Potential Enhancements in Titanium Dental Implants Using Graphene Coatings: A Preliminary Scoping Review

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Abstract:
In the evolving field of dental implantology, graphene coatings represent a significant innovation with the potential to improve implant success. This scoping review synthesises research on graphene-coated dental implants' biocompatibility, antibacterial properties, and effectiveness. It aims to offer a comprehensive overview, identify research gaps, and direct future studies, highlighting graphene's potential to revolutionise implant technology and enhance patient outcomes.
Keywords: Graphene Coatings, Dental Implants, Biocompatibility

الملخص:

في مجال زراعة الأسنان المتطور، تمثل طلاءات الجرافين ابتكارًا مهمًا مع إمكانية تحسين نجاح زراعة الأسنان. تجمع مراجعة النطاق هذه الأبحاث حول التوافق الحيوي لزراعة الأسنان المغطاة بالجرافين، وخصائصها المضادة للبكتيريا، وفعاليتها. ويهدف إلى تقديم نظرة شاملة، وتحديد الفجوات البحثية، وتوجيه الدراسات المستقبلية، وتسليط الضوء على إمكانات الجرافين لإحداث ثورة في تكنولوجيا الزرع وتعزيز نتائج المرضى.

الكلمات المفتاحية: طلاءات الجرافين، زراعة الأسنان، التوافق الحيوي

Introduction

Dental implants have revolutionised restorative dentistry since their introduction by Branemark in the 1970s [1], offering a durable and realistic solution for missing teeth. The predominant choice for implants has been titanium, known for its strong osseointegration properties and exceptional biocompatibility, allowing integration with the jawbone to provide a stable base for prosthetic teeth [2]. Moreover, advancements in materials have introduced zirconia implants, offering a metal-free alternative for patients with metal sensitivities or aesthetic concerns. Particularly advantageous for front teeth replacements, zirconia implants' white, tooth-like colouration makes them ideal in cases where metallic implants might be visible [3].

In contrast, Polyetheretherketone (PEEK), a thermoplastic material, is emerging in dental implantology due to its mechanical properties that closely resemble natural bone, potentially reducing stress transfer to adjacent bone structures. However, while PEEK's flexibility is beneficial, its long-term durability and efficacy warrant further research, especially when compared to materials like titanium or zirconia [4]. Although less commonly used, PEEK is gaining attention for patient-specific solutions, but its performance in varied clinical situations still demands comprehensive evaluation. Additionally, choosing the suitable implant material involves considering factors such as bone quality, aesthetic needs, and material sensitivities [4]. Furthermore, the advancement in implant materials and surface engineering heralds a new era of personalised patient care. Nevertheless, dental professionals must maintain a balance of cautious optimism and adherence to evidence-based practice. This approach ensures that newer materials like PEEK effectively contribute to the integration, function, and aesthetic harmony of dental implants, thereby enhancing outcomes in oral rehabilitation. Dental implants are known for benefits like enhanced chewing ability, more explicit speech, and improved facial aesthetics, yet they are not without drawbacks, including a notable susceptibility to failure. For example, Castellanos-Cosano et al. [5] reported an overall failure rate of about 2.1%, while another study noted a failure rate of 3.11% [6]. Although relatively low, these figures call for an in-depth examination, considering the influence of factors like study methodologies, patient demographics, and types of implants and procedures used. Additionally, peri-implantitis is a significant complication, with a reported occurrence range of 28-77% in subjects and 12-43% in implant sites [7, 8]. This wide range suggests variability in clinical outcomes, possibly reflecting differences in patient care, surgical techniques, and maintenance protocols.

Moreover, the crucial role of pre-implant surgery as a risk factor underscores the need for patient-specific risk assessment and tailored treatment planning. Indeed, these statistics should be interpreted with the understanding that individual cases can vary markedly. Dental professionals should apply these findings cautiously, ensuring that each patient's unique circumstances are factored into their treatment plans. This approach minimises the risk of implant failure and adheres to personalised medicine principles, which is increasingly essential in both dental and medical fields. While failure rates and complications associated with dental implants offer crucial insights, they should be integrated into a broader, patient-centred dental care strategy, focusing on individualised risk assessment and treatment planning. Furthermore, a study highlights that the survival rate of dental implants depends on several factors, including the patient's age, implant length and diameter, bone quality, and implant location [9]. Dental implant failures are classified into early and late based on their occurrence relative to the abutment connection. Early failures, which happen before the implant bears the functional load, indicate a lack of osseointegration. In contrast, in cases of immediate loading, late failures occur after the implant begins to bear load or after the first removal of a provisional restoration [10].

Despite the relatively low failure rates of dental implants, there's a significant interest in the potential of graphene as an implant coating due to its unique properties that could address the underlying causes of dental implant failures. While the current failure rate may appear minimal, each instance of failure carries significant implications for a patient’s health, quality of life, and healthcare costs. Moreover, using graphene could enhance biocompatibility, reduce bacterial adhesion, and improve the mechanical strength of implants, offering a proactive approach to advancing dental implant technology. Therefore, this pursuit is about reducing the failure rate and improving the overall success and longevity of implants, especially considering the rising demand for dental restorations and the evolving expectations for long-term outcomes in oral rehabilitation.

Using graphene coatings on titanium implants in dental implantology offers a landscape characterised by innovation and various challenges. While the biocompatibility and strength of titanium are well-established [11], applying graphene coatings introduces new dimensions to explore. However, integrating such advanced materials into clinical practice is more complex due to their complexity. Moreover, the variability in outcomes necessitates extensive, well-designed studies to ascertain their effectiveness and safety [12]. Similarly, patient-specific factors like bone density and immune responses must be considered, adding complexity to this field [13]. Nevertheless, the potential benefits, such as enhanced osseointegration and reduced infection risks, are significant and warrant further investigation.

Continuing the exploration, the critical analysis of the usage of graphene coatings on titanium dental implants requires a balanced approach. On the one hand, these coatings have shown promise in improving implant characteristics like biocompatibility and antibacterial properties [14,15]. On the other hand, the challenges associated with their clinical application, including potential cytotoxicity and long-term stability, cannot be ignored [16]. Furthermore, the technological and economic aspects of manufacturing and applying these coatings must be considered. Despite these challenges, the potential for improved patient outcomes and longevity of implants makes this a vital area of research. Therefore, ongoing studies and clinical trials are essential to fully understand the benefits and limitations of graphene-coated titanium implants in dental applications.

In addition, understanding the essential nature and characteristics of graphene is crucial before exploring its derivatives as innovative coatings for dental implants. Graphene, a material that has revolutionised many fields of science and technology due to its unique structural and functional properties, along with its derivatives graphene oxide (GO) and reduced graphene oxide (rGO), presents unique characteristics that make them potential candidates for dental implant coatings, albeit with specific considerations and challenges [17]. Graphene's superior mechanical strength and electrical conductivity could enhance the durability and functionality of dental implants. However, its application in a biological context, like dental implants, raises critical questions about biocompatibility and integration with natural tissue, which are crucial for implant success [18].

Furthermore, graphene oxide, produced by oxidising graphite, introduces oxygen-containing groups that increase hydrophilicity, a desirable trait for biomedical applications [19]. This modification improves solubility in biological environments and allows for chemical alterations to tailor the material for specific needs, such as promoting bone cell growth. Conversely, reduced graphene oxide, obtained by reducing GO, partly restores graphene's electrical and mechanical properties while maintaining some chemical reactivity due to residual oxygen functionalities. Yet, the incomplete removal of oxygen groups and structural defects might affect its performance and reliability as an implant coating [20]. Lastly, regarding current research, applications of graphene and its derivatives in dental implants are still mainly in the experimental stages. Although laboratory studies show promise, the transition to clinical use requires thorough investigation to address challenges such as long-term biocompatibility, the complexity of manufacturing implant coatings and ensuring consistent quality and safety. Therefore, while the theoretical advantages of graphene-based materials in dental implants are significant, their practical application remains an active research and development area.

Exploring the complexities of graphene coatings on titanium dental implants, it's crucial to understand the interplay between material science and biological response. Although graphene's unique properties, like high strength and electrical conductivity, offer significant potential for enhancing implant functionality, these advantages must be weighed against possible biological reactions [7]. Moreover, the interaction of graphene with surrounding tissues and its long-term stability within the body are critical factors to consider [7]. Despite promising in vitro results, the translation to clinical applications requires careful evaluation of biocompatibility and the immune response. Further, the economic and technological aspects of integrating graphene coatings in dental implantology must be considered. While the benefits of improved implant performance and patient outcomes are clear, the feasibility of widespread clinical adoption depends on the cost-effectiveness and manufacturability of these advanced materials [4]. Furthermore, although progressing, the current state of research still has gaps in understanding the long-term effects of graphene-coated implants in diverse patient populations [8]. Thus, ongoing research must focus on the scientific and clinical aspects and consider the practicality and accessibility of these advancements in dental healthcare.

In the evolving field of dental implantology, the integration of graphene coatings on titanium implants represents a significant shift. While titanium has long been the benchmark for dental implants due to its robustness and biocompatibility [9]. graphene coatings offer new prospects. However, the effectiveness of these coatings in enhancing osseointegration and minimising bacterial infections, which are common challenges with dental implants, is still under investigation. Furthermore, the unique interaction between graphene and bone tissue suggests potential improvements in implant longevity and patient outcomes [10]. The exploration of graphene coatings on titanium dental implants is a testament to the interdisciplinary nature of contemporary medical research. While the properties of graphene, such as high electrical conductivity and strength, are well-documented [7], their application in dental implantology is a relatively new endeavour. However, this venture is not without challenges, as the long-term biocompatibility and interaction of graphene with bodily tissues are still subjects of rigorous investigation [7]. Furthermore, the cost-effectiveness and manufacturability of graphene coatings in dental applications are critical factors that must be considered, balancing innovation with practicality [11].

In addition to the technological aspects, the clinical implications of using graphene-coated titanium implants must be considered. Although these coatings have shown potential in improving osseointegration and reducing infection risks[12], comprehensive studies are required to fully understand their impact on human health and implant success rates. Moreover, transitioning from laboratory research to clinical application requires careful consideration of regulatory standards and patient safety [13]. Thus, the journey of integrating graphene into dental implantology is a scientific challenge and an endeavour that requires careful navigation of the medical, technological, and ethical landscapes.

While titanium's biocompatibility and strength are well-established, graphene's unique properties, like high electrical conductivity and remarkable mechanical strength, offer new avenues for improving implant performance [14,15]. However, challenges exist in translating these laboratory findings into clinical practice, particularly concerning graphene's long-term biocompatibility and interaction with bodily tissues. Moreover, the cost and feasibility of manufacturing graphene-coated implants play a significant role in determining their practicality for widespread clinical use [11].

Continuing this exploration, the article critically evaluates the clinical implications of graphene-coated titanium implants. Although these coatings have shown potential in enhancing osseointegration and reducing infection risks [16], comprehensive studies are needed to fully understand their impact on human health and implant success rates. Furthermore, transitioning from laboratory research to clinical applications necessitates stringent adherence to regulatory standards and a focus on patient safety [17]. This critical analysis underscores the complex interplay of scientific innovation, clinical application, and ethical considerations in integrating graphene into dental implantology.

While combining graphene's mechanical and electrical properties with titanium's biocompatibility and strength offers significant advancements, translating these laboratory-based innovations into clinical settings presents multiple challenges[14,18]. Moreover, economical and practical considerations in manufacturing and applying graphene coatings must be carefully assessed to ensure their feasibility in dental practice[7].

The clinical implications of using graphene-coated titanium implants are critically analysed in the article. Although there is potential for improved osseointegration and reduced infection risks, comprehensive research is required to understand the long-term effects on human health and the overall success rate of implants[16]. Furthermore, adherence to regulatory standards and prioritisation of patient safety is essential in transitioning from laboratory to clinical application, highlighting the complex interplay between scientific advancements and ethical considerations in dental implantology[17].

This review meticulously examines the intricate relationship between material innovation, clinical outcomes, and the practicality of integrating graphene coatings on titanium dental implants. While research indicates that graphene can enhance implant performance and biocompatibility, translating these findings into a clinical setting involves navigating scientific, technological, and ethical challenges. Therefore, this scoping review aims to synthesise existing knowledge, critically examine gaps and frontiers, and answer the crucial question: "What is the current state of scientific evidence regarding the efficacy, safety, and practicality of graphene-coated titanium dental implants, and what future directions and unexplored territories exist in this field?" By addressing this question, the review intends to steer future research towards bridging the divide between laboratory discoveries and clinical applications, ultimately enhancing patient care in dental practice.

Materials and Methods

The Rationale for Conducting a Scoping Review

Although systematic reviews are traditionally seen as the gold standard in evidence synthesis, they may only be the most appropriate for some research questions, particularly in emerging fields like dental implantology [19]. In contrast, scoping reviews offer a broader, more comprehensive approach to exploring a wide spectrum of literature, which is especially useful when evidence is extensive and varied [20-26]. This methodology is particularly effective at synthesising a diverse array of empirical and theoretical evidence from many disciplines, which is crucial for our study of graphene coatings for titanium dental implant [27].

This scoping review evaluates the current literature on graphene coatings for titanium dental implants. Its goal is to identify gaps in the application of graphene in this field and direct future research towards maximising its unique properties in dental implantology. The scoping review methodology is essential in mapping the research landscape, providing a comprehensive overview of current knowledge, and identifying areas that lack information or that require further investigation. This approach not only synthesises the existing body of knowledge but also guides future research directions to address identified gaps strategically [28-33]. This scoping review adheres to the Preferred Reporting Items for Systematic Review and Meta-Analyses PRISMA guidelines [34]. The study's protocol was registered on the Open Science Framework OSF Project [u667348.ct.sendgrid.net]., ensuring transparency and replicability. Employing the Population/Problem, Concept, and Context PCC framework, this study systematically investigates the aspects related to graphene coatings in dental implantology. The PCC framework facilitates a structured and comprehensive approach to data collection and analysis, essential for thoroughly evaluating the current state of research in this innovative field.

The Scoping Review methodology utilised the PCC (Population/Problem, Concept, and Context) framework to ensure a focused and thorough approach. This framework emphasised antibacterial properties and cellular interactions, which significantly enhanced the rigour and comprehensiveness of the review. As a result, key research gaps in applying graphene coatings in dental implants were identified[33,35].

Eligibility criteria

The scoping review's eligibility criteria are designed to focus on graphene as a coating for titanium dental implants. It includes primary research such as in vitro models, animal studies, and clinical trials involving humans while emphasising peer-reviewed studies for scientific integrity. The review excludes studies not specifically addressing graphene coatings on titanium implants, non-experimental or observational studies, non-peer-reviewed materials like editorials, and studies not in English. This approach ensures a targeted and comprehensive evaluation, offering valuable insights into graphene coatings' efficacy and potential in dental implantology and guiding future research and clinical applications.

Quality Assessment.

A collaboration with a university librarian skilled in scoping literature reviews was formed to enhance the precision and comprehensiveness of the scoping review. Experienced researchers advised a broad initial literature search to capture a wide range of relevant articles, ensuring no significant research was missed. This was followed by applying specific inclusion and exclusion criteria during the title and abstract screening to refine article selection.

The review included a comprehensive search of the Ovid MEDLINE/R database covering publications from 1946 to August Week 5, 2023, using keywords related to dentistry, titanium implants, and graphene/graphite. The search extended to multiple databases including Embase, MEDLINE via Ovid, 'Dentistry and Oral Sciences', and CINAHL Plus via EBSCOhost, known for their extensive biomedical, dental, and oral health literature collections.

Additionally, citation mining of reference lists from selected studies was conducted to uncover any potentially missed relevant studies. This combined approach of database searches and citation mining ensured the inclusion of all pertinent studies on the use of graphene in dental implants.

Study selection.

In this scoping review, the initial phase of study selection commenced with a filtration process, wherein duplicate citations and studies not entirely in English were excluded. This was followed by thoroughly screening titles and abstracts against pre-established inclusion criteria conducted by reviewer NA. To ensure a comprehensive and unbiased assessment, a secondary screening was undertaken for all remaining full-text articles by three reviewers [NA, LO, TW]. This multifaceted approach aimed to maintain the integrity and objectivity of the review process. The screening procedure was methodical, beginning with evaluating titles and abstracts to ascertain their alignment with the predefined inclusion and exclusion criteria. One reviewer primarily executed this task, with selected papers undergoing an in-depth examination to confirm adherence to the criteria. A detailed analysis of the full-text versions was conducted Upon verifying that the titles and abstracts met the inclusion guidelines. Moreover, a second reviewer independently assessed 5% of the records to augment consistency and minimise bias in the selection process. Using EndNote and Rayyan as reference management tools facilitated efficient organisation and review of the selected articles. This meticulous process culminated in the identification of 39 pertinent articles. Initially, the search encompassed a broad range of dental implant materials. However, it was narrowed to focus exclusively on titanium implants, including CP and alloy types. This refinement led to a more focused and relevant selection of studies, with the final count being 18.

Furthermore, a systematic search strategy was implemented to ensure a thorough review of the literature, as illustrated in the study selection PRISMA flowchart (Figure 1). The initial search across various databases yielded a total of 1150 records. These were then methodically screened for duplicates, evaluated for eligibility based on the inclusion criteria, and reviewed for relevance. The final compilation of studies included in the review amounted to 18, each meeting the pre-established conditions for inclusion. The PRISMA flow diagram, depicted in Figure 1, provides a detailed visual representation of the study selection process. This flowchart is an essential tool for illustrating the comprehensive and systematic approach adopted in this scoping review.

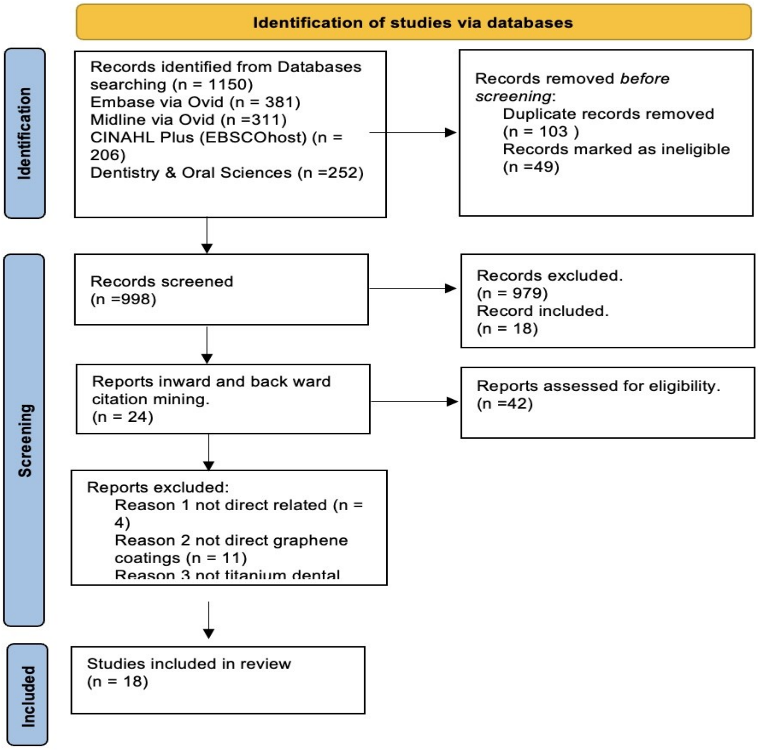

Figure 1. a PRISMA flowchart for the included studies.

Data extraction

The scoping review's methodological approach entailed a comprehensive data extraction and analysis process, crucial for ensuring the robustness and depth of the research findings. Initially, data were independently extracted by three reviewers [NA, LO, TW], with the process being guided by a pre-developed and pilot-tested data extraction file. This initial stage involved thoroughly examining relevant information from the chosen articles. Subsequently, supervisory team members [TW and LO] re-examined the extracted data from a representative sample of the studies to enhance accuracy and reliability. The data, once extracted, was systematically organised in Excel, providing a clear and accessible repository for the studies included in the review. Furthermore, the stages of data extraction, charting, and synthesis were conducted with careful attention to detail, ensuring a thorough and systematic analysis of the collated data.

Data Analysis and Synthesis

In the data analysis and synthesis phase, the information was first synthesised by reviewer NA and then rigorously checked by the rest of the research team. The findings from various studies on graphene coatings for dental implants were summarised in a narrative format, highlighting key findings, trends, and themes. To enhance the presentation of the results and make it more comprehensible, we utilised tables. This synthesis was closely aligned with the research objectives set out at the beginning, shedding light on the implications of these findings and pinpointing areas for future research endeavours.

This review evaluates current research on graphene coatings for titanium dental implants. It focuses on studying the different types of graphene coatings, like graphene oxide and reduced graphene oxide, their effects on biocompatibility, antibacterial properties, and success rates. The review considers in vitro and in vivo research and clinical trials. It also identifies research gaps, particularly in long-term studies and comprehensive clinical trials, providing a foundation for future research in implantology. The main objective of this review is to contribute to implantology by providing a comprehensive knowledge source that can guide future studies. Since graphene coatings have high strength, conductivity, and biocompatibility, so they are seen as a promising development in advancing dental implant technology. The review includes a detailed table that categorises current research based on the type of titanium implant and the specific graphene coating used, offering a summary and a guide for further research in this field.

Results

Table 1 shows that the overarching aims of the 18 studies were to inspect various aspects of graphene-coated titanium implants, ranging from their antibacterial properties to their impact on cellular behaviour and overall biocompatibility. Investigations by Ji, Kang, Cheng and their teams [20,36,37]. were designed to understand the initial antibacterial effects and cell interaction enhancements using novel surface techniques, focusing on in vitro assessments. Other studies took this further by incorporating in vivo elements, providing a broader perspective on the potential for clinical applications [38-40]. These studies aimed to evaluate the long-term implications of surface modifications on implants, such as thermal treatments to improve adhesion and the osteogenic impact of nano-modifications on bone integration.

Table 1 also presents that the study designs predominantly employed in vitro methodologies, as seen in the works of these studies [41-44]. Which allowed for precise control over experimental conditions to isolate the effects of graphene coatings on cell activity. However, several studies expanded their design to include in vivo experiments, such as those by Radunovic and Wang [44,45] utilising animal models to confirm the findings' applicability within a living organism. These in vivo designs are instrumental in confirming the potential translational impact of the in vitro findings. The studies indicate a rigorous methodological approach to validate the efficacy of graphene-coated dental implants, with a strong inclination towards combining in vitro analyses with in vivo models to ensure the robustness and reliability of the results.

Table 1: Overview of Research Objectives and Methodologies in 18 Dental Implant Studies.

Cited Study	Aim of the Study	Study Design
[20]	Assessed rGO coating's impact on human mesenchymal stem cells and implant bio-functionality.	In vitro
[26]	Investigated the influence of graphene coating on osteoblast maturation and biofilm formation.	In vitro
[36]	Investigated antibacterial effects, cell interactions, and differentiation enhancement on titanium implants using a novel surface technique.	In vitro
[37]	Developed a graphene oxide and antimicrobial peptide composite coating for titanium, studying its antibacterial properties.	In vitro

[38]	Explored the impact of thermal treatment on graphene sheets' adhesion and bioactivity on titanium, along with biocompatibility studies.	In vitro and in vivo
[39]	Examined the in vitro and in vivo effects of rGO coating on cellular behaviour and bone integration.	In vitro and in vivo
[40]	Explored nano-graphene oxide's impact on osteogenesis on titanium implant surfaces both in vitro and in vivo.	In vitro and in vivo
[41]	Explored the antimicrobial properties of graphene-coated Ti-6Al-4V against oral pathogens.	In vitro and in vivo
[42]	Evaluated graphene-coated titanium surfaces as potential antimicrobial agents.	In vitro
[43]	Evaluated the viability, cytotoxic response, and osteogenic differentiation of DPSCs on GO-coated titanium surfaces.	In vitro
[44]	Studied graphene-oxide coatings' effects on biofilm formation, material topography, and biocompatibility using zebrafish.	In vitro and in vivo
[45]	Investigated rGO as a biocompatible coating for dental implants to enhance soft tissue integration.	In vitro
[46]	Characterized the osteogenic potential of graphene-coated titanium both in vitro and in vivo.	In vitro and in vivo
[47]	Assessed the antibacterial activity of graphene-coated titanium disks against *Staphylococcus aureus*.	In vitro
[48]	Investigated antibacterial properties and cellular effects of modified titanium surfaces against *S. aureus* and *S. mutans*.	In vitro
[49]	Studied the effect of rGO coating on cell growth and osteogenic differentiation.	In vitro

Table 2 shows that the research studies spanned across multiple countries, with a notable concentration in Asia, indicating a regional interest in advancing dental implant technology. Research conducted in Korea focused on commercially pure titanium implants and employed graphene and reduced graphene oxide[20,36,39]. Similarly, studies from China utilised commercial pure titanium implants but varied their graphene coatings from CVD graphene to rGO and graphene oxide GO [38,45-48]. The trend of commercially pure titanium implants was consistent across these studies, pointing to a standard material choice for dental implant research within the region.

In contrast, research efforts in Singapore[26,42], as well as those spanning between the United States and Singapore[46], explored Grade IV commercial pure titanium implants, opting for graphene oxide and CVD-grown graphene coatings. Their investigations indicate a preference for higher-grade titanium and a similar inclination towards advanced graphene-related coatings. The use of Grade IV titanium suggests a focus on exploring the potential for enhanced durability and performance in dental implants.

European contributions, such as those from Italy and Poland[43,47-50], along with additional research from Singapore[51], deviated from using pure titanium implants by incorporating Ti-6Al-4V alloys. This choice may reflect a regional interest in exploring different titanium alloys' mechanical and biofunctional properties in dental applications. The coatings in these studies ranged from graphene nanoplatelets and graphene monolayers to graphene nanocoating (GN), indicating a diversity in research focus towards exploring various graphene forms and their interactions with titanium alloys.

Table 2 Categorization of Dental Implant Materials and Graphene Coating Types in 18 included Studies.

Cited Study	Location	Dental Implant Type	Graphene Coating Type
[20]	Korea	Commercial pure titanium implant	Reduced graphene oxide (rGO)
[26]	Singapore	Commercial pure titanium implant, Grade IV	Chemical Vapor Deposition CVD-grown graphene
[36]	Korea	Commercial pure titanium implant	Graphene Oxide
[37]	China	Commercial pure titanium implant	Graphene Oxide
[38]	China	Commercial pure titanium implant	Chemical vapor deposition (CVD)
[39]	Korea	Commercial pure titanium implant, Grade II SLA Ti	Reduced graphene oxide (rGO)
[40]	China	Commercial pure titanium implant, Grade IV	nano Graphene oxide (nGO)
[41]	China	Ti-6Al-4V alloy	Chemical Vapor Deposition CVD
[42]	Singapore	Commercial pure titanium implant, Grade IV	Graphene Oxide
[43]	Italy	Commercial pure titanium implant, Grade IV	Graphene oxide (GO)
[44]	Serbia	Commercial pure titanium implant	Graphene oxide (GO)
[45]	China	Commercial pure titanium implant	Reduced graphene oxide (rGO)
[46]	United States, Singapore	Commercial pure titanium implant, Grade IV	Chemical Vapor Deposition CVD-grown graphene
[47]	Italy	Titanium disk (sandblasted, acid-etched Ti)	Graphene nanoplatelets GNPs
[48]	China	Commercial pure titanium implant	Graphene oxide (GO)
[49]	China	Ti-6Al-4V alloy	Reduced graphene oxide (rGO)
[50]	Poland	Ti-6Al-4V alloy	graphene monolayers
[51]	Singapore	Ti-6Al-4V alloy	Graphene nanocoating (GN)

Time Points of Assessment

The assessment time points in the 18 studies under review varied significantly, reflecting the diversity of objectives and methodologies employed across this body of research see Table 2. Early time points ranged from immediate assessment to 48 hours, focusing on initial cellular responses like adhesion and gene expression [20,26,36]. These immediate to short-term assessments are critical for understanding the initial interactions between the graphene-coated implants and the biological environment. On the other end, some studies extended their evaluation period considerably, which spanned up to 8 weeks, allowing for the observation of long-term effects such as osteoinductive activity and osseointegration, a crucial factor for the success of dental implants[38,39].

The mid-range assessments, which took place from several hours to a week, provided insights into intermediate biological responses, such as cell proliferation and early antibacterial effects[37,41]. Studies adopted varied time frames, from several days to weeks, to observe both in vitro and in vivo responses, giving a comprehensive perspective on cellular activity over time[40,43,44]. Such a range of assessment periods, from short 2-hour incubations [41] to 8-day corrosion resistance evaluation[51], showcases the breadth of factors being considered when examining the efficacy and compatibility of graphene-coated dental implants. The diversity in time points underscores the complex nature of implant integration and the need for multiple time-based observations to understand the biomaterial performance fully.

Antibacterial Effect

The studies collectively demonstrate a strong emphasis on the antibacterial properties of graphene and its variants when coated on dental implants. A study found that Graphene Oxide (GO) was effective against *S. mutans* and *P. gingivalis*, bacteria commonly implicated in dental diseases[36]. Similarly, Strong antibacterial properties of GO, particularly when combined with antimicrobial peptides (AMPs), against the same pathogens were reported, indicating a potential synergistic effect [37]. The antibacterial activity of graphene-coated substrates against both Gram-negative and Gram-positive bacteria, specifically E. coli and S.

aureus, was also demonstrated, highlighting the broad-spectrum potential of graphene as an antibacterial coating [38] (see Table 2).

Further investigations into the antibacterial effects revealed that graphene coatings could inhibit biofilm formation, a crucial factor in dental implant success due to the role of biofilms in infection. Reduced biofilm formation by various oral pathogens on graphene-coated surfaces was noted [26,42,44]. This biofilm resistance was also observed where biofilm development was notably reduced [47]. Moreover, it was reported that the release of Ag ions from graphene coatings induced oxidative stress in bacteria, leading to a higher antibacterial rate [48]. Lastly, it was demonstrated that Graphene Nanoparticles (GN) could significantly decrease bacterial adhesion and biofilm formation, especially against S. mutans, providing an additional route for enhancing the antibacterial efficacy of implant surfaces[51]. Although varied in their specifics, these findings consistently underline the potential of graphene-related materials to provide antibacterial properties to titanium implants, which could lead to improved outcomes in dental applications.

Cellular Activity

As observed across the 18 studies, the cellular response to graphene-coated implants has been largely positive, indicating promising biocompatibility and potential for bone regeneration. Studies have shown that graphene coatings on titanium implants can significantly enhance osteoblast activity, improve cell adhesion, and promote osteogenic differentiation in various cell lines, including stem cells and osteoblast-like cells[36,38,40]. This is indicative of a conducive environment for bone growth and implant integration. These findings are supported by other work Fields[20,26] with reported enhancements in osteogenic differentiation and gene expression related to bone formation, which are critical factors for the success of dental implants (see Table 2).

Further reinforcing the biocompatibility of graphene coatings, it was found that such coatings were non-cytotoxic to human gingival fibroblasts and other cells, suggesting a safe interaction with the host tissue [37,42]. Observation indicates that nano-graphene oxide (nGO) modifications improved cell proliferation and were non-toxic to human mesenchymal stem cells and zebrafish embryos, a model organism Field[40,44]. The study highlighted a positive effect on metabolic activity in the short term [52-57], while it was suggested that potential anti-inflammatory benefits and improved biocompatibility are advantageous for implant success [51]. Collectively, these studies present a consensus that graphene and its derivatives can positively influence cellular activities related to the healing and integration process of dental implants.

Physicochemical Characteristics

The physicochemical characteristics of graphene-coated dental implants were extensively investigated across the 18 studies to understand how these properties affect biocompatibility and functionality. Techniques such as Atomic Force Microscopy (AFM), Raman spectroscopy, Scanning Electron Microscopy (SEM), and contact angle measurements were commonly employed. Studies utilised these techniques to assess water contact angles, surface energy, and topography, crucial parameters determining the hydrophilicity and potential cellular response of the implant surfaces [20,26,37]. Moreover, the presence and quality of graphene coatings were also confirmed using AFM and Raman spectroscopy, ensuring the consistency and reliability of the applied coatings [38,39] (see Table 2).

Further analysis of the surface properties provided insights into the wettability and biological interactions of reduced graphene oxide (rGO), which can influence protein adsorption and subsequent cell adhesion [37,45]. This understanding was expanded by examining surface roughness, a factor that can modulate cellular behaviour [40,44]. The assessment of the graphene further contributed to a comprehensive understanding of how these nanomaterials interact with their environment Field [28,29,33]. The precise evaluation of these physicochemical characteristics across the studies underscores the importance of a well-characterized implant surface for improved clinical outcomes.

Table 3 Characteristics of Included Studies in Scoping Review on Graphene -Based Coatings for Biomedical Applications

Cited Study	Time Points of Assessment	Antibacterial Effect	Cellular Activity	Physicochemical Characteristics
1.[20]	Immediate up to 21 days	Not detailed.	Enhanced osteogenic differentiation of hMSCs observed.	AFM analysis of water contact angle and surface energy.
2.[26]	Assessed at 24 and 48 hours	Lowered biofilm accumulation for E. faecalis and S. mutans.	No adverse effects on cell adhesion; promoted osteogenic differentiation.	AFM and contact angle measured surface topography and hydrophilicity.
3.[36]	From 24 hours up to 21 days	Graphene Oxide achieves antibacterial effects against S. mutans and P. gingivalis.	Significant increase in osteoblast activity.	Water contact angle and thickness were assessed post-treatment.
4.[37]	From 24 hours to 7 days	Strong antibacterial properties against S. mutans and P. gingivalis with GO and AMPs.	GO coating with AMPs was biocompatible and non-cytotoxic.	FESEM, Raman, FTIR, and nano-scratch tests were used.
5.[38]	From 24 hours to 8 weeks	Active against E. coli and S. aureus.	Improved cell adhesion and osteogenic activity in stem cells.	AFM and Raman spectroscopy confirmed graphene presence.
6.[39]	In vitro and in vivo from 1 day to 8 weeks	Not detailed.	Better effects on cell attachment and osteogenic gene expression.	Various techniques assessed rGO-coated implants.
7.[40]	In vitro at 4, 7, and 14 days; in vivo at 2 to 6 weeks	Not detailed.	nGO-modified surfaces improved proliferation and bone formation.	FE-SEM
8.[41]	After 6 and 12 hours of culture	Not detailed.	rGO showed improved fibroblast adhesion and gene expression.	Examined wettability and biological properties of rGO.

9.[42]	Evaluated after 24 hours	Inhibited biofilm formation of oral pathogens on graphene.	Cytocompatible with human gingival fibroblasts.	Raman spectroscopy and AFM analyzed the coating.
10.[43]	3, 7, 14, 21, and 28 days for metabolic activity	Not specified	The positive short-term effect on DPSCs metabolic activity	Surface roughness examined with AFM and SEM, GO presence confirmed by Raman
11.[44]	Zebrafish at 6 and 36 hpf, bacterial assessments at 24 h and five days	Significant antibiofilm effect against oral bacteria	GO coatings were biocompatible with hMSCs and non-toxic to zebrafish embryos	Surface topography, roughness, and wettability were evaluated using SEM, AFM, and contact angle
12.[45]	Microbial incubation for 2 hours, Candida for 24 hours	Reduction in bacterial and fungal pathogens	Not specified	Explored surface roughness, wettability, and elemental composition
13.[46]	Bone formation at 4 and 8 weeks, gene expression at 1, 2, 3, and 5 days	Not specified	Increased genetic expression for osteogenesis in MG-63 cells	Assessed surface roughness, wettability, and elemental composition
14.[47]	24 and 48 hours post bacterial inoculation	Reduction in biofilm development only	Not specified	The size of GNPs and coverage percentage evaluated
15.[48]	Ag ion release is monitored every 24 h for up to 7 days	Higher antibacterial rate with Ag ions causing oxidative stress to bacteria	No significant effect on HGFs cell morphology	Surface topography and chemical composition were analyzed using AFM and other techniques.
16.[49]	Various evaluations from 1 to 14 days of culture	Not specified	Enhanced osteogenic differentiation and proliferation in MC3T3-E1 cells	Surface properties after coating were analyzed using SEM, EDS, XPS, and BET

17.[50]	Prior to polarization experiments, immersion for 1 hour	Not applicable	Not specified	Investigated mechanical and corrosion properties using Raman, XPS, and hardness tests
18.[51]	Over 8 days for corrosion resistance	GN reduced bacterial adhesion and biofilm formation, particularly against S. mutans	Potential in reducing inflammation and enhancing biocompatibility with macrophages	Detailed GN structural characteristics were assessed using Raman and AFM

The limitations identified in the 18 studies reveal common challenges and gaps in the research on graphene-coated dental implants, primarily centred around the scope of biological models and the depth of investigations conducted. Many studies
were restricted by their in vitro nature, lacking in vivo validations crucial for assessing clinical applicability [20,36,37]. This limitation was echoed across multiple studies, where the absence of in vivo experiments potentially limits the understanding of the implants' behaviour in a living organism [41,42,47]. A standard limitation was the narrow focus on specific bacterial species or cell types, which may not fully represent the complex interactions in human oral environments [48,51].
Furthermore, several studies did not explore the long-term effects of graphene coatings, an essential aspect of dental implant success[38-40]. The need for more diversity in investigating different graphene parameters, such as thickness and concentration, was noted in some research potentially limiting the understanding of how varying graphene modifications could impact implant performance[20,26,43]. Further studies also faced limitations due to their short-term scope and simplified models that might not adequately replicate the complexities of human oral conditions [41,50]. These limitations highlight the need for more comprehensive, long-term, and clinically relevant studies to understand and optimise the use of graphene-coated dental implants fully.

Discussion:

The aim of this scoping review is to explore the range of graphene coatings applied to titanium dental implants and their influence on implant properties such as biocompatibility and antibacterial effectiveness. This investigation is crucial in synthesising current research findings to enhance our understanding of graphene's role in dental implantology and pinpoint areas for future research. The review delves into the key themes and findings from 18 pivotal studies, offering a comprehensive overview of this field's current state of knowledge.

The primary findings from these studies reveal a significant focus on the antibacterial properties and biocompatibility of graphene-coated implants, as evidenced by recent research [20,36,37]. These studies predominantly utilised in vitro methods, providing a controlled environment to understand the initial interactions between graphene coatings and biological tissues. However, there is a probability that these findings, while promising, may only partially reflect the complexity of in vivo conditions. Studies incorporated in vivo elements to assess these coatings' long-term effects and clinical applicability, suggesting a potential enhancement in implant performance due to graphene application [38,39]. Including in vivo elements signifies the growing importance of extending laboratory findings to real-world applications [44,45]. Theoretically, these findings underscore the promise of graphene coatings in enhancing dental implant efficacy, potentially leading to improved patient outcomes.

Practically, integrating these findings into clinical settings could revolutionise implantology by offering implants with superior biocompatibility and antibacterial properties, thus reducing the likelihood of implant failure and infection.

The scope of research encapsulated in this review highlights a strong regional focus, particularly in Asia, on enhancing dental implants through graphene coatings. The works of researchers from Korea and China underscore a consistent preference for commercially pure titanium implants paired with various graphene derivatives like graphene oxide and rGO [20,36]. This trend reflects a shared regional interest and underscores the likelihood of these materials becoming a standard in dental implant technology in these regions.

On the other hand, research from Singapore and the collaboration between the United States and Singapore suggest a shift towards Grade IV titanium implants, possibly indicating a desire for implants that offer enhanced durability [26,42]. This inclination towards higher-grade materials, coupled with advanced graphene coatings, opens the possibility of developing superior-quality implants tailored for longevity and performance.

Meanwhile, European studies and additional research from Singapore diverge from this path, opting for Ti-6Al-4V alloys. This variation in material choice might indicate a regional inclination towards exploring different mechanical and bio functional properties of titanium alloys[43,47,51].

From a theoretical standpoint, these diverse research endeavours suggest that different regions are exploring various possibilities in implant material and coating technologies. Practically speaking, this could lead to a range of region-specific dental implant solutions, each optimised for distinct clinical needs and preferences. The use of various graphene forms, from nanoplatelets to nanocoating, indicates a potential for creating customised implant surfaces with tailored properties, thus expanding the horizons of implant dentistry globally.

Time Points of Assessment

In exploring time points of assessment across various studies on graphene-coated dental implants, a significant variance was observed, shedding light on the multifaceted nature of implant research. The initial phases of assessment, concentrated on the immediate to 48-hour post-implantation period, are crucial for evaluating primary cellular responses like adhesion and gene expression [20,26,36]. This early-stage evaluation is essential as it provides initial insights into how the biological environment interacts with graphene coatings. In contrast, some studies broadened their horizon to include evaluations up to 8 weeks, offering a lens into the long-term effects critical for implant success, such as osseointegration and osteoinductive activity [38,39]. These extended periods of observation could unveil deeper insights into the longevity and effectiveness of the implants.

Mid-range assessments spanned from hours to a week, bridging the gap between immediate cellular reactions and long-term implant integration by providing a glimpse into cell proliferation and initial antibacterial effects [37,45]. Interestingly, the studies with their varied assessment periods ranging from several days to weeks, present a more comprehensive view, encompassing both in vitro and in vivo responses [40,43,44]. This variety in evaluation periods, from the brief incubations to the extended analysis [41,51], demonstrates the complexity of assessing graphene-coated dental implants' efficacy and compatibility. Such diversity in time frames suggests a potential for different stages of implant integration to exhibit unique responses to graphene coatings, implying a possibility for more nuanced and compelling implant treatment protocols. Theoretically, this highlights the potential for tailor-made treatment plans based on specific time-dependent biological responses. At the same time, practically, it suggests an opportunity to enhance the overall success rate and effectiveness of dental implants in clinical settings.

Antibacterial Effect

The collective findings from various studies underscore a significant emphasis on the antibacterial properties of graphene and its derivatives when applied to dental implants. Notably, studies discovered that Graphene Oxide (GO) exhibited antibacterial solid effects against pathogens like *S. mutans* and *P. gingivalis*, commonly associated with dental infections [36,37]. This suggests a potential for graphene coatings, mainly GO, to significantly enhance dental implants' antibacterial capabilities. One included study by Gu expanded this understanding by demonstrating the effectiveness of graphene coatings against a broader spectrum of bacteria, including Gram-negative and Gram-positive strains like *E. coli* and *S. aureus* [38]. This finding highlights the versatility of graphene as a broad-spectrum antibacterial coating.

Further exploration into graphene's antibacterial effects revealed its potential to inhibit biofilm formation, a critical aspect considering the role of biofilms in implant infections. Studies observed a notable reduction in biofilm formation on graphene-coated surfaces, indicating graphene's efficacy in preventing bacterial colonisation [26,42,44]. Additionally, a study reported that Ag ions released from graphene coatings induced oxidative stress in bacteria, enhancing the antibacterial rate [48]. A recent study found that Graphene Nanoparticles (GN) could significantly reduce bacterial adhesion and biofilm formation, particularly against S. mutans[51]. These findings collectively suggest a high likelihood that graphene coatings can substantially improve the antibacterial properties of dental implants. Theoretically, this could lead to a significant reduction in implant-related infections. At the same time, practically, it could enhance the overall success and longevity of dental implants in clinical settings, offering a promising avenue for future dental implant technologies.

Cellular Activity

The cellular response to graphene-coated implants, as demonstrated in the 18 studies, has generally been positive, showcasing promising biocompatibility and potential for bone regeneration. Research highlighted that graphene coatings significantly enhance osteoblast activity, improve cell adhesion, and promote osteogenic differentiation in various cell lines, including stem cells and osteoblast-like cells [36,38,40]. These findings suggest a favourable environment for bone growth and implant integration. Similarly, some studies supported these observations, noting enhancements in osteogenic differentiation and gene expression, which are crucial for dental implant success [20,26].

Further affirming graphene's biocompatibility, researchers discovered that graphene coatings were non-toxic to human gingival fibroblasts and other cell types, indicating a safe interaction with host tissues [37,42]. Other studies observed that nano-graphene oxide (nGO) modifications not only improved cell proliferation but were also non-toxic to human mesenchymal stem cells and zebrafish embryos used as model organisms[40,44]. Carlo highlighted a positive impact on short-term metabolic activity[43], while Rosa [51] proposed potential anti-inflammatory benefits and enhanced biocompatibility. These findings collectively suggest a high likelihood that graphene and its derivatives can positively affect cellular activities crucial for the healing and integration process of dental implants. Theoretically, this indicates a potential for improved healing and integration of implants. At the same time, practically, it suggests that graphene-coated implants could be a game-changer in clinical applications, potentially enhancing the success and longevity of dental implants.

Physicochemical Characteristics

In dental implant research, the physicochemical characteristics of graphene-coated implants have been a focal point, as evidenced by the thorough investigations in the 18 studies reviewed. Employing techniques like Atomic Force Microscopy (AFM), Raman spectroscopy, Scanning Electron Microscopy (SEM), and contact angle measurements, studies have meticulously assessed water contact angles, surface energy, and topography. These characteristics are pivotal in determining the implant surfaces' hydrophilicity and potential cellular response [20,26,36]. Additionally, different research has validated the presence and quality of graphene coatings, ensuring the coatings' consistency and reliability [38,39].

Further exploration into surface properties shed light on the wettability and biological interactions of reduced graphene oxide (rGO), crucial factors that can affect protein adsorption and cell adhesion [37,45]. Research has broadened this perspective by examining surface roughness, a significant factor influencing cellular behaviour [40,43,44]. Moreover, assessing elemental composition and structural characteristics added depth to our understanding of how these nanomaterials interact within their environment [46,47,51]. These comprehensive evaluations highlight the importance of well-characterized implant surfaces, suggesting the probability of improved clinical outcomes with finely tuned physicochemical properties. Theoretically, this attention to detail in surface characterisation could lead to implants better suited for human use. At the same time, it implies that such enhancements in implant design could significantly improve patient outcomes in dental implantology.

The strengths and the limitations.

The strengths of this scoping review are multifaceted. Firstly, it provides a comprehensive aggregation of current research on graphene-coated dental implants, which is beneficial for synthesising a broad spectrum of data into a singular narrative. The review offers a global perspective on the subject by collating studies from various geographical regions and methodologies. This wide-ranging approach ensures a holistic understanding of the topic, contrasted with narrow, focused studies. Additionally, the review serves as a valuable resource for researchers and practitioners in dental implantology, offering insights into the latest trends and advancements. It highlights key areas where graphene coatings have shown potential, like improving biocompatibility and antibacterial properties, thus facilitating the identification of future research avenues and clinical applications.

However, the review has its limitations. One significant constraint is the reliance on published studies, which may inherently contain biases or limitations, as noted in their respective methodologies. This reliance could skew the overall findings of the review despite efforts to present an unbiased overview. Moreover, while comprehensive, the scope of the review might not encompass all existing studies on the topic, particularly those published in languages other than English or less accessible journals. This could lead to a potential underrepresentation of specific research perspectives or findings.

Additionally, the review's synthesis of data from various studies, while providing a broad overview, might overlook specific nuances or detailed findings of individual studies. Lastly, the dynamic nature of research in graphene applications means that newer studies or emerging technologies might not be included, which could impact the review's currency and relevance over time. Despite these limitations, the review is a substantial contribution to the field, offering a consolidated view of current research while acknowledging areas for further exploration and improvement.

The Implications

The findings from the 18 studies in this scoping review collectively point towards significant theoretical and practical implications in dental implantology. Theoretically, the demonstrated efficacy of graphene coatings in enhancing the biocompatibility and antibacterial properties of dental implants paves the way for new understanding in biomaterial science. With its unique properties, this implies that graphene could redefine the standards for implant surface modifications, encouraging a shift towards materials that actively promote osseointegration and reduce infection risks.

Practically, applying graphene coatings on dental implants could revolutionise patient care in dentistry. Enhanced biocompatibility and reduced infection rates could lead to higher success rates of implant surgeries, improved patient outcomes, and potentially shorter recovery times. However, these benefits are not without challenges, as the review also highlights the necessity of in vivo studies and long-term evaluations to fully comprehend the implications of graphene coatings in real-world clinical settings.

Recommendation for future studies

For future research, a primary suggestion is to conduct a systematic review that delves deeper into the specificities of graphene's interactions with dental implant surfaces. Such a review should consolidate findings from both in vitro and in vivo studies, providing a more nuanced understanding of graphene's role in various biological environments. Additionally, there is a need to explore the long-term effects of graphene coatings on implants, mainly focusing on the durability of the coatings and their long-term impact on osseointegration and antibacterial efficacy. Moreover, future studies should investigate the varying graphene formulations and their specific interactions with different types of titanium alloys used in dental implants. Understanding these interactions at a molecular level could lead to more targeted and effective implant surface treatments. Lastly, it is imperative to conduct a systematic review to identify and confirm gaps in the current literature. Such a review would not only validate the findings of this scoping review but also provide a clear direction for future research endeavours, ensuring continued advancement in dental implantology.

Bridging Knowledge Gaps: A Systematic Review on Graphene Coated Dental Implants

Building on the scoping review, a crucial research question emerges: "What are the comparative effects of different graphene coatings on the osseointegration, biocompatibility, and antibacterial properties of titanium dental implants in both in vitro and in vivo settings?" This inquiry is pivotal, as it seeks to compare various graphene coatings, including graphene oxide and reduced graphene oxide. Unlike the previous review, this question delves into a comprehensive range of implant characteristics. Significantly, it focuses on osseointegration, essential for implant stability; biocompatibility, crucial for patient safety; and antibacterial properties, vital to prevent postoperative infections. By examining both in vitro and in vivo studies, this systematic review aims to bridge the gap between controlled experiments and real-world clinical applications. Thus, the findings could provide essential insights, potentially guiding future research and clinical practices in dental implantology, ultimately enhancing patient care and treatment outcomes.

Conclusion

In conclusion, this scoping review has systematically gathered and examined research on graphene-coated dental implants, focusing on understanding their biocompatibility, antibacterial properties, and overall effectiveness. The review has revealed that graphene, in its various forms, like graphene oxide and reduced graphene oxide, appears to enhance the performance of dental implants significantly. Particularly, it has been shown to improve osseointegration, offer superior antibacterial effects, and ensure better cell adhesion. Additionally, the findings indicate that while most studies have relied on in vitro assessments, there is a growing trend of incorporating in vivo methods to validate these results. This approach is crucial as it bridges the gap between laboratory research and clinical application, enhancing the understanding of how these innovations could translate into real-world dental care. Moreover, the geographic diversity of the studies underscores a global interest in advancing dental implant technologies yet also highlights varying regional focuses in research methodologies and material choices.

Importantly, this review has identified gaps in the current research landscape, particularly in long-term studies and comprehensive in vivo analyses. These gaps present opportunities for future research, suggesting the need for a systematic review to further explore and compare the effects of different graphene coatings. Ultimately, this scoping review not only enhances our understanding of graphene-coated dental implants but also sets the stage for future investigations that could revolutionize dental implantology and patient care.

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