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# Advances of graphene nanoparticles in dental implant applications – A review



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#### ABSTRACT

Nanoparticles have shown significant potential in dental implants as they have distinctive properties and potential benefits. They have distinct physicochemical features that differ from their bulk equivalents. These characteristics make nanoparticles highly appealing for application in commercial and medical research. The main objective of nanotechnology research and development is to advance overarching social goals, including enhancing human potential and pushing the limits of environmentally sound growth. Considering this, graphene nanoparticles are rapidly overtaking other nanostructures as the favoured option for contemporary biomedical applications. This paper reviews the significance of nanoparticles in various fields and critically examines the importance of graphene nanoparticles in dental implant applications. It also discusses techniques for graphene synthesization and characterization. Additionally, it featured multiple applications of graphene in dental implants along with the present difficulties and potential outcomes. Numerous potential applications in dentistry research exist for this highly adaptable nanotechnology. Due to its distinctive characteristics and possible advantages, graphene nanoparticles have demonstrated promise in dental implants.

#### 1. Introduction

The spectrum of nanoscale atoms used in nanotechnology, which ranges from 1 to 100 nm, makes it an essential 21st-century technology [1–4]. It has made many research projects in various fields, such as chemistry, physics, medicine, and other areas, possible [5]. Nanoparticles have proven distinct catalytic, thermal, optical, electrical, and biological properties used in various industries due to their high surface energy, large surface area-to-volume ratio, and comparatively tiny size compared to bulk material [6]. Although nanoparticles of the same substance have a higher surface-to-volume ratio (per unit mass), they are more reactive. The laws of quantum physics apply to particles smaller than 50 nm [7,8].

Regarding scientific knowledge and practical uses, nanoparticles are currently in the most advanced stage [9]. Nanoparticles' size-dependent physical and chemical properties led to their investigation 10 years ago [10]. They are now in the commercial exploring phase [11,12].

Nanotechnology is leading the rapid development of healthcare goods because of its numerous potential advantages and risks to human health [13]. In particular, compared to its competitors, graphene nanotechnology has exhibited long-term clinical success from the start of the study period. Some essential characteristics include the significant mechanical strength, high surface area, and superior electrical conductivity of graphene nanoparticles [14]. The primary distinctions between micro and graphene oxide nanoparticles are their size, surface area, dispersion behavior, and potential applications [15]. Nanoparticles are more useful candidates for cutting-edge applications in a variety of fields because they generally have advantages in terms of reactivity [16], dispersion [17], and biological interactions [18].

Graphene nanoparticles in dental implants improve biocompatibility by promoting osseointegration through improved cell adhesion [19] and proliferation [20], ensuring the implant's stability and longevity. Additionally, they lower inflammation and promote tissue regeneration, which promotes healing and enhances functional and aesthetically

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Abbreviation: NPs, Nanoparticles; GO, Graphene Oxide; ZnO, Zinc Oxide; ZrO<sub>2</sub>, Zirconium Dioxide; TiO<sub>2</sub>, Titanium Dioxide; AgNPs, Silver Nanoparticles; SiO<sub>2</sub>, Silicon Oxide; H<sub>2</sub>O<sub>2</sub>, Hydrogen Peroxide.

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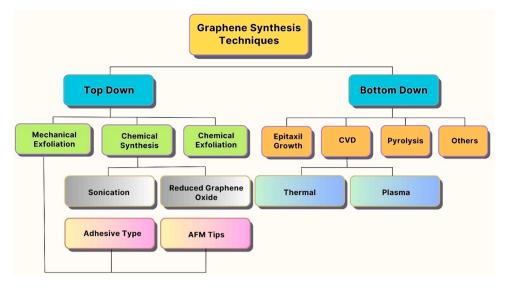


Fig. 1. An illustration of the Graphene production types.

pleasing results [21]. By limiting bacterial growth, reducing the chance of complications, and averting peri-implantitis, the inherent antibacterial properties of graphene nanoparticles improve biocompatibility in dental implants [22].Additionally, Graphene-doped poly(methyl-methacrylate) materials have been identified as beneficial to enhancing dental implants' biocompatibility and mechanical characteristics [23].

Using graphene nanoparticles in dental implants has several significant advantages, one of which is that they can enhance the osseointegration of the implant with the surrounding bone tissue [24]. This is so that the implant can be firmly secured in place. Graphene nanoparticles can induce the creation of new bone tissue [25]. Dental implants made of graphene nanoparticles are a unique and intriguing area of study that could significantly increase the success rates of these treatments and lower the risk of problems like infection and implant failure. Despite several disadvantages and potentially hazardous circumstances, research on this phenomenon is highly dependable.

Graphene nanoparticles possess remarkable biological properties that render them highly suitable for augmenting dental implant materials. These materials' distinctive two-dimensional configuration and biocompatible nature facilitate effective integration with adjacent bone tissue, expediting the healing process and mitigating the likelihood of implant rejection [26]. In addition, the exceptional electrical conductivity of graphene has the potential to further the progress of smart implants, enabling the real-time monitoring of oral health and the status of implants [27]. As scientists continue to explore the utilization of graphene nanoparticles for biomedical purposes, the prospective advancements in dental implant technology hold great promise. These advancements can provide patients with tooth replacement options that are more resilient, effective, and compatible with biological systems [28].

The process of osseointegration in dental implants, which incorporates graphene nanoparticles, is a complex phenomenon that occurs in several distinct phases. At the outset, following the introduction of graphene nanoparticles into the body, their notable characteristics, such as a substantial surface area and compatibility with biological systems, contribute to the prompt formation of blood clots and the attraction of inflammatory cells to the location of the implant. This denotes the primary inflammatory phase, wherein the human body initiates the process of healing [29]. In the subsequent phase, known as the proliferative phase, the utilization of graphene nanoparticles facilitates the adhesion and proliferation of osteoblasts, thereby stimulating the development of fresh bone tissue near the implant [30]. Ultimately, in the final phase, the utilization of graphene's conductivity can contribute to preserving a consistent bone-implant interface, thereby enhancing the long-term effectiveness of the implant [31].

This paper focuses on the critical discussion of graphene for dental implant applications. It reviewed the importance of NPs in different fields. In addition, characterization methods and graphene fabrication strategies were covered in this study. The uses of graphene in various dental implant applications have also been addressed. Furthermore, the discussion has focused on current challenges and prospects.

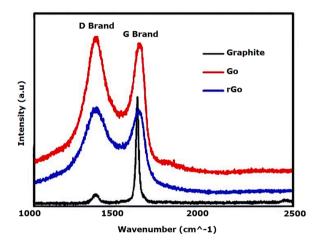
# 2. Synthesis approaches of graphene nanoparticles

Graphene Oxide is regarded as a highly promising nanomaterial due to its exceptional physical and chemical properties. In a recent study, Inchingolo et al. [32] inferred that graphene coatings can significantly enhance osteogenic differentiation in bone marrow mesenchymal stem cells when cultured in vitro. This effect is likely achieved by regulating the FAK/P38 signaling pathway. Furthermore, these coatings can promote the integration of dental implants within living organisms. Nevertheless, additional research is required to substantiate these potential applications, particularly in the context of human subjects. The study observed that incorporating surface roughness through graphene oxide (GO) coatings on implant surfaces exhibited stability and non-reactivity and promoted favourable cellular processes such as adhesion, diffusion, and proliferation. Utilizing GO in implant veneers shows promise in addressing multiple significant concerns. Two major factors contributing to implant failure are the presence of germs on the tissues surrounding the implant and the antibacterial properties of graphene oxide. Moreover, several studies have demonstrated that Graphene Oxide (GO) can facilitate the process of osseointegration. Additionally, graphene oxide (GO) can effectively bind biomolecules and active ingredients, potentially enhancing osseointegration and expediting healing. According to Inchingolo et al., its recovery at graphene oxide (GO) coatings shows considerable potential in maintaining a favourable equilibrium between a coated dental implant's ability to inhibit biofilms formation and stimulate a beneficial cellular reaction [32]

Typically, the covalent functionalization of graphene involves sharing  $sp^2$  orbitals and their conversion to  $sp^3$  hybridized orbitals. This process significantly impacts the graphene material's local symmetry and electronic structure [33]. In addition to utilizing covalent functionalization, the non-covalent approach has garnered attention in bio-application. Specifically, the formation of polymer/graphene nanocomposites is often the focus of interest in this context. As

#### Brief Top-down Graphene History [42].

Method	Typical dimension	Lateral	Advantage directly from graphite	Disadvantage	References
Exfoliation using microtechnology Graphite is sonicated directly.	Few layers layers, both single and numerous	lm to cm lm or sub- lm	Large-scale, unaltered graphene sheets affordable, unaltered graphene	tiny scale production Separation; low yield	[43] [44,45]
Graphene is functionalized or exfoliated electrochemically.	few and just one layer	500–700 nm	Functionalized graphene's high electrical conductivity; one-step functionalization and exfoliation	Ionic liquids' price	[46]
Super acids dissolve graphite.	primarily one layer	300–900 nm	Scalable, unmodified graphene	Hazardous chlorosulfonic acid use and the price of acid cleanup	[46]



**Fig. 2.** Graphite, Graphene Oxide, and Reduced Graphene Oxide were all given Raman spectra readings [63].

previously discussed, the potential mechanisms underlying the interaction between graphene and polymeric compounds include Van der Waals forces,  $\pi$ - $\pi$  interaction, electrostatic interactions, and chemical binding. The interaction between graphene and polymers is primarily governed by the combination of Van der Waals forces and other interactions, which arise due to the unique structure of graphene. Furthermore, polymers containing  $\pi$ -bonds, such as polyvinyl alcohol (PVA) and polymethyl methacrylate (PMMA) [34], are capable of engaging in  $\pi$ - $\pi$  interactions with graphene [35]. The stability of graphene is enhanced by non-covalent interactions, which also contribute to improving its thermal, electrical, and mechanical properties [36–38]. Graphene nanosheets have the potential to enhance the bioactivity, mechanical, and thermal properties of bioceramics and metallic structures, similar to the way polymers do [39].

Nanoparticles in medicine require producing particles with different shapes, monodispersity, chemical compositions, and sizes [40]. Top-down and bottom-up methodologies can categorize the many methods utilized to generate the nanoparticles [41].Graphene productionusesvarious synthesis methods, such as chemical vapor deposition, liquid phase exfoliation, liquid phase growth, mechanical exfoliation, epitaxial growth, and electrochemical exfoliation. Graphene made in various ways can have various advantages and disadvantages depending on how it is used [42].Fig. 1 shows some Synthesis process of Graphene Nanoparticles.

#### 2.1. Top-down techniques

In a top-down technique, graphite or graphite derivatives like graphite oxide (GO) and graphite fluorides are separated from one another or exfoliated to create graphene or modified graphene sheets. A researcher's contribution might be inferred from Table 1. Using topdown approach, precision like graphite is broken down into only one atom thick layers. Graphite is transformed into graphene using mechanical exfoliation, chemical exfoliation, and chemical synthesis [42].

# 2.2. Bottom-up techniques

Atoms and molecules are used in bottom-up approaches to building larger-featured objects through additive processes [47]. By heating hydrocarbon gasses like methane to roughly 1000 °C, bottom-up manufacturing includes growing sheet graphene on a metal substrate like copper or nickel foil. The catalytic function of the metal substrate facilitates the separation of hydrogen and carbon. When this carbon is depleted on the metal substrate, it forms the graphene sheet by self-assembling [48]. The bottom-up approach allows the graphene layer thickness to be managed by applying various surface catalysts and growth criteria [49]. Atomic control over the geometry of the materials, including edge state, defects, size, and other elements, is possible when fabricating graphene nanoribbons (GNRs) from the bottom up [50].

# 2.3. Others

Other processes for making graphene include thermal fusion of PAHs [51], graphite arc discharge [52], PMMA nanofibres exposed to an electron beam [53], and nano-diamond conversion [54]. Arc discharge in an H2 atmosphere can produce graphene in two to three layers with flake sizes between 100 and 200 nm [55]. Mechanical exfoliation and CVD are two techniques that can result in high-quality graphene [56].

# 3. Characterization approaches of graphene nanoparticles

An essential component of research and examination into graphene is its characterization. Graphene's shape, characteristics, flaws, and layers are investigated through characterizations using spectroscopic and microscopic observations [57]. Characterization methods include atomic force microscopy (AFM), scanning electron microscopy (SEM), transmission electron microscopy (TEM), X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS), Mossbauer spectroscopy, Raman spectroscopy, and UV–visible spectroscopy [58].

#### 3.1. Raman spectroscopy

Raman spectroscopy is commonly employed to investigate graphene's structure and electrical properties [59]. Raman spectroscopy is performed on graphene, and a few review articles on the optical phonon spectrum and the Raman graphene spectrum have been released [60]. Graphene's molecule vibration reacts with monochromatic Raman spectroscopic radiation to cause a scattering change in the radiation [61]. In graphene, three primary peaks can be seen: the D, G, and 2D elevations. The D point can observe an irregularity in sp<sup>2</sup> hybridization at 1350 cm [62].Fig. 2 illustrates the Raman spectra readings of Graphite, Graphene Oxide, and Reduced Graphene Oxide.

# 3.2. X-ray diffraction (XRD)

The primary purpose of the X-ray diffraction technique is to

determine the material's phase using units of cell dimension [64]. X-ray diffraction (XRD) examinations of powder were done using a Bruker D8 Advance diffractometer with Cu KR radiation. The 2 points between 2.1° and 2.2° for which the diffraction measurements were collected [65]—Fig. 2 implies graphite, graphite oxide, and graphene XRD patterns. Graphite exhibits a distinct and significant diffraction point at 26.6°. Although oxygen molecules are present, the apex moves to 13.3°. There is no peak following manufacturing, suggesting that graphene was produced synthetically [66].

# 3.3. X-ray photoelectron spectroscopy (XPS)

The elemental compositions of graphene-emitter surfaces or functionalized graphene can be investigated using the XPS method to fully comprehend the surface chemical states directly related to their electrical properties [64–67].

# 3.4. Mossbauer spectroscopy

Mossbauer spectroscopy can effectively determine nanomaterials' magnetic characteristics and phase makeup based on iron oxides. Because of their comparable spinel crystal structures, magnetite  $Fe_3O_4$  and maghemite  $Fe_2O_3$  are particularly challenging to distinguish by structural techniques, mainly when the sample contains a combination of various phases [68].

# 3.5. Transmission electron microscope (TEM)

TEM is the method most frequently employed in graphene's layer count and structural structure research. When the electron beam engages the object of investigation, TEM pictures are created [69].

# 3.6. Fourier transform infrared analysis (FTIR)

Thermo Nicolet iS10 instrument, manufactured by Thermo Fisher Scientific, Madison, Wisconsin, USA, was used to capture the FTIR spectra of GO and GO-AgNPs. (ATR) [70].

## 3.7. Scanning electron microscopy (SEM)

Graphene's morphology is investigated using SEM [71]. The graphene's shape is studied using SEM. Graphene folds, impurities, and gaps during the manufacturing process can all be found using SEM photography. Graphene's ultrathin layers present a sharpness challenge [72].

# 3.8. Atomic force microscopy (AFM)

The SuperSharpSilicon - Non-Contact/Tapping mode - High Resonance Frequency - Reflex Coating feature captured images on an Asylum Research MFP-3D Stand Alone (MFP-3D-SA). (SSS-NCHR) [73].

## 4. Importance of graphene nanoparticles in dental implant

To cure and prevent oral disorders, dental prostheses and implants containing many nanoparticleshave been employed recently [74–77]. The texture of nanoparticles is quite similar to that of actual teeth. Also, because it is made for any conceivable shape, it is straightforward to produce suited sizes [78,79]. Many nanoparticles possess antibacterial properties that prevent the spread of germs [80]. High-temperature resistance and surface coating capabilities are two advantages of NPs [81]. Nano dentistry will save time and money while relieving the patient's emotional agony, which is why patients are lured to the dental field. Without a doubt, the development of nanomaterials will address dental difficulties [82].

Dental implants are made to function and provide stability when

missing teeth are integrated with the oral tissues around them [83]. Dental implants' long-term success and the reduction of complications depend heavily on the biocompatibility of the materials used [84]. Graphene nanoparticles, in this context, offer unique benefits that support improved biocompatibility and improved results in dental implant applications [85]. Graphene NPs promote osseointegration, the direct structural and functional connection between the implant and the bone [86]. Given their large surface area and distinctive physicochemical characteristics, the formation of new bone tissue around the implant is facilitated by improved cell adhesion and proliferation [87]. This strong integration ensures the stability and longevity of the implant, lowering the risk of implant failure.

The biocompatibility of graphene nanoparticles aids in reducing inflammation and fostering tissue regeneration. When performing dental implant procedures, the surrounding tissues may experience an inflammatory response that, if not properly controlled, could obstruct healing and jeopardize the success of the implant [88]. Graphene nanoparticles have anti-inflammatory properties that lower inflammation and support an environment conducive to healing. Additionally, their capacity to promote tissue regeneration helps to develop strong bone and gum tissue, ensuring proper functional and esthetic results [89].

Graphene nanoparticles' antibacterial properties aid their biocompatibility in dental implants [32]. Peri-implantitis, an inflammatory condition that affects the soft and hard tissues supporting the implant, can result from bacterial colonization around dental implants [90]. The inherent antibacterial properties of graphene nanoparticles effectively inhibit bacterial growth and stop infections [91]. This antimicrobial activity lowers the risk of complications and implant failure by preserving the health and integrity of the surrounding tissues [92].

Significantly, as graphene-based materials become more prominent in dentistry, the biocompatibility of these materials is thoroughly researched [93]. Many tests have been conducted to determine whether graphene is biocompatible [94]. Physical interaction involving graphene particles and cell membranes and the production of reactive oxygen species explain graphene's toxicity alongside numerous other factors (ROS) [95]. The nucleus can be harmed because the smaller particles can more readily puncture cell membranes. Furthermore, a relationship has been discovered between increased production of reactive oxygen species and higher concentrations of graphene sheets [96].

Dental and biomedical implants constructed out of steel can benefit from adding graphene or its covering due to the metal's improved strength, durability, and toughness due to graphene compounds. In one instance, copper was given graphene to boost its elasticity and hardness. Its tensile strength was improved when graphene was added to an alloy of 1% Al and 1% Sn [97].

A pure graphene layer was recently created on nitinol (NiTi), a shape memory metal that can be used for dental and orthopedic implants [98]. Such a graphene covering significantly enhanced the osteogenic differentiation of mesenchymal stem cells and integrin-mediated focal adhesion on the implant surface. Different research examined the effectiveness of GO-coated collagen scaffolds in promoting alveolar bone repair and osteoblastic cytocompatibility of tooth extraction sockets [99].

Due to its remarkable physical strength, transparency, flexibility, and cheap cost, graphene is a perfect material for more robust, longerlasting, and substantially more economical dental fillings, bridges, crowns, and implants [100–102]. Additionally, graphene has been demonstrated as beneficial in the long run in dental whitening procedures, enhancing the action of bleaching by sensitizing hydrogen peroxide's market penetration and functioning as a catalyst for the hydrogen peroxide's activity, reducing the time of treatment, which decreases the aggression to the gums and causes less sensitivity [103]. An enhanced Osseointegration has been the focus of research on altering implant surfaces. In these conditions, graphene may produce an ideal implant

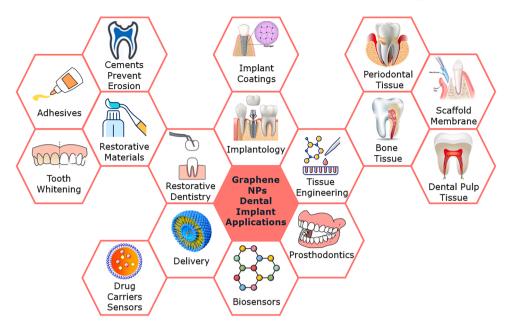


Fig. 3. Applications of graphene nanoparticles and their derivatives in the field of dentistry.

layer for complex tissue engineering to quicken bone regeneration [104]. An effort was made to increase the effectiveness of a dental implant using graphene, which currently has the maximum potential, in studies on administering medications like dexamethasone and BMP-2 [103,105]. After implant insertion, the soft tissue and bone that support the teeth usually degenerate. So, by employing a graphene scaffold for a dental implant and its capacity to repair tissue, a chronic problem might be resolved [106–108].

To be considerably more precise, the present application of GO in dentistry has led to incredible results in treating oral cancer, drug delivery, bone tissue engineering, regenerative dentistry, and antibacterial activity [109–112]. Investigations in solutions against dental infections demonstrated the possibility of employing graphene-based materials (GM), such as graphene oxide (GO) or graphene Nanoplatelets (GNP), in dental materials [113,114].

#### 5. Application of graphene nanoparticles in dental implants

Many innovative treatments and technological innovations based on materials have been developed in the last few decades to treat various ailments. Due to their superior mechanical qualities, new metallic alloys like stainless steel and nitinol (NiTi) are frequently utilized in biomedical implants [115]. The integrating biological system and tooth implant underwent fibro-osseous fusion following dental insertion. Osteogenic characteristics of the implant substance are necessary for osseointegration at the complex tissue interface. In contrast, at the soft tissue interface, it is imperative to guarantee a firm epithelial seal to avoid bacterial invasion [116]. Recent nanotechnology investigations have reported that osseointegration rates and quality can be altered by changes to titanium implant-related characteristics like surface foundation, hydrophilicity, surface roughness, topography, and shape [117]. Dentistry, often known as oral medicine, focuses on the early detection, diagnosis, and treatment of dental disorders. Recently, a substantial study on graphene-based nanoparticles for dentistry has been carried out by experts [118].Fig. 3 shows the significant aspects of graphene in the dentistry field.

# 5.1. Tissue engineering

Multiple imperfections brought on by tumors, injuries, illnesses, and other conditions are repaired and replaced using tissue engineering. It is generally recognized that scaffolds provide a surface on which different stem cells can adhere, proliferate, and differentiate during tissue creation. Numerous research demonstrated the potential of employing graphene-based materials to construct or defend tissue engineering scaffolds [119]. The formation of osteoblasts by various stem cell types is stimulated by graphene in numerous investigations. The hybrid sheet made of graphene and HAp exhibited excellent biomimetic weathering [120]. Furthermore, graphene's unique properties, such as high surface area, mechanical strength, and electrical conductivity, make it an appealing candidate for promoting cell adhesion, proliferation, and differentiation. Bone, neural, cardiac, and skin tissue regeneration have all been successfully aided by graphene-based scaffolds [121]. However, more investigation is required to fully comprehend the long-term biocompatibility and safety of graphene-based materials in tissue engineering applications [122]. Graphene's potential in tissue engineering holds great promise for addressing various medical issues and enhancing patient outcomes as the field develops [123].

Various materials have been studied as scaffolds for periodontal tissue regeneration. These materials include collagen [124], poly (3-hydroxybutyrate-Co-4-hydroxybutyrate) [125], β-calcium phosphate [126], poly-lactic acid [127], poly-glycolic acid [128], polycaprolactone [129], and chitosan [130]. To be considered ideal for periodontal tissue engineering, a scaffold should effectively and precisely guide the proliferation and differentiation of stem cells into specific tissue lineages [131]. Using scaffolds in various applications raises concerns regarding their mechanical strength and rigidity, as highlighted in reference [132]. To address this challenge, novel materials are being explored to enhance scaffold performance, and one such promising addition is graphene derivatives. Researchers have successfully incorporated graphene oxide (GO) into hydroxyapatite (HA) scaffolds using techniques like spark plasma sintering [133] or sol-gel synthesis combined with biomimetic treatment [134]. These modified scaffolds exhibit notable strength and have demonstrated the capability to enhance the viability of mesenchymal stem cells (MSCs) while promoting osteoblastic differentiation.

The introduction of reduced graphene oxide (rGO) as a reinforcement in hydroxyapatite led to an impressive 203% increase in fracture strength compared to pure HA. Furthermore, this scaffold exhibited the capacity to stimulate both cell proliferation and osteoblastic differentiation, as elucidated in reference [135]. Another noteworthy development by Nie et al. involved the creation of a three-dimensional porous scaffold using rGO and nanohydroxyapatite. This scaffold demonstrated its ability to encourage cell proliferation, enhance alkaline phosphatase (ALP) activity, and promote the expression of osteogenic genes in rat bone MSCs, as reported in reference [136]. In pursuit of bolstering the mechanical and biological attributes of scaffolds, researchers have turned to the development of multi-composite structures. Wang et al. embarked on a project to synthesize a scaffold by combining graphene oxide (GO) with a nanocomposite consisting of collagen and nanohydroxyapatite. The resultant product, characterized by its substantial porosity, showcased enhanced hydrophilicity and mechanical strength, along with exceptional proliferation potential [137]. Under the leadership of Zhang, a research group has achieved a breakthrough by creating a technique that employs water-soluble graphene oxide-copper (GO-Cu) nanocomposites for the coating of porous calcium phosphate (CaP) scaffolds. This pioneering coating has proven to greatly improve the attachment and osteogenic differentiation of stem cells derived from rat bone marrow (BMSCs). Furthermore, when these scaffolds were implanted into rats with calvarial defects, they actively promoted both angiogenesis and osteogenesis [138]. In periodontal tissue regeneration and engineering, Table 3 offers a concise summary of the key findings and applications of graphene nanoparticles and their derivatives.

### 5.2. Osseointegration and implant surfaces

Enhancing osseointegration for ceramic and titanium implants is a major challenge. Surface treatments are being explored to improve success rates by enhancing antimicrobial properties and tissue-implant interaction. This interface is crucial for processes like inflammation, cell recruitment, protein adsorption, and biofilm formation [139]. Graphene's utilization in implants stems from its remarkable characteristics. These include its high biocompatibility, its capacity for physical interaction with biomolecules such as proteins, enzymes, or peptides [140], its effective promotion of stem cell stimulation and differentiation [141], its long-term durability [142], its significant surface area that facilitates subsequent bioactivity [143], its enhancement of wear resistance [144], and its reinforcement of toughness [145]. Various methods, including chemical vapor deposition [146], plasma treatment [147], electrophoretic deposition [148], solution spray, dip-coating [149], and wet/dry transfer [150], have been employed to apply graphene oxide-based coatings onto zirconia and titanium substrates. The treatment of inert surfaces with graphene oxide enhances mechanical characteristics and fosters cell adhesion and growth. This improvement is attributed to the presence of hydrophilic functional groups, such as hydroxyl or carboxyl, which facilitate these processes [151,152].

# 5.2.1. Graphene NPs coated titanium implants

The application of GO-coated titanium implants had several positive effects, including the stimulation of cell proliferation, increased levels of alkaline phosphatase (ALP) activity, enhanced gene expression related to osteogenesis, and the promotion of protein expression associated with bone formation markers such as BSP, Runx2, and OCN [153]. Furthermore, it was observed that as the thickness of the graphene oxide layer increased, there was an improvement in ALP-positive areas and an increase in the mineralization of the extracellular matrix [154]. However, the initial graphene-based coatings lacked the crucial three-dimensional morphology necessary for the osseointegration process. Consequently, the research team led by Qiu developed the first 3D porous coatings utilizing GO and rGO on pure titanium plates. These products demonstrated high osteoinduction capacity and biocompatibility [155]. In their observations, Li et al. noted that when titanium was coated with GO, it resulted in greater new bone formation and fewer gaps between the implants and the surrounding peri-implant bone tissue [156].

Efforts were made to enhance implant surfaces by incorporating graphene oxide (GO) and bioactive proteins. Within this realm, bone morphogenetic proteins (BMPs), a protein class renowned for their ability to stimulate bone growth, were explored. Particularly, BMP-2 emerged as a potent factor in promoting stem cell differentiation into bone cells, thereby boosting implant integration by fostering bone regeneration at the implant-recipient site interface [157]. The implant surface underwent treatment involving graphene oxide, which served as a carrier for both BMP-2 and substance P. While no discernible disparities were noted in substance P release between the titanium and GO/Ti groups, the release of BMP-2 from Ti/GO exhibited a gradual pattern over a span of 14 days. In contrast, without GO treatment, the release of BMP-2 content occurred rapidly within the initial 24 h on the titanium surface [158]. Ren et al. [159] conducted a study that examined how DEX-GO-Ti and DEX-rGO-Ti, titanium foils loaded with dexamethasone and graphene oxide or reduced graphene oxide, impacted the proliferation and osteodifferentiation of rat bone mesenchymal stem cells (rBMSCs). The findings indicated that DEX-GO-Ti notably boosted cell proliferation, while rBMSCs cultured on DEX-GO-Ti displayed increased expression levels of calcium, proteins, and mRNA-markers closely linked to osteogenic differentiation.

## 5.2.2. Graphene NPs coated zirconia-based implants

While there is a substantial body of literature dedicated to enhancing the surface properties of titanium implants using graphene-based materials, research exploring the combination of these materials with zirconia-based implants is relatively scarce [160]. Zirconia ceramics (ZrO2) hold significant appeal due to their exceptional mechanical, physical, and chemical stability, as well as their resistance to corrosion and toxicity. These qualities contribute to reduced peri-implant inflammation and favorable esthetic results [161]. Investigations in this area have primarily pursued two avenues: the introduction of graphene-based nanomaterials into zirconia coatings [162,163] and the homogenous integration of graphene-based nanomaterials within zirconia ceramics [164–166].

Graphene-based 2D nanomaterial (GBN) fillers for ceramic composites can be categorized into two groups based on the number of graphene sheets they contain. Graphene nanoplatelets (GNP) have more than ten layers and a thickness below 100 nm, while multi-layered graphene (MLG) consists of fewer than ten layers. MLG can be further classified into two subgroups: reduced graphene oxide (rGO) and fewlayer graphene (FLG), containing two to approximately five layers [167]. Another form of graphene sheets arranged as coaxial tubes with a nanoscale internal diameter is known as carbon nanotubes (CNT), which come in two distinct varieties: single-wall (SWCNTs) and multiple-wall (MWCNTs) [168]. It's worth noting that both graphene sheets and carbon nanotubes tend to aggregate in their pure state due to excess free surface energy, resulting in instability and the folding of layers [169], primarily due to van der Waals forces [170]. When zirconia is combined with GBN, it has been demonstrated to enhance material toughness through various mechanisms, including but not limited to graphene pullout, bridging, crack deflection, and crack branching [167]. However, the accumulation of filler material can create stress concentration regions that may significantly compromise the material's mechanical strength [168]. Table 4 presents the utilization of dental implants coated with graphene-based nanoparticles materials.

# 5.3. Antimicrobial activity

Graphene derivatives exhibit antimicrobial mechanisms stemming from their chemical and mechanical properties [171]. Concerning their mechanical aspects, both graphene oxide (GO) and reduced graphene oxide (rGO) are characterized by sharp edges capable of potentially damaging bacterial cell membranes [172]. The mechanical factors influencing this phenomenon encompass edge density and the angle at which the sheet contacts the cell membrane. Studies have demonstrated that smaller-sized GO sheets with smoother edges exhibit a higher edge density, resulting in a more potent antibacterial effect. This effect becomes evident at a contact angle of 37° and peaks at 90° [173]. Notably, rGO has been found to exert a more pronounced impact than GO [174].

An additional antimicrobial mechanism relies on cellular uptake, wherein bacterial cells become trapped and isolated from their environment upon contact with graphene sheets. This isolation deprives them of access to nutrients [175]. Interestingly, this effect is bolstered when GO sheets have larger lateral dimensions [176]. Consequently, we encounter a paradox: smaller dimensions are essential for a more pronounced cutting effect, while larger GO sheets can lead to increased cellular uptake. As research indicates, GO can induce lipid peroxidation within bacteria [177]. This action is bactericidal, as it results in the disruption of microbial cell membranes. Graphene derivatives are thought to generate elevated levels of reactive oxygen species (ROS), leading to oxidative stress within bacterial cells [178]. Fig. 1 illustrates the primary mechanisms responsible for the antibacterial properties of both GO and rGO.

Peng et al. [179] researched to explore the antibacterial properties of graphene derivatives against periodontopathogenic bacteria. They compared the effectiveness of rGO and silver (rGp-NS-Ag) composites to combat Candida albicans, Lactobacillus acidophilus, S. mutans, and Aggregatibacter actinomycetemcomitans with that of silver nanoparticles (AgNP) and standalone rGO nanosheets. The rGp-NS-Ag composites exhibited significantly improved antimicrobial effects, as reported in their study. In another study, treating titanium surfaces with GO-Ag nanocomposites demonstrated a notable antibacterial impact against P. gingivalis, with an impressive percentage of 95.45%. Furthermore, it displayed a minimal bacterial adhesion rate of 4.55%. This effect was attributed to various factors, including alterations in microstructures, bacterial quantity, disruption of cell membranes, induction of bacterial apoptosis, and changes in bacterial gene expression, as indicated by the collected data [180]. In their study, Wang and colleagues delved into the antimicrobial attributes of graphene-coated Ti-6Al-4 V when confronted with oral pathogens, including P. gingivalis, F. nucleatum, and C. albicans. Their findings indicated that the Ti-6Al-4 V alloy, once coated with graphene, displayed increased resistance to these oral pathogens compared to the uncoated counterpart. Notably, the graphene-coated Ti-6Al-4 V alloy exhibited a heightened capacity to generate reactive oxygen species (ROS) within the tested pathogens, surpassing the ROS production of the uncoated Ti-6Al-4 V allov [181].

Furthermore, the introduction of zinc oxide-functionalized graphene oxide into polyetheretherketone demonstrated substantial antibacterial efficacy against a range of oral pathogens, including P. gingivalis, F. nucleatum, S. sanguinis, and S. mutans. Additionally, this approach effectively deterred the formation of biofilms through the induction of oxidative stress [182,183]. Research findings have also indicated that the utilization of DNA-aptamer-nanographene oxide led to the generation of reactive oxygen species specifically targeted at P. gingivalis, ultimately resulting in bactericidal effects [184]. Table 5 contains the primary research studies centered on investigating the antibacterial properties of graphene nanoparticles and their derivatives.

## 5.4. Collagen membranes

As a protective membrane to prevent soft tissue from penetrating the newly formed bone, the collagen membrane is frequently used in guided bone regeneration (GBR) and showed tissue regeneration (GTR) [185]. Collagen membrane still requires various changes to increase biocompatibility even though it has many positive characteristics, such as ease of manipulation and minimal surgical involvement [186]. Graphene's exceptional mechanical strength [187], surface area [188], and electrical conductivity [189] make it an appealing additive for improving the scaffold's properties. According to studies, compared to conventional collagen membranes, graphene-enhanced collagen membranes exhibit greater stability, improved cell adhesion, and quicker tissue regeneration [190]. The antimicrobial qualities of graphene also provide an added benefit in preventing infections during the healing process [191]. Additional study is still needed to fully comprehend the long-term effects and improve the formulation of collagen membranes modified with graphene for secure and efficient clinical applications. This cutting-edge strategy could revolutionize tissue engineering to regenerate bone and soft tissues, improving patient outcomes and minimizing surgical procedures.

## 5.5. Teeth whiting

As is well known,  $H_2O_2$ has been used for in-office bleaching for a very long period. To carry out the bleaching procedure, the  $H_2O_2$  molecules must enter deeply into the molars. However, the relatively elevated  $H_2O_2$  concentrations resulted in several adverse reactions, including irritated gums and dental sensitivity [192,193]. As a result, several improvements in teeth-whitening procedures have been created to expedite the process and reduce its adverse effects. A cobalt (Co)/tetraphenyl porphyrin (TPP)/rGO nanocomposite was described by Su et al., and it demonstrated superior tooth-whitening effectiveness when teeth were discolored by dyes, tea, and betel nuts compared to  $H_2O_2$  alone [194]. Graphene-based materials are a possible catalyst for teeth-whitening applications when employed in the proper sorts and amounts. Table 6summarizes the materials made of graphene primarily used in dentistry research areas.

# 5.6. Prosthodontic restorations

In modern dentistry, a wide array of medical materials are employed, each with unique strengths and weaknesses. Within prosthodontics, a rich diversity of materials is utilized for indirect restorations, particularly those integrated into CAD/CAM systems [195]. Given graphene's superior mechanical attributes, ease of manipulation, potential for functionalization, and promising applicability in dental and biomedical contexts, a significant drive exists to develop novel, enhanced restorative materials. These materials would possess distinctive compositions and microstructures, allowing for a comprehensive exploration of their physical and mechanical properties. Furthermore, this research aims to provide insights into their clinical performance and potential failure risks [196].

Over the past eight decades, polymethylmethacrylate (PMMA) resin has maintained its prominent status in prosthetic dentistry. This enduring popularity primarily stems from its utility in crafting complete and removable partial dentures. The reasons underpinning its favorability include its ease of fabrication, cost-effectiveness, pleasing esthetic qualities, and a low modulus of elasticity. Furthermore, PMMA resin possesses a notable advantage in its ease of repair, rendering it a versatile choice among dental professionals. PMMA-based resins have found extensive utility in provisional restorations due to their characteristic attributes, such as low mechanical properties, which make them unsuitable for permanent repairs. They also exhibit considerable polymerization shrinkage and a limited ability to inhibit biofilms, restricting their use in permanent restorations [197]. Endeavors to augment the mechanical properties of PMMA resins have yielded successful outcomes by integrating reinforcing phases, including glass and polyethylene fibers [198].

Graphene nanofibers and nanosheets, propelled by recent advancements in nanotechnology, have notably contributed to the evolution of glass fiber-reinforced materials (GFMs). These advancements have extended to incorporate their reinforcement phase in various polymers, including those based on polymethylmethacrylate (PMMA) resins [199, 200]. Noteworthy is the fact that even at low concentrations, solutions containing graphene oxide (GO) and reduced graphene oxide (rGO) appear dark, and pristine graphene exhibits a significant absorption of white light [201].

Bacali et al. conducted a study that focused on enhancing PMMA (polymethyl methacrylate) by incorporating graphene-silver nanoparticles (Gr-Ag). The primary objectives of the research were to

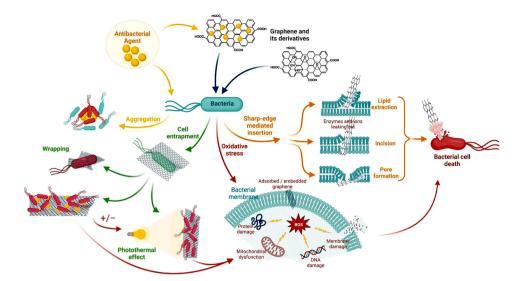


Fig. 4. Graphene derivatives exhibit antibacterial mechanisms encompassing cell entrapment, oxidative stress induction, and insertion through sharp edges [247].

 Table 2

 Summaries of each bottom-up method's benefits and drawbacks and the nature, average size, and thickness of the graphene sheets produced by each method.

Method	Typical dimension	Lateral	Advantage	Disadvantage	References
Restrictive self-assembly	Single layer	100's nm	Thickness regulation	Defects are present	[248]
CVD	Few layers	Very large (cm)	Large size; high quality	Small production scale	[249-254]
voltage spike	Single, bi, and few	Few 100 nm to a few l	Can produce10 g/h of graphene	Low yield of graphene; carbonaceous	[255,256]
	layers	m		impurities	
Epitaxial development on SiC	Few layers	Up to cm size	area of extremely pure graphene	Tiny scale	[257–263]
Carbon nanotubes are unzipped	Multiple layers	few l m long nanoribbons	Size is decided by picking the first nanotube.	beginning point that is too expensive; oxidized graphene	[44,264]

#### Table 3

The key findings and applications of graphene nanoparticles and their derivatives.

Year	Materials derived from graphene	Consequences	Refs.
2020	GO/chitosan	Osteogenic differentiation	[265]
2020	GO/IONPs/H	Biocompatible; osteogenic activity; calcium deposits	[266]
2020	GO/HA/Au	Biocompatibility; osteogenic differentiation	[267]
2019	monocytes activator GO complexed with CaP	Activation of monocytes; stimulated osteogenesis	[268]
2019	GO-collagen aerogel	Biomineralization; biocompatibility; osteogenic activity	[269]
2019	HA/rGO	Proliferation; osteogenic activity	[270]
2019	Silk fibrinoid/GO/BMP-2	Biocompatibility; adhesion;	[271]
		proliferation; osteogenic differentiation	
2018	Ti/GO/BMP-2/ vancomycin	Osteogenic activity	[272]
2018	3D collagen sponge/GO	Osteogenic differentiation; PDL- like and cementum-like tissue regeneration	[273]
2017	CaP/rGO	Speed up bone neoformation	[274]
2017	Collagen-GO membrane	Stiffness and roughness;osteogeni differentiation	[275]
2016	Poly(L-lactic-co-glycolic acid) with Tussah silk fibroin; GO	Strong adherence; rapid growth; ALP; mineral deposition	[276]
2016	Silk-fibroin/GO	Osteogenic and cementoblast differentiation	[277]
2015	rGO/HA nanocomposites	Elevated levels of ALP; mineralization; and osteopontin; osteocalcin expression	[278]

evaluate the material's mechanical characteristics, hydrophilicity, and morphology [202]. The study's results revealed a noteworthy impact of Gr-Ag fillers on compression parameters, bending strength, and tensile strength, leading to an overall enhancement in the material's mechanical properties compared to pure PMMA. In another investigation by Bacali, the effectiveness of Gr-Ag-modified PMMA in combatting bacterial infections, along with its potential toxicity, monomer release, and mechanical properties, was examined. The findings demonstrated that this material exhibited robust antibacterial properties against various bacterial strains, including Gram-negative bacteria, S. aureus, Escherichia coli, and S. mutans [203]. Table 7 lists the primary research studies exploring the applications of graphene nanoparticle derivatives in direct and indirect dental restorations.

## 5.7. Restorative materials

Graphene derivatives have found versatile applications across various dental fields due to their immense potential. Restorative dentistry often deals with materials like composites, adhesives, and cement, which must possess esthetic qualities and high hardness. However, these materials face limitations, such as significant polymerization shrinkage and poor antibacterial properties. To overcome these challenges, researchers have integrated graphene nanoplates (GNPs) into porous and dissolution-prone substances like resins, cement, and adhesives. This innovative approach effectively reinforces commonly used dental composites and simultaneously exerts an anticaries effect [204].

The introduction of graphene nanosheets into two different bioactive calcium silicate cement powders, Biodentine, and Endocem Zr, has shown promising results in bonding time and hardness improvement. However, it's noteworthy that Endocem Zr experienced notable bonding

The utilization of dental implants coated with graphene-based nanoparticle materials.

Year	Materials derived from graphene	Consequences	Refs
2022	Graphene nanoplatelets and yttria-stabilized zirconia	Resistance to aging	[279]
2022	Reduced graphene oxide (rGO)-coated sandblasted	Enhanced bone fusion resulting in a quicker healing process	[280]
2021	GO/Zirconia	Osteogenic differentiation	[281]
2021	rGO nanosheets	Osteogenic differentiation	[282]
2020	GO/Ti	Biocompatibility; osteogenic differentiation	[283]
2020	GO	Re-osteogenesis	[284]
2020	GO/Ti	Proliferation; adhesion, osteogenic differentiation, and osteointegration	[285]
2019	GO/HA/chitosan	Promoted apatite formation	[286]
2019	Magnesium alloy with	High cytocompatibility and	[287]
	graphene nanoparticles	osteogenic properties	50003
2019	GO/chitosan/HA	Osteogenic differentiation	[288]
2018	Single-layer graphene sheets	Osteogenic differentiation	[289]
2018	GO/aspirin/Ti	Proliferation; osteogenic differentiation	[290]
2017	rGO/Ti	Rough surface biocompatibility; high hydrophilicity; increased ALP activity; collagen secretion; osteogenic differentiation	[291]
2017	GO/Ti/Dex	Stimulated cell growth; hastened the process of bone formation	[292]
2017	nGO/PEG/PEI/siRNA	Osteogenic differentiation; osteointegration	[293]
2016	GO	Osteogenic differentiation	[153]
2015	rGO/Dex	Osteogenic differentiation	[294]
2013	Functionalized multiwalled carbon nanotubes on zirconia	Enhanced cell attachment	[295]

property impairments when adding GNPs. This suggests that while GNPs enhance the physical-mechanical properties of materials, their compatibility with all materials in terms of bonding may vary [205]. Moreover, incorporating graphene and graphene oxide (GO) into bioactive materials has demonstrated enhancements in the differentiation and proliferation of human dental pulp stem cells and periodontal ligament stem cells. This advancement can potentially facilitate the regeneration of dental pulp and periodontal ligament tissues [206].

A unique graphene variant, Fluorinated Graphene (FG), has been developed and incorporated into glass ionomer cement, presenting a more appealing option than conventional gray GNPs due to its visually pleasing bright white color. FG has been used to modify poly(acrylic acid)-based glass ionomer cement types (GICs), improving mechanical, tribological, and antibacterial properties. Consequently, GIC/FG composites exhibit enhanced Vickers microhardness, compression, flexural strength, and reduced friction coefficients. This widens the application of glass ionomer cement in restorative dentistry for various procedures, including restoring non-carious and carious lesions, class III and class V restorations, and crown cementation. Furthermore, these compounds exhibit potent antibacterial activity against Staphylococcus aureus and S. mutans while maintaining a favorable fluoride ion release rate [207].

The advantages of graphene-based materials (GBMs) have led to their integration into adhesive materials, where they play a crucial role in replacing infected dental tissues and preventing the progression of decay [208]. Adhesive materials are essential for bonding dental composites to dental hard tissues, especially dentin. GBMs, specifically graphene quantum dots, have been developed in conjunction with 1-ethyl-3-(3-dimethyl aminopropyl) carbodiimide (EDC) to inhibit the degradation of collagen fibrils. These quantum dots effectively inhibit collagenase activity and matrix metalloproteinases (MMPs) by covalently linking collagen fibers, reducing the enzymatic hydrolysis of

### Table 5

Antibacterial	properties o	f graphene	nanoparticles	and their	derivatives.
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Year	Materials derived from graphene	Microorganism causing disease	Consequences	Refs.
2022	Nanographene oxide	P. gingivalis	Biofilm and the decrease in bacterial metabolic activity	[296]
2022	Ti/6Al/4V	C. albicans P. gingivalis F. nucleatum	Inhibition of bacteria through the production of reactive oxygen species (ROS)	[297]
2021	Ti/0.125G	S. mutans F. nucleatum P. gingivalis	Inhibited the proliferation of bacteria	[298]
2021	PEEK/GO	S. mutans F. nucleatum P. gingivalis	Inhibition of bacteria	[299]
2020	Nano-graphene oxide with antisense vicR RNA plasmid	S. mutans	Gene expressions linked to virulence were decreased, biofilm formation was suppressed, and the accumulation of extracellular polymeric substances (EPS) was inhibited	[300]
2020	GO	E. coli	Antibacterial effectiveness	[301]
2020	GO	S. mutans	Achieving an antimicrobial effectiveness of up to 80%	[302]
2020	GO	S. mutans; P. gingivalis; F. nucleatum	Getting rid of any remaining bacteria and preventing the reformation of biofilm	[303]
2019	G/AgNp	S. aureus S. mutans E. coli	Activity that inhibits or kills bacteria	[304]
2019	rGO/Ag	S. mutans	The antimicrobial effect achieved through the capture of cells and the bactericidal properties of silver ions	[305]
2019	GQD	A. actinomycetemcomitans P. gingivalis P. intermedia	Inhibition of bacteria through the production of reactive oxygen species (ROS)	[306]
2018	Ag/GNP	E. coli	Cell entrapment to induce antimicrobial effects	[307]
2018	GO-AgNPs	S. aureus	The inhibition of microorganisms through the induction of cell membrane disruption and the generation of reactive oxygen species (ROS)	[308]
2018	GO/AgNPs	C. albicans	The destruction of	[304]

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#### Table 5 (continued)

Year	Materials derived from graphene	Microorganism causing disease	Consequences	Refs.
			and the induction	
			of oxidative stress	
			are responsible	
			for the	
			antimicrobial	
2010			effects	5000
2018	GO	E. coli S. aureus	Inhibition of microbial growth	[309
		5. aureus	through the	
			destabilization of	
			bacterial cell	
			membranes	
2017	rGNs/Ag	C. albicans	Greater	[179
		L. acidophilus	antimicrobial	
		S. mutans A.	efficacy	
		A. actinomycetemcomitans	compared to R- GN and AgNPs	
		uctinoiny ceteniconntains	separately	
2017	Ti/GO/Ag	S. aureus	The antimicrobial	[310
	5	S. mutans	effect involves	
		P. gingivalis	bacterial cells	
			shrinking, getting	
			punctured,	
			breaking apart, and ultimately	
			bursting	
2017	Ag-rGO	E. coli	Silver ions kill	[311
	0		bacteria by	
			trapping them in	
			cells, damaging	
			cell membranes,	
			and causing oxidative stress	
2016	GMgO-Ag	E. coli	The antimicrobial	[312
			effect resulting	
			from the	
			disruption of cell	
		_	membranes	
2016	GO and rGO-	S. aureus	Antimicrobial	[313
	poly(dopamin)		effectiveness through the	
			induction of cell	
			membrane	
			disruption, the	
			generation of	
			reactive oxygen	
			species (ROS),	
			and electron transfer	
2015	GO	S. mutans	The disruption of	[314
- 10		F. nucleatum	cell membranes	.017
		P.gingivalis	leads to	
			antimicrobial	
		0	effects	Fort-
	PLGA/	S. aureus	The antibacterial	[315
2015	abitarra (CC) (		effects through	
2015	chitosan/GO/		cilver's catalytic	
2015	chitosan/GO/ AgNPs		silver's catalytic oxidation.	
2015			silver's catalytic oxidation, disruption of cell	
2015			oxidation,	
2015			oxidation, disruption of cell membranes, and the generation of	
2015			oxidation, disruption of cell membranes, and the generation of reactive oxygen	
	AgNPs	E seli	oxidation, disruption of cell membranes, and the generation of reactive oxygen species (ROS)	Foto
2015 2014		E. coli	oxidation, disruption of cell membranes, and the generation of reactive oxygen species (ROS) Inhibition of	[316
	AgNPs	E. coli	oxidation, disruption of cell membranes, and the generation of reactive oxygen species (ROS) Inhibition of microorganisms	[316
	AgNPs	E. coli	oxidation, disruption of cell membranes, and the generation of reactive oxygen species (ROS) Inhibition of microorganisms through	[316
	AgNPs	E. coli	oxidation, disruption of cell membranes, and the generation of reactive oxygen species (ROS) Inhibition of microorganisms	[316
	AgNPs	E. coli	oxidation, disruption of cell membranes, and the generation of reactive oxygen species (ROS) Inhibition of microorganisms through producing	[316
	AgNPs	E. coli	oxidation, disruption of cell membranes, and the generation of reactive oxygen species (ROS) Inhibition of microorganisms through producing reactive oxygen species (ROS), light-induced	[316
	AgNPs	E. coli	oxidation, disruption of cell membranes, and the generation of reactive oxygen species (ROS) Inhibition of microorganisms through producing reactive oxygen species (ROS),	[316]

Table 5 (continued)

Year	Materials derived from graphene	Microorganism causing disease	Consequences	Refs.
2013	GO	E. coli	The antimicrobial effectiveness is achievedthrough methods such as insertion, cutting at the edges, and lipid extraction.	[317]

collagen fibers, and enhancing the durability of dental bonding material [209]. Furthermore, GNPs are frequently employed as fillers in polymer-based dental adhesives due to their potent antimicrobial and antibiofilm properties. These nanocomposites filled with GNPs effectively suppress the activity of S. mutans cells while maintaining their bonding properties [210]. Additionally, research has explored using silver nanoparticles with reduced nanographene oxide and graphene nanoplates to enhance adhesive properties, promoting better bonding between resin and dentin while maintaining cell viability [211]. Another innovative approach involves the incorporation of graphene oxide and hydroxyapatite into resin-dentin bonds, resulting in improved durability, adhesive properties, and remineralization capabilities [212].

Researchers have also successfully developed a composite material known as nHAP/MWCNT-GO, comprising nanohydroxyapatite, multiwalled carbon nanotubes, and graphene oxide. This material forms a surface film that effectively resists acid and minimizes dentin erosion [213]. Additionally, graphene oxide (GO) modifications by incorporating different nanoparticles, such as calcium fluoride and silver, have shown promise in preventing dentin decalcification. GO combined with silver and silver-calcium fluoride has exhibited inhibition of S. mutans, with low cytotoxicity observed except at higher concentrations [214]. To address the bonding challenges with zirconia, the application of a silane primer has been found to be influential. Incorporating GO sheets into silane primers has emerged as a viable option for improving the mechanical properties of the adhesive layer in resin composites bonded to ZrO<sub>2</sub>, leading to enhanced shear bond strength, surface roughness improvement, and a slight increase in water contact angle [215,216].

# 6. Present challenges and future prospects

#### 6.1. Present challenges

Much research has been done on the biological applications of graphene and its derivatives. However, this subject is still in its infancy, and certain significant obstacles must be solved before this sector can be widely marketed [217]. One problem in creating dental implants that should be avoided is mechanical failure following insertion brought on by flaws. Defects in graphene implants vary in size and shape according to how they were made. As a result, the first hurdle for graphene and its derivatives is to study created flaws during the fabrication of graphene implants for large-scale applications [218].

Long-term toxicity and in vivo toxicity mechanisms present another challenge in the clinical approaches to graphene and its derivatives [219]. Additionally, recent research has looked into the toxicity of graphene and its products in biological systems [220,221]. According to specific reports, biomaterials based on graphene may generate oxidative debris that could cause cytotoxicity. Consequently, it is important to closely check the quality of graphene and its derivatives throughout the bio-functionalization process [222]. Furthermore, some studies show that graphene and graphene oxide (GO) are toxic to mice in a dose-dependent manner [223,224]. In contrast, functionalized graphene oxide is less damaging in vitro and in vivo (for example, by covering it with a biocompatible polymer) [225].

Further research must determine whether graphene and its

Materials made of grapheneare primarily used in dentistry research areas.

Applications	Types of graphene	Properties	Application types	References
Periodontal tissue regeneration	GO/ 3D collagensponge	periodontal ligament-like tissue regeneration	Scaffolds	[318]
Collagenemmenber	GO	Osteogenic differentiation Inflammation effect Roughness and stiffness	Coatings	[319]
Dental implant and abutment	Single-layer graphene sheets	Osteogenic differentiation Osteogenic differentiation	Coatings	[320]
	rGOnanosheets	Osteogenic differentiation	Coatings	[321]
	GO/Minocycline hydrochloride (MH)	Antibacterial property	Coatings	[322]
Bone tissue engineering	Monolayer graphene	Osteogenic differentiation	Coatings	[323]
Dental pulp regeneration	Graphene/HA Graphene dispersion	Biomimetic mineralization Neural differentiation	Scaffolds Scaffolds	[324] [325]
	NFs/rGO/PCL	Neural differentiation	Scaffolds	[326]

derivatives have adequate drug-loading capacity for practical applications. The toxicity profiles of graphene and its products in vitro and in vivo, as well as their biocompatibility and biodegradability, should be taken into consideration before determining the precise chemical modification processes of graphene and its derivatives for cell membrane barrier penetration and intracellular release for drug delivery [226]. The in vivo toxicity and manufacturing characteristics of graphene and its products, both of which need rigorous analysis, are two critical barriers to their usage.

Since graphene can be harmful on a fundamental level, the enzymatic degradation of graphene is an important topic. Instead, if there are microorganisms that can break down graphene and its derivatives, the permanence of these materials in the body will be considerably reduced. These studies must determine the nature of the graphene particles' degradation products. Enzymes can break down graphene and release potentially harmful byproducts. We must investigate the composition of these subsidiaries and their impact on health [227].

The amount of graphene to coat biomaterial granules can affect bone response. The predominant component of porcine bone tissue, hydroxyapatite, was visible in the FTIR spectra of porcine bone. The phosphate group caused the stretching band at approximately 1036 cm<sup>-1</sup>; the carbonate band at 874 cm-1 was caused by carbonate; and the P-O bending caused the bands at 565 and 604 cm<sup>-1</sup>. O—H group's stretching band was roughly 3430 cm<sup>-1</sup>, while its bending band was approximately 1640 cm<sup>-1</sup>. It's unlikely that this technique is sensitive enough to detect the small amount of GO used to coat the porcine bone granules [228].

# 6.2. Future prospects

Graphene nanoparticles have become versatile instruments with a wide range of potential applications [229]. Their large surface area and functionalization capability make it possible to deliver drugs with pinpoint accuracy, increasing drug efficacy and reducing side effects [230]. They have been used in imaging as contrast agents in MRI [231] and CT scans [232] and for bioimaging [233]. Graphene nanoparticles can also potentially treat cancer using photothermal and photodynamic methods [234]. They are also helpful for developing biosensors because they can detect biomolecules and pathogens quickly and with high sensitivity [235].

In the last ten years, graphene-based nanomaterial has found widespread application in industries other than medicine [236]. The primary emphasis of research on using graphene in dental materials has been on two methods: first, creating novel dental materials solely from GFNs, and second, modifying existing dental materials by adding the proper GFNs to various substrates. The primary emphasis of research on using graphene in dental materials has been on two methods: first, creating novel dental materials solely from GFNs, and second, modifying existing dental materials by adding the proper GFNs to various substrates [117].

While graphene nanoparticles have shown promise in imaging and drug delivery, there is still room for more research in fields like targeted therapy [237], biosensing [238], and regenerative medicine [239]. For various medical applications, researchers could look into graphene nanoparticles' biocompatibility, toxicity, and long-term effects [240]. Furthermore, Graphene-based materials have been shown to have excellent mechanical strength and conductivity, which makes them the best choice for energy storage devices. Graphene nanoparticle optimization for supercapacitors, lithium-ion batteries, and other advanced energy storage technologies could be the main topic of future research [241].

It is possible to use the special qualities of graphene nanoparticles to clean up the environment [242]. Investigating their potential for pollutant adsorption [243], water purification [244], and air filtration [245] could lead to efficient and long-term solutions to environmental problems. Moreover, Graphene nanoparticles have the potential to be used as catalysts in a variety of chemical reactions due to their large surface area and high reactivity [246]. Investigating their catalytic properties might create more effective and eco-friendly procedures in sectors like chemical production and renewable energy generation.

The development of graphene and its derivatives as biological materials has become an interesting research area in recent years. This study topic will need appropriate future research orientations to develop into a market-oriented research area because it is still in its early phases. Despite its other qualities, including mechanical strength, electrical conductivity, and thermal stability, graphene is a promising candidate due to its functionalization potential with various biomaterials and biomolecules. One of the most important future objectives for the biomedical therapeutic application of graphene and its derivatives, such as antibacterial and anti-cancer medications, is conceptualizing its toxicity profile (Fig. 4,Table 2). Additionally, more research should be done on the surface chemistry design of graphene and its products for potential use in vivo gene delivery or treatment of genetic disorders [227].

# 7. Conclusion

Several distinctive qualities of graphene nanoparticles make them desirable for use in dental implants. They can interact with biological tissues more effectively because they have a larger surface area-tovolume ratio. The strength and longevity of dental implants might be increased by their superior mechanical and highly conductive qualities. Dental implants with graphene nanoparticles are a very new and

The applications of graphene nanoparticle derivatives in both direct and indirect dental restorations.

Year	Materials derived from graphene	Consequences	Refs.
2022	PMMA/GO—Commercial CAD-CAM resin block	Enhanced flexural strength	[327]
2022	PMMA/GNP—3D printed resin	Improved strength, hardness, and elasticity; antimicrobial activity	[328]
2022	Soft denture liner PMMA based/GO—incorporated into the liquid	No impact on the firmness of denture liners	[329]
2022	GO/montmorillonite	Enhancing the stability of mineralization in enamel and dentin	[330]
2021	PEEK/GNP—injection molding	Higher flexural, tensile, and compression strength	[331]
2021	Bone cement PMMA-based/ GO incorporated into the liquid	Enhanced bone cement compression strength	[86]
2021	PMMA/GO—Commercial CAD-CAM resin block	Reduced hardness	[332]
2020	PMMA/GO—Commercial CAD-CAM resin block	Enhanced flexural strength	[333]
2020	PMMA/GO—incorporated into the liquid	Reduced bending strength	[334]
2019	PMMA/GO—Commercial CAD-CAM resin block	The addition of GO into PMMA did not have any effect on hardness or flexural strength	[335]
2019	G/AgNp	Reduced harmful effects and enhanced bending characteristics	[336]
2019	GO	Improved adhesion strength in shear	[337]
2019	Graphite Fluoride bioactive glass	Enamel and dentin mineralization	[338]
2018	PMMA/GO—incorporated into the liquid	Elevating the GO concentrations to a level of 0.5 wt% or higher resulted in enhanced hardness and flexural strength in PMMA	[339]
2018	Fluorinated graphene	Elevated microhardness and enhanced compressive strength; reduced friction coefficient	[340]
2017	Gp-NSs	Improved physical and mechanical characteristics of bioactive cement	[341]
2017	nHA/MWCNTO/GO	Formation of a protective layer for dentin against erosive processes	[342]
2017	rGO—HA	The elasticity is now ten times better than that of HA	[343]
2017	GO-based fluorhydroxyapatite	Enamel and dentin mineralization	[344]
2013	PMMA/rGO—incorporated into the liquid	Elevated levels of concentration led to a reduction in the tensile strength of PMMA, while lower concentrations did not result in any alterations	[345]

exciting study area. While further research is needed to fully understand the potential benefits and risks of using these particles in dental implants, preliminary data suggest they may be effective in improving these procedures' success rates and long-term outcomes. By analyzing recent research on graphene NPs, this review paper can advance scientific knowledge in dental implants. It is possible to aggregate the available data, identify research gaps, and suggest potential directions for future research. Dental implants containing graphene nanoparticles have the potential to advance clinical practice, highlight prospective growth areas, and foster interdisciplinary collaboration. Dental professionals can confidently decide whether to utilize zirconium nanoparticles in dental implant procedures using this knowledge. In this report, the use of graphene nanoparticles in dental implants is studied along with areas that might need improvement. This might help to focus future research and lead to the development of more effective dental implant tools and procedures. In the future, many more plant species can be used and reported in the green, quick production of metal oxide nanoparticles.

#### **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

Data will be made available on request.

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