initial adhesion and obstruct biofilm formation. Graphene oxide (GO) is recognized as a significant candidate for such coatings owing to its inherent antimicrobial properties, modifiable surface chemistry, and compatibility with composite bioactive systems.

GO operates through multiple complementary mechanisms, encompassing physical disruption of membranes, induction of oxidative stress via reactive oxygen species (ROS), interference with metabolic processes related to electron transfer, electrostatic interactions with bacterial membranes, and photothermal heating under near-infrared (NIR) irradiation. This multifaceted approach amplifies its efficacy against biofilms and potentially diminishes reliance on any singular antibacterial pathway.

Physical antibacterial mechanisms

Graphene oxide (GO) sheets have the ability to inhibit bacteria through direct mechanical interactions; their sharp edges can penetrate cellular membranes, leading to leakage and bacterial cell death [11]. When applied to GO-coated zirconia, a reduction in the viability of *Streptococcus mutans* and *Aggregatibacter actinomycetemcomitans* has been observed, correlating with membrane deformation and decreased adhesion areas [11]. An increased surface area enhances the likelihood of contact, whereas surface hydrophilicity may hinder the adhesion of bacteria on more hydrophobic surfaces. Furthermore, GO sheets may fold or partially enclose bacteria, thereby facilitating entrapment and inducing stress on the membranes. When deposited on sandblasted/acid-etched or micro-arc-oxidized substrates, GO imparts a nanoscale texture that interferes with microbial settlement. Additionally, GO-mineralized collagen hybrid abutments are capable of creating hierarchical micro- and nano-scale roughness, effectively limiting bacterial adhesion while preserving compatibility with fibroblasts [12].

https://doi.org/ 10.11138/oi.v18i1.204

Chemical and oxidative mechanisms

The oxygenated groups present on graphene oxide (GO) facilitate the generation of reactive oxygen species (ROS), thereby inducing oxidative stress that damages lipids, proteins, and DNA. This process disrupts cellular membranes and results in a decrease in colony-forming units on GO-modified titanium in comparison with control samples [13]. The antibacterial efficacy of GO can be modulated by adjusting the degree of oxidation and the thickness of the coating to attain an optimal balance between microbial eradication and compatibility with mammalian cells [13]. Furthermore, GO functions as an electron acceptor, withdrawing electrons from bacterial respiratory proteins, which disrupts the electron transport chain and reduces ATP synthesis. In the context of GO-modified PEEK abutments, this mechanism has been associated with diminished metabolic activity of *Streptococcus mutans* while maintaining fibroblast attachment [14]. The electrostatic attraction between negatively charged GO and positively charged regions of bacterial membranes enhances proximity to reactive groups, thereby accelerating bacterial inactivation. Conversely, variations in mammalian membrane composition and oxidative tolerance may diminish susceptibility to oxidative damage [13–14].

Synergistic composites

The integration of graphene oxide (GO) with metallic ions, ceramics, or polymers can augment antibacterial efficacy through multiple simultaneous mechanisms. Silver-decorated GO within a chitosan matrix facilitates sustained release of Ag^+ ions alongside GO-mediated mechanical and oxidative effects, while chitosan enhances coating stability and compatibility with soft tissues [15]. Zinc-doped hydroxyapatite combined with GO also improves antibacterial performance; zinc interferes with cellular membranes and enzymatic processes, whereas GO diminishes adhesion and early biofilm formation [16]. More broadly, GO-based composites that incorporate metals, ceramics, and biopolymers consistently exhibit superior antibacterial performance compared to single-component coatings and are advanced as preventive measures against peri-implantitis [17].

Photothermal and electro-stimulated effects

Graphene oxide (GO) absorbs near-infrared (NIR) light and converts it into localized heat, which can denature bacterial proteins and compromise biofilm matrices, thereby facilitating targeted antimicrobial action. GO-collagen composites subjected to NIR irradiation have resulted in over 90% reduction in bacterial populations while preserving fibroblast viability, aligning with the higher tolerance of mammals to brief, mild hyperthermia [12]. The electroactivity of GO may additionally augment bacterial eradication under low-level electrical stimulation by enhancing electron-transfer interactions, although this particular mechanism remains less extensively investigated.

Biocompatibility balance

Contrary to numerous ion-releasing antibacterial coatings, which present risks of cytotoxicity or impaired osteoblast function, appropriately immobilized graphene oxide (GO) can provide antibacterial effects while simultaneously supporting mammalian cell adhesion, proliferation, and differentiation. Surfaces coated with GO have exhibited compatibility with gingival fibroblasts, stem cells, and pre-osteoblasts, thus indicating that antibacterial oxidative actions can be achieved at levels below the thresholds of mammalian toxicity [13,14,18]. Furthermore, a decrease in the expression of pro-inflammatory cytokines, such as IL-6 and TNF-α, has been observed on GO-modified substrates in comparison to control samples, aligning with potential anti-inflammatory properties that may enhance soft-tissue integration.

Biocompatibility and soft-tissue integration

A stable peri-implant soft tissue interface is essential for the long-term success of implants. The biological seal created by the gingival epithelium and connective tissue serves to protect the underlying bone by restricting bacterial infiltration and inflammatory damage [19–20]. As this mucosal seal must withstand colonization while maintaining homeostasis, implant surfaces should be both cytocompatible with soft tissue cells and resistant to bacterial adhesion [21]. GO presents itself as a promising modifier in this context owing to its hydrophilicity, protein-adsorptive functional groups, and an oxidative profile capable of supporting antibacterial effects without compromising host cells.

Soft-tissue responses are influenced by variables including surface chemistry, energy, wettability, nano-topography, and bioactivity [22–23]. Although titanium facilitates soft-tissue attachment, its inherent inertness constrains the adhesion strength of epithelial cells and fibroblasts. Graphene oxide (GO) provides oxygen-rich functional groups and a nanosheet architecture, which may enhance initial biological interactions and promote tissue integration through increased cytocompatibility, protein adsorption, modulation of inflammation, and cell-specific attachment.

Cell viability and cytotoxicity

Any surface modification must remain non-cytotoxic and comply with biocompatibility expectations [24]. GO's effects vary

https://doi.org/ 10.11138/oi.v18i1.204

with oxidation level, flake size, deposition method, and thickness, but thin, uniformly immobilized layers are consistently biocompatible [9–10,25–26]. On titanium, covalently functionalized GO increased viability and proliferation of dental pulp stem cells, with elongated cytoskeletal organization and abundant filopodia indicating strong compatibility [18]. Pre-osteoblasts on GO-modified SLA titanium also showed high viability and minimal cytotoxicity, supporting the safety of controlled, covalently attached GO layers [13]. Similar findings extend to polymers: GO-modified PEEK abutments promoted stronger adhesion and faster proliferation of human gingival fibroblasts than pristine PEEK [14].

Protein adsorption and wettability

Protein adsorption subsequent to placement influences subsequent cell adhesion and tissue integration [22]. Graphene oxide (GO) enhances surface free energy and presents carboxyl, hydroxyl, and epoxy groups, which facilitate the adsorption of adhesion proteins such as fibronectin, vitronectin, and laminin, thereby supporting integrin-mediated attachment. GO-coated titanium has demonstrated increased adsorption of fibronectin and vitronectin, along with increased osteoblast adhesion [13]. Additionally, GO-mineralized collagen hybrid abutments have been shown to support dense fibroblast attachment and organized matrix deposition, aligning with improved soft-tissue sealing [12]. Elevated wettability further encourages epithelial and fibroblast spreading and stabilizes early attachment [22].

Inflammatory response and oxidative balance

Excessive inflammation hampers healing processes and increases the likelihood of peri-implant mucositis and peri-implantitis [21]. When properly immobilized, the oxidative capacity of graphene oxide (GO) appears to be adequate for antimicrobial efficacy while remaining below cytotoxic thresholds for mammalian cells, aligning with the varying sensitivities of bacteria and host cells. GO-modified polyetheretherketone (PEEK) has been demonstrated to correlate with decreased expression of pro-inflammatory cytokines, indicating a more stable environment conducive to tissue repair [14]. The integration of GO into biopolymer composites may further enhance this balance: GO-silver-chitosan coatings have been shown to reduce inflammation-related gene expression while maintaining antibacterial properties, with chitosan functioning as a biocompatible matrix and possible antioxidant agent [15]. Emerging evidence also suggests that GO may influence immune responses (e.g., macrophage polarization, osteoclast activity), thereby supporting a microenvironment conducive to concurrent angiogenesis and osteogenesis [27].

Fibroblast and epithelial integration

Effective transmucosal sealing requires robust fibroblast and epithelial adhesion, stable extracellular matrix formation, and epithelial hemidesmosome attachment [19–21]. Graphene oxide (GO) can enhance fibroblast attachment and matrix production through nanoscale roughness and chemical functionalities. Gingival fibroblasts cultured on GO-modified PEEK demonstrate improved cytoskeletal organization and increased collagen type I expression, characterized by an elongated morphology and anchoring filopodia [14], indicating stronger integration. Similar adhesion cues have been observed in dental pulp stem cells and pre-osteoblasts cultured on GO-functionalized titanium [13,18]. Furthermore, GO-collagen hybrid abutments support the formation of a continuous epithelial layer and close epithelial contact under microscopy, consistent with the development of hemidesmosome-like attachments essential for epithelial sealing [12]. Composite coatings combining GO with collagen, hydroxyapatite, or chitosan may further enhance soft tissue stability and inhibit apical epithelial migration, which is associated with early pocket formation [14–16,21,28].

Compatibility of composite coatings

GO readily integrates into composite materials designed to enhance soft-tissue integration while preserving antibacterial functionality. Hydroxyapatite-GO coatings can facilitate both bone and soft-tissue responses through hydroxyapatite bioactivity and GO-driven hydrophilicity and protein adsorption, maintaining high stromal cell viability alongside soft-tissue compatibility [28]. Zinc-doped hydroxyapatite-GO systems incorporate osteogenic and antimicrobial properties derived from zinc while maintaining fibroblast viability, thereby supporting their application in transmucosal regions [16]. Silver-GO-chitosan coatings similarly combine sustained ion release with GO-mediated mechanisms and chitosan-enhanced hydrophilicity and gingival compatibility, achieving antibacterial efficacy with minimal cytotoxicity [15].

Osteogenic potential and osseointegration

The achievement of successful osseointegration is essential for the long-term viability of implants and relies on coordinated biochemical and mechanical interactions that secure the implant surface to newly formed bone tissue. During the initial healing phases, osteoblasts and osteoprogenitors derived from stem cells are required to adhere, proliferate, differentiate, and deposit mineralized extracellular matrix directly onto the implant surface. Although titanium demonstrates biocompati-

https://doi.org/ 10.11138/oi.v18i1.204

bility, it is not inherently osteoinductive; consequently, surface treatments such as sandblasting combined with acid etching, micro-arc oxidation, hydroxyapatite coatings, and bioactive polymer deposition are necessary. The focus on nanostructured interfaces is increasing due to their ability to emulate critical features of the extracellular matrix and regulate cellular behavior at the molecular level [29–30].

GO offers a multifunctional nanoscale interface that enhances osteogenesis via its oxygenated functional groups, substantial surface area, hydrophilicity, and strong interactions with adhesion proteins [31]. The suggested mechanisms include improved protein adsorption and integrin-mediated adhesion, activation of osteogenic signaling pathways, and facilitation of mineral nucleation.

Cellular adhesion and early differentiation

Early attachment constitutes the initial phase of osseointegration, wherein the nanoscale roughness and hydrophilicity of graphene oxide (GO) facilitate cell spreading and cytoskeletal organization. Covalently immobilized GO on titanium surfaces enhances the adhesion and early proliferation of dental pulp stem cells, exhibiting extensive filopodia attachment indicative of accelerated osteoblastic differentiation [18]. Furthermore, GO-modified SLA titanium enhances pre-osteoblast adhesion within 24 hours and increases the number of vinculin-rich focal adhesions, which transmit signals to promote differentiation [13]. GO-mineralized collagen hybrid coatings similarly enable rapid attachment of osteoblast-like cells while supporting favorable soft-tissue responses [12].

Osteogenic gene expression and signaling

Graphene oxide (GO) influences the differentiation-associated gene networks by modulating the adhesion-signaling axis. On GO-modified titanium, an increase in RUNX2 expression has been documented alongside elevated levels of alkaline phosphatase and osteopontin, which are associated with the activation of focal adhesion kinase signaling [13]. Similarly, dental pulp stem cells cultivated on GO-functionalized titanium exhibit upregulation of transforming growth factor beta, bone morphogenetic protein 2, RUNX2, and type I collagen, indicating the promotion of both early and late stages of osteogenesis [18]. When combined with osteogenic ions, GO can enhance biological responses: for example, zinc-doped hydroxyapatite integrated with GO has been shown to increase osteogenic marker expression, aligning with zinc's effects on alkaline phosphatase activity and collagen synthesis, thereby suggesting that GO can effectively present ions or molecules [16].

Protein adsorption and integrin interactions

Osteoblasts primarily adhere to an adsorbed protein layer rather than directly to the substrate. Graphene oxide (GO) enhances the adsorption of integrin-interacting proteins such as fibronectin, vitronectin, and osteopontin through negatively charged oxygenated groups, thereby supporting integrin-mediated adhesion and downstream signaling pathways [29]. GO-coated titanium surfaces demonstrate increased adsorption of fibronectin and vitronectin relative to unmodified surfaces, correlating with heightened focal adhesion formation and activation of maturation-related pathways [13]. Furthermore, GO-collagen hybrids leverage this protein-binding capacity to facilitate the deposition of an organized matrix, providing evidence of integrin engagement [12].

Mineralization and matrix deposition

A characteristic feature of osseointegration is the deposition of mineralized extracellular matrix at the surface. GO-coated titanium has demonstrated significant calcium phosphate nodule formation and increased alizarin red staining after 21-28 days, signifying enhanced mineral deposition [18]. Likewise, Hydroxyapatite-GO coatings have been shown to augment late-stage osteogenic activity, including elevated levels of osteocalcin and osteopontin, as well as the development of a robust mineralized interface [28]. In vivo studies have indicated that GO incorporated into micro-arc oxidation coatings elevates mineral deposition and osteoid thickness at two and four weeks, implying benefits during both early and later stages of bone formation [32]. These phenomena are generally ascribed to GO's negatively charged functional groups, which attract calcium ions and facilitate the nucleation and growth of calcium phosphate phases.

In vivo evidence

Animal studies corroborate in vitro findings. Implants coated with reduced GO in rabbit femurs demonstrated superior bone-to-implant contact compared to controls, with histological analysis revealing mature lamellar bone directly adjacent to the GO surface [33]. GO-incorporated micro-arc oxidation coatings in rat femurs facilitated increased new bone formation and enhanced peri-implant bone microarchitecture [32]. Additional in vivo research reports combined angiogenic and osteogenic responses surrounding GO-deposited implant surfaces [11], suggesting pro-regenerative effects at the bone-implant interface.

https://doi.org/ 10.11138/oi.v18i1.204

Synergistic composite systems

Graphene oxide (GO) can be integrated with ceramics, doped ions, polymers, and bioactive molecules to develop multifunctional coatings that facilitate osseointegration while mitigating infection risks. Zinc-doped hydroxyapatite with GO has demonstrated increased alkaline phosphatase activity alongside enhanced bactericidal properties [16]. Silver-decorated GO-chitosan coatings combine osteogenic potential, corrosion resistance, and antibacterial efficacy [15]. Additionally, GO-zirconia composites have been shown to improve mechanical strength and promote osteoblast attachment [34]. Furthermore, GO-wrapped carbon fiber-PEEK composites support osseointegration and resist bacterial colonization [35–36].

Mechanical and structural enhancements

While graphene oxide (GO) coatings are often considered for their biological advantages, the long-term effectiveness of implants also relies on mechanical stability under cyclic occlusal loads, as well as resistance to chemical challenges such as pH variations, enzymes, and metabolites, in addition to wear and corrosion. Consequently, coatings must maintain their structural integrity, adhere effectively to the substrate, withstand wear, and provide protection against corrosion over an extended period. GO enhances these properties through its two-dimensional architecture, high elastic modulus, and chemical versatility, thereby facilitating reinforcement across diverse coating systems. Electrophoretic deposition and layer-by-layer assembly are particularly attractive fabrication techniques, given their ability to produce uniform, adherent films and their compatibility with industrial scale-up [37–38].

Mechanical strength and wear resistance

Graphene oxide (GO) demonstrates exceptional inherent mechanical characteristics, with tensile strength reported to be approximately 130 GPa and a Young's modulus near 1 TPa [29]. In composite materials, GO can enhance load transfer, deflect cracks, dissipate energy, and establish barrier-like networks that inhibit defect propagation. In ceramics, the reinforcement of 3Y-ZrO_2 with GO has led to increased fracture toughness and wear resistance, with crack bridging, sheet pull-out, and interfacial debonding playing a role in energy dissipation and diminishing brittleness [34]. Similar reinforcement effects have been observed in polymers: GO-wrapped carbon fibre-PEEK has enhanced flexural strength and elastic modulus compared to pristine PEEK, owing to robust interfacial interactions between GO functional groups and the polymer matrix that hinder microcrack initiation [35].

Corrosion and chemical stability

Environmental fluctuations in oral environments can promote titanium corrosion, ion release, surface roughening, and progressive deterioration. GO-based coatings act as protective barriers that reduce electrochemical interactions and enhance corrosion resistance. Silver-decorated GO-chitosan coatings have demonstrated a capacity to decrease corrosion current density and increase polarization resistance by restricting the ingress of chloride ions and salivary constituents, with chitosan providing a uniform stabilizing film [15]. Hydroxyapatite-GO coatings on Ti6Al4V similarly enhance corrosion resistance by minimizing microdefects and promoting passivation, thereby potentially protecting alloy performance during the initial stages of inflammatory healing [28]. Micro-arc oxidation coatings incorporating GO and graphite further augment corrosion resistance, with GO reducing porosity and graphite supporting durability [32].

Adhesion and interfacial integrity

Robust adhesion between coating and substrate is essential because delamination under mechanical stress undermines osseointegration and exposes surfaces to microbial colonization and corrosion. Graphene oxide (GO) can improve adhesion via chemical bonding, mechanical interlocking, and redistribution of stress. Its hydroxyl, carboxyl, and epoxy groups are capable of interacting with titanium oxide; APTES-mediated covalent functionalization has produced GO-Ti interfaces that endure sterilization cycles and abrasion [18]. On micro-roughened SLA titanium, GO sheets can penetrate surface pits and valleys, thereby supporting strong adherence of thin sprayed films through interlocking and chemical affinity [13]. The planar structure of GO may also help to alleviate stress concentrations at the interface, consequently delaying crack initiation and delamination. In hybrid materials such as hydroxyapatite-GO, additional ionic and hydrogen bonds further reinforce cohesion and adhesion [28].

Reinforcement in hybrid and multifunctional systems

Graphene oxide (GO) demonstrates compatibility with numerous bioactive and structural materials, thereby facilitating the development of coatings that incorporate antibacterial, osteogenic, and mechanical functionalities. Hydroxyapatite-GO systems have shown increased microhardness and elastic recovery, while also promoting mineralization [28]. Zinc-doped hydroxyapatite combined with GO offers osteogenic and antimicrobial benefits derived from zinc, in addition to GO-driven reinforcement and antibacterial activity [16]. Similarly, silver-GO-chitosan coatings synergistically combine sustained anti-

https://doi.org/ 10.11138/oi.v18i1.204

microbial effects with GO reinforcement, alongside the durability, corrosion resistance, and cytocompatibility associated with chitosan [15]. In ceramic applications, GO-enhanced zirconia has exhibited improved toughness and wear resistance, indicating its potential utility in abutments and other load-bearing components [34]. The effects of dosage are significant: in bioceramics, 1 wt% GO increased microhardness without impairing cell viability, whereas 3 wt% resulted in greater hardness but demonstrated early cytotoxicity [39]. In polymers, GO-modified polyetheretherketone (PEEK) has shown improved mechanical properties, along with enhanced biological performance, supporting its application in abutments.

Surface nano-topography, wettability, and fatigue behavior

Surface topography substantially influences protein adsorption, cell adhesion, and mechanical anchorage. Graphene oxide (GO) can introduce nanoscale features while maintaining advantageous microscale roughness. On selective laser sintering (SLA) titanium, GO preserved the microtopography and added a nanoscale layer that enhanced wettability and protein adsorption, thereby supporting serum protein binding and osteoblast attachment [13]. In micro-arc oxidation coatings, GO contributed to micro-nano hybrid structures featuring nanoscale wrinkles and ridges that facilitate cell attachment and mechanical interlocking with bone [32]. GO-collagen coatings establish a biologically relevant nano-architecture that supports fibroblast alignment and soft-tissue sealing [12].

Long-term reliability is also contingent upon fatigue resistance under repeated chewing cycles. GO sheets can bridge and deflect microcracks, distribute load through a high-modulus network, and limit corrosive infiltration when embedded in matrices such as hydroxyapatite, PEEK, or zirconia. Although dedicated long-term fatigue studies remain limited, available reports indicate enhanced toughness and resistance to damage accumulation in GO-zirconia and GO-carbon fibre-PEEK systems compared to conventional counterparts [34–36].

The key antibacterial, soft tissue, osteogenic, and mechanical effects of GO coatings, along with representative systems and clinical implications, are outlined in Table 1.

Table 1. Functional Domains, Mechanisms, and Translational Relevance of Graphene Oxide-Based Coatings for Dental Implants. This table summarizes the contributions of graphene oxide (GO) to antibacterial activity, soft tissue integration, osteogenic potential, mechanical performance, and the development of multifunctional composite materials. It includes key example systems and discusses potential clinical implications. Abbreviations: GO, graphene oxide; ROS, reactive oxygen species; NIR, near-infrared; HA, hydroxyapatite; PEEK, polyetheretherketone; CF, carbon fibre.

Functional domain	GO based mechanisms	Representative effects	Example systems	Potential clinical relevance
Antibacterial activity	Physical membrane disruption by sharp sheet edges; oxidative stress via ROS; electron transfer from bacterial membranes; electrostatic attraction between negatively charged GO and positively charged bacterial surfaces; NIR activated photothermal heating	Reduced bacterial adhesion and viability; inhibition of early biofilm formation; disruption of mature biofilm matrix; broad activity against Gram positive and Gram negative species	GO on Ti, zirconia, or TiO_2 nanotubes; Ag GO chitosan coatings; Zn HA GO composites; GO collagen abutments	Lower early peri implant bacterial load and biofilm formation, reduced peri implantitis risk, potential for on demand photothermal disinfection after placement
Soft tissue integration	Hydrophilic functional groups that increase protein adsorption; favourable nano topography for fibroblasts and epithelial cells; moderated oxidative environment; reduced pro inflammatory cytokine expression	Enhanced fibroblast and epithelial adhesion; improved extracellular matrix organisation; reduced IL 6 and TNF α release; more stable peri implant mucosal seal	GO modified PEEK abutments; GO collagen hybrid abutments; HA GO coatings incorporating soft tissue facing regions	Stronger soft tissue seal around abutments, reduced epithelial down growth, better protection of marginal bone from bacterial and inflammatory insult

https://doi.org/ 10.11138/oi.v18i1.204

Functional domain	GO based mechanisms	Representative effects	Example systems	Potential clinical relevance
Osteogenic potential and osseointegration	Increased adsorption of fibronectin, vitronectin, osteopontin; activation of FAK, p38 MAPK, BMP2 and RUNX2 pathways; promotion of calcium phosphate nucleation; support of osteoblast and stem cell adhesion and spreading	Higher osteoblast and stem cell adhesion and proliferation; upregulation of osteogenic genes; increased ALP, osteocalcin and mineralised nodule formation; greater bone to implant contact in vivo	GO functionalised Ti; GO mineralised collagen; Zn HA GO composites; GO wrapped CF PEEK implants; reduced GO coatings	Faster and more robust osseointegration, potentially shorter healing times, improved long term bone stability around implants
Mechanical and structural performance	High intrinsic tensile strength and modulus; crack deflection and bridging; barrier effect against corrosive species; improved coating adhesion via chemical bonding and mechanical interlocking	Increased fracture toughness and wear resistance; enhanced flexural strength and elastic modulus in composites; reduced corrosion current density and improved passivation; reduced risk of coating delamination	GO reinforced 3Y ZrO_2; GO CF PEEK; HA GO coatings; Ag GO chitosan on Ti; GO containing micro arc oxidation layers	More durable implant and abutment components, reduced risk of mechanical failure or coating breakdown under cyclic occlusal loading and corrosive oral conditions
Composite and multifunctional systems	Combination of GO with bioactive ceramics, metals, and polymers to integrate multiple functions in a single coating	Simultaneous antibacterial, osteogenic, soft tissue friendly and corrosion resistant behaviour; tunable release of ions or drugs; improved mechanical integrity of the coating	Zn HA GO, Ag GO chitosan, HA GO, GO collagen hybrids, GO with Cu or other ions, drug loaded GO layers	Single coating system that addresses infection control, bone regeneration, soft tissue sealing and mechanical stability in an integrated manner
Challenges and future directions	Control of synthesis, oxidation level, sheet size and immobilisation method; long term biostability; optimisation of antibacterial versus osteogenic balance; integration with stimuli responsive and drug delivery functions	Risk of variability in biological responses; possible long term cytotoxicity or particle migration if coatings degrade; limited long term in vivo and no human clinical data so far; need for standardised characterisation and regulatory pathways	GO produced by Hummers and modified Hummers routes; electrophoretic deposition, micro arc oxidation, spray and covalent functionalisation strategies	Requires standardised manufacturing specifications, long term animal and clinical studies, and regulatory alignment; future potential for smart, patient specific, GO based implant surfaces with electrical, photothermal or drug delivery capabilities

Challenges and future directions

Although GO-coated dental implants demonstrate promising antibacterial, osteogenic, and mechanical properties, various scientific, technological, and regulatory challenges must be addressed prior to their extensive clinical adoption. Existing in vitro and animal studies require further validation through comprehensive data on long-term coating stability, manufacturing reproducibility, biological safety, and adherence to regulatory standards.

Variability in synthesis and surface functionalization

GO properties demonstrate considerable variability contingent upon the synthesis method utilized, such as Hummers, modified Hummers, and electrochemical processes, resulting in differences in oxygen content, sheet thickness, flake size, and defect density [[29]]. These attributes can influence antibacterial efficacy, oxidative reactivity, cytotoxicity, protein binding affinity, and osteogenic responses. For instance, increased oxygen content can enhance hydrophilicity but may also elevate oxidative stress; similarly, variations in sheet size and reduction state can affect membrane disruption and electron transfer mechanisms. The coating method is also a crucial factor: APTES-mediated covalent functionalization yields stable coatings capable of withstanding sterilization and handling [18], whereas ultrasonic atomization spraying produces uniform films primarily bonded physically, which may respond differently under cyclic loading conditions [13]. To improve reproducibility, future research should establish specific target parameters for sheet size distribution, oxidation level, surface charge, thickness, bonding stability, and dispersion. Furthermore, standardized reporting metrics, including X-ray photoelectron spectroscopy, Raman spectroscopy, contact angle measurements, zeta potential, and atomic force microscopy, should be adopted.

https://doi.org/ 10.11138/oi.v18i1.204

Cytotoxicity, inflammation, and long-term biostability

Although immobilized graphene oxide (GO) is frequently regarded as cytocompatible in short-term examinations, its long-term safety profile remains uncertain. Factors such as dosage, flake size, oxidation state, and aggregation influence cytotoxicity; excessively oxidized or inadequately dispersed GO may induce intracellular reactive oxygen species (ROS) and trigger apoptosis or necrosis [26]. In cases where coatings undergo degradation or delamination, released GO fragments could migrate locally or systemically. Short-term animal studies have demonstrated good tolerance [32–33]; however, the long-term biodistribution and persistence are not comprehensively characterized. Principal concerns include chronic inflammation, fibrotic encapsulation, nanoparticle transport to distal organs, intracellular accumulation affecting osteoblast and fibroblast functions, and macrophage-mediated foreign body responses. Addressing regulatory requirements will necessitate extended investigations, including chronic toxicity assessments in large-animal models (e.g., 6-12 months), systemic histological examinations, particle tracking, long-term immune and inflammatory profiling, as well as prolonged immersion and degradation testing in relevant simulated fluids and enzymatic environments.

Mechanical fatigue, wear, and delamination under clinical loading

Implants are subjected to multi-axial stresses, including compression, shear, and torsion, as well as millions of loading cycles annually. While graphene oxide (GO) enhances static mechanical properties in ceramics and polymers, comprehensive investigations into fatigue life and wear under realistic multi-axis loading conditions remain limited and do not provide a complete characterization of fatigue and wear behaviors. Potential risks include microcrack initiation at GO interfaces, delamination due to inadequate bonding, brittle failure of composites, chemical alterations under cyclic loads, and accelerated corrosion at defect sites. Future research should incorporate nano-scratch testing, nano-indentation, physiologically relevant fatigue cycling, thermal cycling to simulate fluctuations in the oral environment, and finite element modeling to map stress distributions, particularly in promising micro-arc oxidation systems that include GO [32].

Balancing antibacterial and osteogenic performance

The dual functionality of graphene oxide (GO) also presents an optimization challenge: conditions aimed at maximizing antibacterial efficacy may impair host compatibility, while osteogenic-promoting conditions may diminish antimicrobial effects. Precise regulation of oxidation level, thickness, sheet size, and additives is required. Highly oxidized GO may enhance antibacterial properties but increase oxidative stress in the host; larger sheets may more effectively disrupt bacteria yet hinder fibroblast proliferation; dense, continuous coatings may inhibit cell adhesion but limit protein infiltration, which is essential for osseointegration. Osteogenic responses are evidently sensitive to GO concentration and presentation [13], and incorporating silver or zinc can augment antimicrobial potency, albeit with a risk of dose-dependent cytotoxicity. Future research should focus on mapping dose-response relationships, establishing safe and efficacious oxidation and concentration ranges, identifying optimal sheet thicknesses that enhance wettability and protein adsorption, and employing combinatorial approaches (such as low-dose dopants, polymers, and biological molecules) supported by computational modeling.

Limited long-term in vivo evidence and lack of human trials

The limitations of translation are primarily attributable to the scarcity of long-term animal data and the absence of comprehensive clinical studies. Numerous in vivo investigations predominantly concentrate on early healing stages (2-8 weeks) [32–33], often failing to account for the complexities of the human oral environment or the extended service duration. Critical deficiencies include the necessity for large-animal models (such as canines and ovines), studies that incorporate loading conditions, and clinical outcomes such as peri-implant mucosal health, the prevalence of peri-implantitis, and systemic safety evaluations. Reviews emphasize that regulatory progress is contingent upon the availability of extensive long-term datasets [40–41]. Future research should therefore entail assessments of osseointegration in large animals under load, survival studies spanning 6 to 24 months, comprehensive in vivo evaluations of soft tissue responses, and investigations utilizing models of peri-implant mucositis and peri-implantitis.

Emerging perspectives

Future research endeavors may leverage the electrical, optical, and chemical properties of GO beyond its role as a passive coating. Electroconductive GO/reduced GO surfaces could facilitate controlled electrical stimulation to expedite bone regeneration [42]. Photothermal GO coatings provide on-demand near-infrared (NIR)-triggered disinfection, as demonstrated in GO-collagen systems that achieve significant bacterial reduction while maintaining mammalian cell viability [12]. GO may also function as a carrier for the localized delivery of antibiotics, growth factors, peptides, or anti-inflammatory agents. Ultimately, the development of multi-component “intelligent” surfaces that combine zinc (osteogenesis), silver (antibacterial), collagen (soft-tissue sealing), and hydroxyapatite (mineralization) could enable adaptive healing strategies. Furthermore,

https://doi.org/ 10.11138/oi.v18i1.204

with the advent of digital dentistry, these surfaces may be tailored to individual patients' specific needs, moving away from generic, one-size-fits-all coating solutions.

Conclusions

Graphene oxide has become a prominent candidate for advanced dental implant coatings due to its ability to combine broad-spectrum antibacterial activity with enhanced osseointegration and soft tissue sealing. By synergistically combining ROS-mediated membrane disruption, electron transfer, and electrostatic mechanisms with improved protein adsorption and the activation of osteogenic signalling pathways, GO coatings reliably diminish biofilm formation and facilitate early osteogenesis both in vitro and in vivo. When integrated into multifunctional composites with hydroxyapatite, chitosan, or metal ions, GO further enhances mechanical stability and permits precise modulation of antibacterial and osteogenic responses. Additionally, it may exert advantageous immunomodulatory effects at the implant interface.

From a translational perspective, scalable manufacturing approaches such as electrophoretic deposition and layer-by-layer assembly, together with tailored functionalisation strategies, provide practical pathways for producing durable graphene oxide (GO)-modified implants. Significant obstacles remain, including variability in GO synthesis, limited comprehension of long-term biostability and immune responses, and the current absence of standardised, long-term in vivo and clinical data. Future efforts should therefore focus on harmonised characterisation, chronic safety and performance evaluations, and the integration of GO coatings with intelligent drug delivery systems and other bioactive cues. If these challenges are effectively addressed, GO-based coatings possess the potential to support a new generation of multifunctional dental implants, offering enhanced protection against infection and more predictable long-term integration.

Funding: None

Conflict of interest: The authors declare no conflict of interest

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