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Review Article

Graphene and its Application in Orthodontics

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Graphene is a one-atom-thick layer of carbon atoms arranged in a hexagonal lattice. The unique structure allows its customization to suit the requirements of various fields of biomedical sciences. Owing to their physical and biochemical properties, graphene is a near ideal material for incorporation into dental materials, and hence of great use in Orthodontics. Not only as dental materials such as metallic and acrylic components, graphene and its several derivatives have properties that aid tissue regeneration as well. Besides these applications, the capability of biofunctionalization and photoluminescent render graphene-based materials useful in various protein based targeted therapies and as biological sensors. Although, the full potential of applications of graphene has not yet been realized in Orthodontics, several studies indicate a great potential for its use. This review summarizes various studies on graphene and suggests future directions for research in the field.

Introduction

Carbon is the basic requirement for life and is one of the most diffused elements found abundantly in nature. Graphite chemistry began in 1859, when the syntheses of graphene oxide (GO) and reduced graphene oxide (rGO) were reported. Microscopic images of single-layer graphene (SLG) oxide sheets were observed in 1948 [1]. However, the isolation of pristine graphene was achieved in 2004 when it was first isolated by Novoselov et al. using mechanical exfoliation method with a sticky tape [2]. Graphene is formed by carbon atoms arranged in honeycombed lattice. Its structure is composed of six-membered rings stacked in parallel with no chemical groups on the surface [3]. Graphene is a two-dimensional allotrope of carbon, consisting of a single layer of carbon atoms arranged in a hexagonal lattice structure. It has useful properties of exceptional strength and electrical and thermal conductivity. Moreover, these materials offer a greater antimicrobial action, cost effectiveness and scalability in production as compared to other graphite-based nanomaterials, such as carbon nanotubes [4]. Owing to its exceptional properties, graphene has found great importance in several fields of science and technology, including orthodontics. This article highlights the applications and literature update on graphene in orthodontics.

Structure of Graphene

Each carbon atom in graphene is bonded to three neighbouring carbon atoms through strong covalent bonds, forming a planar honeycomb lattice (figure 1). The carbon-carbon bonds within the lattice are exceptionally strong, making graphene a robust material. This unique arrangement of bonds results in a flat, atomically thin sheet that is one atom thick. The hexagonal lattice of graphene provides it with excellent electrical properties. The carbon atoms in the lattice form a conjugated π electron system, allowing for efficient electron mobility. This leads to high electrical conductivity. Furthermore, the sp^2 hybridized carbon atoms in graphene give it its distinctive thermal conductivity. The tightly packed lattice enables efficient heat transfer through the material [4]. The large surface area of graphene, combined with its exceptional mechanical, electrical, and thermal properties, has aroused immense interest in its potential applications, including uses in the field of Dentistry.

Properties of Graphene

The structure of graphene plays a crucial role in determining various extraordinary characteristics. The physical properties of graphene and its biocompatibility render it useful in the field of medicine

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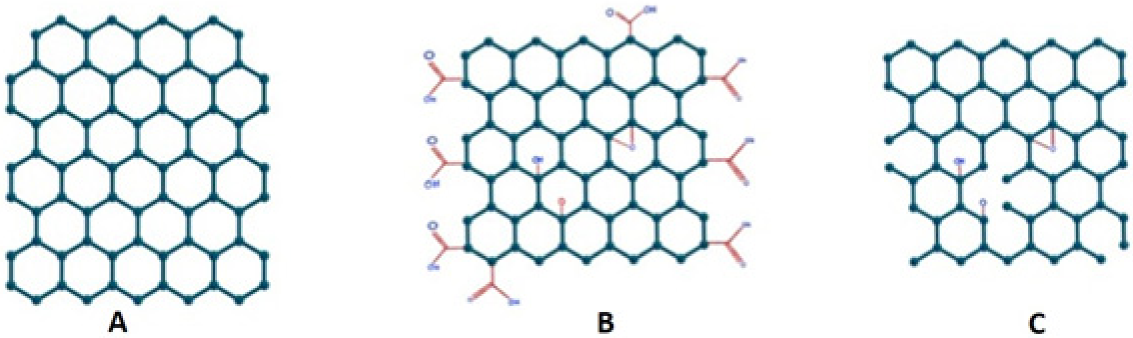

Figure 1: Schematic diagram of the graphene (A), where bonded carbon atoms form a honeycomb lattice; graphene oxide (B) where in reactive oxygen groups are situated on basal planes and edges and reduced graphene oxide (C) where in the carbon atoms are arranged in a hexagonal manner through covalent bonds, thereby forming a honeycomb structure

and biomedical fields, including the field of Dentistry. The field of Orthodontics requires the use of several dental materials, each with specific requirements. Graphene with its versatility is highly suited for incorporation into several orthodontic appliances and materials [5-7].

Biocompatibility: Graphene has been found to be biocompatible, meaning it does not elicit toxic or harmful reactions when in contact with living tissues. This property is crucial for various materials and implants to ensure they are well-tolerated by the oral environment and do not cause adverse effects on surrounding tissues [5].

High strength and durability: Graphene is one of the strongest materials known. Its exceptional mechanical properties make it ideal for dental applications that require strength and durability, such as dental implants, fillings, and prosthetics.

Electrical conductivity: Graphene exhibits excellent electrical conductivity, allowing it to conduct electrical signals and interactions effectively. This property is valuable for developing oral sensors and diagnostic devices in dentistry, enabling the accurate measurement and monitoring of various oral parameters and conditions.

Antibacterial properties: Graphene has shown potent antibacterial properties against a broad spectrum of bacteria. Its antimicrobial activity can help to prevent bacterial colonization, biofilm formation, and oral infections, making it valuable for dental materials, such as mouthguards, orthodontic appliances, or dental implant coatings [6].

Thermal conductivity: Graphene possesses exceptional thermal conductivity, allowing efficient heat transfer. This property can be advantageous in dental applications where temperature management is crucial, such as laser treatments, dental drills, or thermal therapies.

Flexibility and Transparency: Graphene is highly flexible and can conform to different shapes and contours, which is beneficial for dental applications that require customized or adaptable materials. Additionally, graphene is transparent, enabling its integration into transparent dental devices or appliances without compromising aesthetics.

Graphene Derivatives

Graphene oxide: Graphene oxide (GO) is obtained by the oxidation of graphene. It presents various reactive oxygen functional groups (e.g., hydroxyl, carboxyl, and epoxy groups) located on the basal plane and the edges, which are beneficial to combine different biomolecules. (Figure-1) GO is more hydrophilic and has defective structure, poor insulating property, and mechanical property compared to Graphene [8].

Reduced graphene oxide (rGO): rGO, produced by the reduction of GO, retains the two-dimensional structure of graphene, consisting of a single layer of carbon atoms arranged in a hexagonal lattice. (Figure-1) It is a unique form of graphene that is chemically or thermally treated to remove oxygen-containing functional groups from the graphene oxide structure [8,9]. This reduction process transforms the insulating graphene oxide into a highly conductive and versatile material with a range of useful properties. However, it shows structural defects as compared to pure graphene.

Graphene nanoplatelets (GNPs): GNPs are two-dimensional carbon structure materials with platelet shaped single or multiple layers of graphene which possesses attractive characteristics including high electrical conductivity, high modulus of elasticity, high strength, high thermal conductivity and high specific surface area [10].

Graphene quantum dots (GQDs): GQDs are graphene blocks with two-dimensional (2D) transverse size (less than 100 nm) [11]. Owing to its smaller size, GQD has a better prospective application in biomedical fields than graphene and its other derivatives [12]. GQDs also have adequate sites for binding with molecules such as peptides, drugs and other markers to be used for detection and treatment of several conditions, while being more biocompatible than graphene. In addition, GQDs offer the advantage of photoluminescence, a property that is useful in fabrication of certain sensors for detection of several organic and inorganic compounds [13].

Other forms of graphene: Graphene foam, aerogel and hydrogel are some of ways in which Graphene has been used. Graphene foam is a 3D structure made of interconnected graphene sheets. Graphene aerogel is a lightweight, porous material made of graphene, while various hydrogel materials incorporate graphene to improve their mechanical and electrical properties. The high surface area of graphene can also improve the adhesive properties of the hydrogel and increase the bonding strength to tooth surfaces. These properties, along with the porous nature of graphene hydrogel render it useful to be used as a scaffold material for tissue engineering in orthodontics [14].

Table 1: Various studies on the orthodontic applications of graphene and its derivatives

Authors (Year)	Mode of graphene application	Results
(A) Graphene in metal alloys for arch wires and implants		
Li et al. [15] (2015)	Nickel-Titanium (NiTi) alloy with graphene film coating	The graphene layer improved the surface bioactivity of NiTi alloy and promoted the osteogenic differentiation of mesenchymal stem cells.
Zhang et al. [16] (2017)	Nickel-Titanium (NiTi) alloy with graphene film coating	Graphene film on the NiTi alloy exhibited good anti-corrosion and biocompatibility activity.
Rokaya et al. [17] (2019)	Nickel-Titanium (NiTi) alloy with graphene oxide /silver nanoparticle (GO/AgNP) coating	The GO/AgNP coated NiTi alloy demonstrated improved mechanical strength and a reduced friction coefficient.
Mallick et al. [18] (2019)	Electrophoretic deposition (EPD) of graphene on Nitinol wires	Nitinol wires with graphene coatings showed a significant improvement in the corrosion resistance property.
Srimaneepong et al. [19] (2020)	Graphene oxide (GO) and GO/silver (GO/Ag) nanocomposite coating on nickel-titanium (NiTi) alloy	Both the GO-coated NiTi and GO/Ag-coated NiTi alloys showed less corrosion resistance, a lower rate of corrosion, and higher protection efficiency than the bare NiTi alloy. The coated NiTi alloys were biocompatible to human pulp fibroblasts and showed upregulation of IL-6 and IL-8 levels.
Dai et al. [20] (2021)	Nickel-Titanium (NiTi) alloy with different concentrations of graphene oxide coatings	Graphene oxide coatings with different concentrations reduced the corrosion tendency if NiTi alloy in the artificial saliva, and enhanced the lubricity as well as anti-*Streptococcus mutans* ability by reducing the adhesion of plaque to the alloy.
Pipanttanachat et al. [21] (2021)	Nickel-Titanium (NiTi) alloy coated with graphene oxide/silver nanoparticles (GO/AgNP)	Modifying the NiTi alloy surface using GO/AgNPs decreased the biofilm formation.
Guo et al. [22] (2022)	Application of graphene oxide (GO) coatings on the selective laser melting NiTi (SLM-NiTi) alloy	GO coating enhanced the corrosion resistance of SLM-NiTi alloy and inhibited the nickel ions release. GO coating promoted the adhesion, growth, and proliferation of osteoblasts.
Wang et al. [23] (2022)	Graphene sheets embedded carbon (GSEC) films on the orthodontic stainless steel archwires	GSEC decreased the friction coefficient and wear rate.
Araujo et al. [24] (2022)	Nickel-Titanium (NiTi) alloy with graphene oxide (GO) and a composite of reduced graphene oxide (rGO) coatings	Both coatings presented the capacity of following several superelastic cycles, maintaining their morphological integrity. Only the rGO coating resulted in a significant improvement of corrosion resistance.
(B) Graphene in orthodontic adhesive		
Bregnocchi et al. [25] (2017)	Adhesive filled with graphene nanoparticles (GNP)	Adhesive containing the 0.2%wt of GNPs had mechanical properties comparable with the adhesive without GNPs.
Lee et al. [26] (2018)	Addition of mixture of graphene oxide (GO) and bioactive glass (BAG) to low-viscosity Transbond XT (LV) in a ratio of 1, 3, and 5%.	The anti-demineralization effect was higher in the BAG plus GO-group than in the LV-group. The higher the BAG plus GO concentration, the more was the anti-demineralization effect.
Nam et al. [27] (2019)	Bonding resins containing Graphite Fluoride Bio active Glass (FGtBAG)	Orthodontic resins containing FGtBAG had more antibacterial activity and remineralization effect.
Ghorbanzadeh et al. [28] (2021)	Curcumin-reduced nano-graphene oxide (rGO-NCUR) with a composite resin	Composite containing 5% w/w rGO-CUR had more antimicrobial activity without adverse effect on the physical-mechanical properties of composites.
Alnatheer et al. [29] (2021)	Silanized graphene oxide (SGO) modified adhesive bonded to orthodontic bracket	Adhesive modified with 0.25 wt% SGO showed higher shear bond strength, sufficient durability, greatest bactericidal and least cytotoxic effect.
Pourhajibagher et al. [30] (2021)	Orthodontic adhesive doped with nano graphene oxide (N-GO)	Adhesive with 5 wt% of N-GO reduced the microbial count and biofilm with no adverse effect on shear bond strength and adhesive remnant index.
Ghorbanzadeh et al. [312] (2021)	Photoactivated orthodontic composite containing nano structured graphene oxide (OC-GO)	Photo-activated 5% wt. OC-nGO had better control on cariogenic bacterial biofilm formation.
Pourhajibagher et al. [32] (2022)	Orthodontic adhesive discs containing 0, 1, 2, 5, and 10% GO	Orthodontic adhesives with 5% and 10% concentrations of GO showed significantly more antimicrobial activity against *Streptococcus mutans* in cariogenic biofilms.
Gamal et al. [33] (2022)	Graphene oxide nanoparticles within self-etch adhesive	Addition of graphene oxide nanoparticles to self-etch adhesive had an antibacterial effect without affecting the bond strength.

Table 1: continued

Llie et al. [34] (2022)	Silica-silver-graphene (SiO_2-Ag-Gr), graphene and silver doped hydroxyapatite (HA-Ag-Gr)	Orthodontic adhesives with Silica-silver-graphene (SiO_2-Ag-Gr), graphene and silver doped hydroxyapatite (HA-Ag-Gr) showed a positive effect on local biocompatibility up to 6 months in an in-vitro simulation of clinically relevant environmental conditions and aging.
Sawan et al. [35] (2022)	Orthodontic adhesive modified with graphene sheets decorated with silver nanoparticles (Ag-GS)	Adhesive with 0.35 wt% Ag-GS increased the antibacterial capabilities significantly and showed promising results for bonding orthodontic brackets to enamel without compromising strength.
(A) Graphene in acrylic resin		
Lee et al. [36] (2018)	Poly-methylmethacrylate (PMMA) with nano-graphene oxide (nGO)	Incorporating nGO to PMMA exhibited an anti-adhesive effect against microbial species in artificial saliva.
Gamal et al. [37] (2019)	Poly-methylmethacrylate (PMMA) with nano- graphene oxide (GO)	Incorporation of nGO into the PMMA at a concentration of 0.5% inhibited the growth of *Streptococcus mutans.*
Bacali et al. [38] (2020)	Poly-methylmethacrylate (PMMA) resin enhanced with graphene and silver nanoparticle	The PMMA resin loaded with G-AgNp had promising antibacterial activity associated with minimal toxicity to human cells, *in-vitro,* as well as improved flexural properties.
Aati et al. [39] (2022)	Acrylate-based resin impregnated with graphene nanoplatelets (GNPs)	The embedment of GNPs in 3D printed resin exhibited high antimicrobial, stiffness and strength properties.
Ionescu et al. [40] (2022)	Graphene nanofibers (GNF)-doped (<50 ppm) polymethyl methacrylate for CAD-CAM	GNF-doping improved the material's performance and increased its antimicrobial potential.
Salgado et al. [41] (2023)	3D-printed resin loaded with graphene nanoplatelets	The use of graphene as a mechanical reinforcement nanomaterial seems to be viable at low concentrations without prejudice to the surface roughness of a 3D-printed poly-methylmethacrylate resin.
Teimoorian et al. [42] (2023)	Functionalized GO nanosheets added to polymethyl methacrylate	Addition of functionalized nGO in appropriate concentrations to polymethyl methacrylate improved the anti-bacterial and anti-fungal biofilm properties without changing or increasing their physical and mechanical properties.
(B) Graphene in bone remodelling and tissue engineering		
Jiao et al. [43] (2022)	Local periodontal injection of gelatin reduced graphene oxide in mouse model	Local injection of gelatin reduced graphene oxide induced more osteoclastic bone resorption and neovascularization by stimulation of bone marrow stem cells and thus accelerated the orthodontic tooth movement.

Orthodontic Applications of Graphene

In Orthodontics, graphene's unique properties and chemical structure make it a promising material for various applications, including orthodontic brackets, wires, and adhesives. Graphene can be incorporated into many orthodontic materials to enhance their mechanical strength, electrical conductivity, and biocompatibility, among other properties.

For reviewing the existing literature on the use various uses of graphene and its derivatives in orthodontics, the PubMed via Medline, Scopus via Ovid, Embase, LILACS and CINAHL databases were systematically searched. Abstracts, editorials, letters to editors, and literature reviews were excluded. In the search, the keywords consisting of "graphene" and "orthodontics", "archwires", "NiTi wires", "implants", "acrylic resin", "caries detection" "nanosensors" or "tissue engineering" were employed in various combinations. The title and abstracts were retrieved from the databases by one author (RM). Following a thorough search and including all relevant articles, duplicates were removed. This was followed by screening of the titles, followed by the abstracts which was done by two authors (RM and MB). Full texts of the articles that fall within the scope of the present study were retrieved and included in the present review after a final consultation with the third author (AKJ). The findings of these studies were summarized in a tabular format. Inferences on the potential applications of graphene in orthodontics were drawn by studying on its current uses based on its various properties in different aspects.

Various applications of graphene and its derivatives as materials and other aids in the field of orthodontics is summarized in table 1. Several metal alloys have various uses in orthodontics. These alloys have been further enhanced to improve their physical properties and biological stability. Graphene offers a near ideal material for enhancing the properties of these metal alloys. The alloy, hence formed, when used in orthodontic implants improves their mechanical properties, biocompatibility, and osseointegration [15-24]. When used in arch wires, graphene increases their strength and decreases friction and corrosion resistance [18,23,24]. Graphene, GO and rGO have been used in orthodontics for coating alloys such as NiTi and stainless steel to be used as orthodontic arch wires and implants [15-24]. Like GO, rGO has also been employed for coating alloys to be used as alloys [24].

The methods used for coating graphene and its derivatives on alloy surfaces include chemical vapor deposition, electrophoretic depositions or dip coatings and all of these techniques have reported an increase in corrosion resistance and biocompatibility in the coated alloy [18,23,24]. While Araujo et al. further incorporated block copolymer of styrene-ethylene-butylene-styrene along with rGo which resulted in decreased the oxygen vacancies in the passive film when compared with the bare NiTi and GO coating, thereby improving properties of the alloy [23]. Therefore, such modifications predict greater opportunities for exploration of other uses of rGO. However, the incorporation of graphene derivatives in these materials has only been tried on a surface level. Further development of materials that disperse graphene into orthodontic material might lead to a further improvement in characteristics of these materials.

A major advantage of graphene and its derivatives includes its biocompatibility and antimicrobial characteristics. Hence, they have been incorporated into composites in order to prevent dental caries. In orthodontics, bonding adhesives form the junction between dental hard tissue and brackets, where enamel demineralization is likely to occur. Graphene incorporated adhesives can prevent this enamel demineralization and hence white spot lesions, which are inevitable in several post-orthodontic cases [25-35]. Another material where graphene can be incorporated is polymethyl methacrylate, which is used in several orthodontic appliances. Orthodontic appliances are a potential niche for bacterial colonies, if adequate hygiene measures are not taken. Incorporation of graphene can render these appliances more biocompatible with added antimicrobial action [36-42].

Advanced Uses and Future Perspectives for Graphene in Orthodontics

The applications and future perspectives of graphene and its derivatives in orthodontics is summarized in figure 2. Graphene can be incorporated in various components of orthodontic mechanotherapy, including those fabricated from metal alloys, composite and acrylic resin. Further, graphene holds great potential for use as scaffold in bone remodelling procedures or to be used directly as local injections. Graphene-based sensors may be modified with defined functional groups to have render them sensitive for caries detection. These sensors may also be used to carry specific antimicrobial peptides for detection and targeted action on microbe. Evidence from the use of graphene in tissue engineering and caries detection from in-vitro and animal models in various biomedical fields suggest that graphene derivates may be of great use in orthodontics in coming future. However, evidence on these from orthodontic perspective is very limited, thereby creating a potential for further research.

Functionalization of graphene according to the orthodontic requirements can open newer avenues in patient care and research. Graphene when functionalized appropriately can help in remineralization of early caries lesions, including post-orthodontic white spot lesions as well. A study by Nizami et al. evaluated the efficacy of functionalized graphene oxide nanocomposites on the decalcification of dentin and found that GO-Ag, GO-Ag-CaF_2, and GO-CaF_2 nanocomposites were most effective for the preventive for decalcification [44]. Moreover, GO-Ag and GO-Ag-CaF_2 almost completely inhibited *Streptococcus mutans* growth. Such methods may be tried in the development of orthodontic adhesives

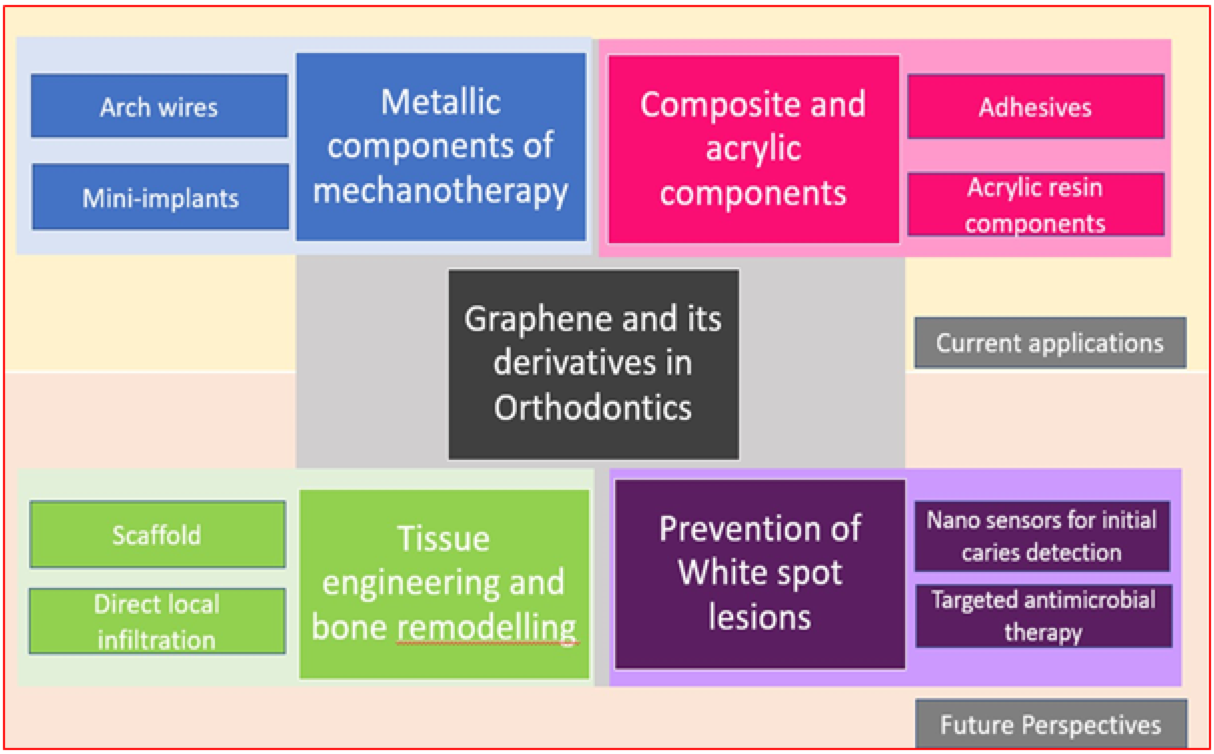

Figure 2: The applications and future perspectives of graphene and its derivatives in orthodontics

as well [44]. Since dental caries results from a disruption of balance between demineralization and remineralization processes, favouring demineralization, the use of graphene functionalized with fluoride moieties would help in achieving adequate remineralization potential.

Advances in the field of orthodontics and identification of bone remodelling techniques have the potential of increasing the pace of orthodontic treatment with the aid of manipulations at molecular level. Tissue engineering approaches can seek to introduce cells to promote tissue repair through transplantation with a scaffold material or direct injection at the target site. Alternatively, approaches can aim to recruit host cells from surrounding tissue or distal locations in the body to cause tissue repair. Graphene, with its porous morphology, great surface area, selective permeability, excellent mechanical, thermal, electrical and optical properties biodegradability appear to be an ideal component for scaffold engineering. Also, in simulated oral micro environment, graphene was found to be efficient in differentiating stem cells into specific cell types [43]. The upregulation of markers in dental pulp stem cells cultured on the group with GO, including dentin sialophosphoprotein (DSPP), dentine matrix protein-1 (DMP-1), Alkaline Phosphatase and Osteopontin have been observed in-vitro [44]. In another study, Silk fibroin protein hydroxyapatite (SF/HAP) scaffolds with nanosized GO with polyethylamine functionalized carry and spatially control the release of the miR-214 inhibitor [45]. This system has been shown to have the ability to enhance osteogenic differentiation in mouse osteoblastic cells in-vitro. These scaffolds also activated the osteoblastic activity of endogenous osteoblast cells to repair critical-sized bone defects in rats without the need for loading osteoblast cells [46]. Such scaffolds may be used to aid in carrying components such as platelet rich fibrin to facilitate faster orthodontic tooth movement. Functionalization of graphene may also be carried out to render them create a conducive environment for tooth movement by acting on specific molecular targets. Direct injections of graphene derivates have also been found to have positive influence on orthodontic tooth movement. Jiao et al. used direct local injections of gelatin reduced graphene oxide for orthodontic tooth movement in mouse models [42]. GOG stimulated bone marrow stem cells to cause accelerated bone remodelling through osteoclastogenesis and angiogenesis [43].

Graphene based biosensors are highly promising because of their remarkable sensitivity, wide detection range, ability of functionalization, fast response time, all in a transparent and miniaturized system that can be easily incorporated into orthodontic appliances. In the recent development of biosensors and electronics, graphene has rapidly gained popularity due to its superior electrical, biochemical, and mechanical properties. Since graphene can be functionalized to have selectivity towards specific chemical and biological or chemical targets [47]. This facilitates development of nanosensors with peptides that enable efficient recognition of pathogenic bacteria [48]. This ability is of great use in the prevention of white spot lesion, which is a common post-orthodontic complication. Such sensors, being lightweight and transparent, may be easily incorporated into orthodontic appliances. In a study by Chen et al. in which graphene, nanosensors were functionalized with a chemically synthesized bifunctional peptide consisting of a graphene based peptide and another domain with antimicrobial peptide (AMP), which showed activity towards both the Gram-negative bacteria like *Escherichia coli* and *Helicobacter pylori*, and the Gram-positive bacteria *Staphylococcus aureu* [49]. Further, these biosensors may also be modified to detect the level of various proteins and salivary markers that are indicate the level of orthodontic tooth movement. Further, GQDs and its unique properties, such as high surface area and fluorescence, aid in the development of bioimaging, biolabeling tools.

Conclusion

Graphene is a two-dimensional material with extraordinary physical and chemical properties that have been investigated for use in various applications, including orthodontic materials. Graphene and its derivatives have been used to improve the mechanical properties, biocompatibility, and antibacterial properties of orthodontic brackets, adhesives, and arch wires. incorporating graphene or its derivatives into orthodontic materials can enhance shear bond strength, reduce frictional resistance, improve sliding mechanics, and increase hardness. The various forms and derivatives of graphene offer unique properties that can be tailored to specific applications, making graphene a promising material for the field of orthodontics. Hence, the material science of graphene and its derivatives is an evolving towards optimizing the use of graphene in orthodontic materials thereby improving their performance and ultimately enhance patient outcomes. With further research to fully explore the potential uses of these materials and to address any potential safety concerns, graphene may emerge as one of the most versatile materials to be used in orthodontics.

References

1. G. Ruess, F. Vogt, Monatsh für Chemie, 78, 222 (1948).
2. K.S. Novoselov, D. Jiang, F. Schedin, T.J. Booth, V.V. Khotkevich, S.V. Morozov, et al. Two-dimensional atomic crystals, Proc. Natl. Acad. Sci. U S A, 102,: 0451 (2005).
3. K.S. Novoselov, A.K. Geim, S.V. Morozov, D. Jiang, Y. Zhang, S.V. Dubonos, et al., Electric field effect in atomically thin carbon films, Science. 306, 666-9 (2004).
4. Y. Zhang, Q. Wan, N. Yang, Recent advances of porous graphene: synthesis, functionalization, and electrochemical applications, Small, 15, 1903780 (2019).
5. G. Wang, F. Qian, C.W. Saltikov, Y. Jiao, Y. Li, Microbial reduction of graphene oxide by Shewanella, Nano. Res. 4, 563-70 (2011).
6. W. Hu, C. Peng, W. Luo, M. Lv, X. Li, D. Li, et al., Graphene-based antibacterial paper, ACS. Nano. 4, 4317-23 (2010).
7. X. Li, X. Liang, Y. Wang, D. Wang, M. Teng, H. Xu, et al., Graphene-based nanomaterials for dental applications: principles, current advances, and future outlook, Front. Bioeng. Biotechnol. 10, 804201 (2022).
8. G. Reina, J.M. González-Domínguez, A. Criado, E. Vázquez, A. Bianco, M. Prato, Promises, facts and challenges for graphene in biomedical applications, Chem. Soc. Rev. 46, 4400-16 (2017).
9. A. Lazauskas, L. Marcinauskas, M. Andrulevicius, Photothermal reduction of thick graphene oxide multilayer films via direct laser writing: morphology, structural and chemical properties, Superlat. Microstruc. 122, 36-45 (2018).
10. C.F. Kuan, C.L. Chiang, S.H. Lin, W.G. Huang, W.Y. Hsieh, M.Y. Shen, Characterization and properties of graphene nanoplatelets/XNBR nanocomposites, Polymers. Polymer. Compos. 26, 59-68 (2018).
11. Y. Yan, J. Gong, J. Chen, Z. Zeng, W. Huang, K. Pu, et al., Recent advances on graphene quantum dots: from chemistry and physics to applications, Adv. Mater. 31, e1808283 (2019).
12. K.S. Novoselov, A.K. Geim, S.V. Morozov, D. Jiang, Y. Zhang, S.V. Dubonos, et al., Electric field effect in atomically thin carbon films, Science. 306, 666-9 (2004).
13. C. Zhao, X. Song, Y. Liu, Y. Fu, L. Ye, N. Wang, et al., Synthesis of graphene quantum dots and their applications in drug delivery, J. Nanobiotechnol. 18, 142 (2020).
14. N. Amiryaghoubi, N. Noroozi Pesyan, M. Fathi, Y. Omidi, Injectable thermosensitive hybrid hydrogel containing graphene oxide and chitosan as dental pulp stem cells scaffold for bone tissue engineering, Int. J. Biol. Macromol. 1, 1338-57 (2020).
15. J. Li, G. Wang, H. Geng, H. Zhu, M. Zhang, Z. Di, et al., CVD growth of graphene on NiTi alloy for enhanced biological activity, ACS. Appl. Mat. Interfac.7, 19876-81 (2015).
16. L. Zhan, Y. Duan, Z. Gao, J. Ma, R. Liu, S. Liu, et al., Graphene enhanced anti-corrosion and biocompatibility of NiTi alloy, Nano. Impact. 7, 7-

14 (2017).

17. D. Rokaya, V. Srimaneepong, J. Qin, K. Siraleartmukul, V. Siriwongrungson, Graphene oxide/silver nanoparticle coating produced by electrophoretic deposition improved the mechanical and tribological properties of NiTi alloy for biomedical applications, J. Nanosc. Nanotechnol. 19, 3804-10 (2019).
18. M. Mallick, N. Arunachalam, Electrophoretic deposited graphene based functional coatings for biocompatibility improvement of Nitinol, Thin. Solid. Films. 692, 137616 (2019).
19. V. Srimaneepong, D. Rokaya, P. Thunyakitpisal, J. Qin, K. Saengkiettiyut. Corrosion resistance of graphene oxide/silver coatings on Ni-Ti alloy and expression of IL-6 and IL-8 in human oral fibroblasts, Sci. Rep. 10, 1-12 (2020).
20. D. Dai, D. Zhou, L. He, C. Wang, C. Zhang, Graphene oxide nanocoating for enhanced corrosion resistance, wear resistance and antibacterial activity of nickeltitanium shape memory alloy, Surface. Coatings. Technol. 431, 128012 (2022).
21. S. Pipattanachat, J. Qin, D. Rokaya, P. Thanyasrisung, V. Srimaneepong, Biofilm inhibition and bactericidal activity of NiTi alloy coated with graphene oxide/silver nanoparticles via electrophoretic deposition, Sci. Rep. 11, 14008 (2021).
22. Y. Guo, Z. Xu, Q. Wang, S. Zu, M. Liu, Z. Yu, et al., Corrosion resistance and biocompatibility of graphene oxide coating on the surface of the additively manufactured NiTi alloy, Progress. Organic. Coatings. 164, 106722 (2022).
23. P. Wang, X. Luo, J. Qin, Z. Pan, K. Zhou. Effect of graphene sheets embedded carbon films on the fretting wear behaviors of orthodontic archwire–bracket contacts, Nanomaterials. (Basel) 12, 3430 (2022).
24. A.F. Araujo, M.V. Ferreira, M.D. Felisberto, D.C. Sicupira, L.A. Santos, Corrosion resistance of a superelastic NiTi alloy coated with graphene–based coatings, Progress. Organic. Coatings. 165, 106727 (2022).
25. A. Bregnocchi, E. Zanni, D. Uccelletti, F. Marra, D. Cavallini, F. De Angelis, et al., Graphene-based dental adhesive with anti-biofilm activity, J. Nanobiotechnology. 15, 1-13 (2017).
26. S.M. Lee, K.H. Yoo, S.Y. Yoon, I.R. Kim, B.S. Park, W.S. Son, et al., Enamel anti-demineralization effect of orthodontic adhesive containing bioactive glass and graphene oxide: An in-vitro study, Materials. (Basel) 11, 1728 (2018).
27. Nam HJ, Kim YM, Kwon YH, Kim IR, Park BS, Son WS et al. Enamel surface remineralization effect by fluorinated graphite and bioactive glass-containing orthodontic bonding resin. Materials (Basel) 2019;12(8):1308.
28. R. Ghorbanzadeh, A.S. Vaziri, A. Bahador, Antimicrobial properties and shear bond strength of composite used in orthodontics following the addition of curcumin-reduced nanographene oxide, Avicenna. J. Clin. Microb. Infect. 8, 139-44 (2021).
29. M. Alnatheer, A. Alqerban, H. Alhazmi, Graphene oxide-modified dental adhesive for bonding orthodontic brackets, Inter. J. Adhes. Adhes. 110, 102928 (2021).
30. M. Pourhajibagher, A. Bahador, Orthodontic adhesive doped with nanographene oxide: physico-mechanical and antimicrobial properties, Folia. Medica. (Plovdiv) 63, 413-21 (2021).
31. R. Ghorbanzadeh, A.H. Nader, A. Salehi-Vaziri, The effects of bimodal action of photodynamic and photothermal therapy on antimicrobial and shear bond strength properties of orthodontic composite containing nano-graphene oxide, Photodiagnosis. Photodyn. Ther. 36, 102589 (2021).
32. M. Pourhajibagher, R. Ghorbanzadeh, A. Salehi-Vaziri, A. Bahador, Invitro assessments of antimicrobial potential and cytotoxicity activity of an orthodontic adhesive doped with nano-graphene oxide, Folia. Medica. (Plovdiv) 64, 110-6 (2022).
33. W.M. Gamal, A.M. Sayed, Post-gel shrinkage strain and degree of conversion of nanohybrid resin composite containing graphene oxide nanoparticles, Egypt. Dent. J. 68, 3691-9 (2022).
34. N. Ilie, N.E. Serfözö, D. Prodan, J. Diegelmann, M. Moldovan, Synthesis and performance of experimental resin-based dental adhesives reinforced with functionalized graphene and hydroxyapatite fillers, Materials. Design. 221, 110985 (2022).
35. N.M. Sawan, E.I. AlSagob, A.A. Ben Gassem, A.A. Alshami, Graphene functionalized with nanosilver particlemodified methacrylatebased bonding agent improves antimicrobial capacity and mechanical strength at tooth orthodontic bracket interface, Polymer. Composites. 42, 5850-8 (2021).
36. J.H. Lee, J.K. Jo, D.A. Kim, K.D. Patel, H.W. Kim, H.H. Lee, Nano-graphene oxide incorporated into PMMA resin to prevent microbial adhesion, Dent. Mater. 34, e63-e72 (2018).
37. R. Gamal, Y.F. Gomaa, A,M, Said, Incorporating nano graphene oxide to poly-methyl methacrylate; antibacterial effect and thermal expansion, J. Mod. Res. 1, 19-23 (2019).
38. C. Bacali, M. Badea, M. Moldovan, C. Sarosi, V. Nastase, I. Baldea, et al., The influence of graphene in improvement of physico-mechanical properties in PMMA denture base resins, Materials. 12, 2335 (2019).
39. S. Aati, A. Chauhan, B. Shrestha, S.M. Rajan, H. Aati, A. Fawzy, Development of 3D printed dental resin nanocomposite with graphene nanoplatelets enhanced mechanical properties and induced drug-free antimicrobial activity, Dent. Mater. 38, 1921-33 (2022).
40. A.C. Ionescu, E. Brambilla, P.M. Pires, A. López-Castellano, A.M. Alambiaga-Caravaca, C. Lenardi, et al., Physical-chemical and microbiological performances of graphene-doped PMMA for CAD/CAM applications before and after accelerated aging protocols, Dent. Mater. 38, 1470-81 (2022).
41. H. Salgado, J. Fialho, M. Marques, M. Vaz, M.H. Figueiral, P. Mesquita, Mechanical and surface properties of a 3D-printed dental resin reinforced with graphene, Revista. Portuguesa. de Estomatologia. 64, 12-19 (2023)S.
42. M. Teimoorian, M. Mirzaie, H. Tashakkorian, H. Gholinia, H. Alaghemand, A. Pournajaf, et al., Effects of adding functionalized graphene oxide nanosheets on physical, mechanical, and anti-biofilm properties of acrylic resin: In vitro- experimental study, Dent. Res. J. (Isfahan) 28, 37 (2023).
43. D. Jiao, J. Wang, W. Yu, K. Zhang, N. Zhang, L. Cao, X. Jiang, Y. Bai, Biocompatible reduced graphene oxide stimulated BMSCs induce acceleration of bone remodelling and orthodontic tooth movement through promotion on osteoclastogenesis and angiogenesis, Bioact. Mater. 15, 409-25 (2022).
44. M.Z.I. Nizami, Y. Nishina, T. Yamamoto, Y. Shinoda-Ito, S. Takashiba, Functionalized graphene oxide shields tooth dentin from decalcification, J. Dent. Res. 99, 182-8 (2020).
45. L. Ou, Y. Lan, Z. Feng, L. Feng, J. Yang, Y. Liu, et al., Functionalization of SF/HAP Scaffold with GO-PEI-miRNA inhibitor complexes to enhance bone regeneration through activating transcription factor 4, Theranostics. 9, 4525-41 (2019).
46. N. Sun, S. Yin, Y. Lu, W. Zhang, X. Jiang, Graphene oxide-coated porous titanium for pulp sealing: an antibacterial and dentino-inductive restorative material, J. Mater. Chem. B. 8, 5606-19 (2020).
47. R. Goldoni, M. Farronato, S.T. Connelly, G.M. Tartaglia, W.H. Yeo, Recent advances in graphene-based nanobiosensors for salivary biomarker detection, Biosens. Bioelectron. 171, 112723 (2021).
48. M. Mannoor, H. Tao, J. Clayton, A. Sengupta, D.L. Kaplan, R.R. Naik, et al., Graphene-based wireless bacteria detection on tooth enamel, Nat. Commun. 3, 763 (2012).
49. L. Chen, Y. Li, J. Li, X. Xu, R. Lai, Q. Zou, An antimicrobial peptide with antimicrobial activity against *Helicobacter pylori*, Peptides. 28, 1527-31 (2007).