IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 4 Ser.3 (April. 2020), PP 21-24
www.iosrjournals.org

GRAPHENE:- A Future Promising Biomaterial In Endodontics & Restorative Dentistry : A Review

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Abstract: *Graphene and its derivatives, graphene oxide (GO) and reduced graphene oxide (rGO), are 2D carbon-based materials.Graphene family and materials, with superior and remarkable mechanical, chemical, and biological properties, are able to grab appreciable attention on the path of researches seeking new materials for future promising biomedical applications. Moreover, they have been shown to influence the differentiation of stem cells and to improve properties of biomaterials. Grapheneanditsderivatives can be combined with several biomaterials used in regenerative, restorative dentistry and medicine. Asitcanbefunctionalizedandcombinedwithseveralbiomolecules,grapheneholdsenormouspotentialtobeusedasdrugsubstratesandscaffoldsforcell- basedtissueengineeringstrategies also.*

Date of Submission: 24-03-2020 Date of Acceptance: 11-04-2020

I. Introduction

With the advancement of biomaterial and its clinical applications, graphene has gained much attention recently. Graphene is a two-dimensional carbon allotrope which has sp2-bonded carbon atoms in a single sheet-like arrangement in a honeycomb pattern with extremely high mechanical strength and modulus of elasticity. Its remarkable structural, chemical, thermal, and biological properties have been demonstrated and can be applied in dentistry. Moreover, graphene has unparalleled electronic properties and offers a large surface area that can be chemically functionalized.

Graphene family nanomaterials (GFNs)include ultrathin graphite, few-layer graphene (FLG), graphene oxide (GO; from monolayer to few layers), reduced graphene oxide (rGO), and graphene nanosheets (GNS) [3]. They differ from each other in terms of surface properties, number of layers, and size [4]. Among other members of graphene family nanomaterial, graphene oxide (GO) is one of the most important chemical graphene derivatives which could be produced through energetic oxidation of graphite through Hummers method using oxidative agents. GO possessed a variety of chemically reactive functional groups on its surface, which facilitate connection with various materials including polymers, biomolecules, DNA, and proteins [5]. Reduced graphene oxide (rGO) can be obtained by chemically, thermally, or electrochemically reducing graphene oxide, which possesses heterogeneous electron-transfer properties [6]. Fluorinated graphene (FG) is an uprising member in the graphene family. FG has favorable biocompatibility, exhibiting a neuro-inductive effect via spontaneous cell polarization and enhancing adhesion and proliferation of mesenchymal cells providing scaffold for their growth. However, because of its properties especially antibacterial properties and tissue regenerative capacities, it has been widely review and studied in medicine field considering limited in vivo and in vitro studies in dentistry. Therefore, this article reviews the recent achievements and provides a comprehensive literature review on the potential applications of graphene that could be translated into clinical reality in dentistry.

HISTORICAL BACKGROUND OF GRAPHENE

(1848-1958) Graphite oxide was prepared by Hummers, Brodie et al.
(1962) Reduced graphene oxide (rGO) was prepared by thermal and chemical reduction of graphite oxide.
(1970) Monolayer graphite was prepared by seggregating carbon on the surface of nickel.

(1986) The term graphene was suggested by Boehm et al. to describe single layer of graphite like carbon.
(1999) Rouff et al. isolate multiple layers of graphene by micromechanical exfoliation.
(2004) Single layer of graphene were isolated by Geim&Novoselov via mechanical exfoliation.
(2010) Geim&Novoselov were awarded with the Nobel Price.

IMPORTANT CHARACTERISTICS OF GRAPHENE THAT POTENTIATE ITS APPLICATION IN DENTISTRY.

Biocompatibility-

The most important point to consider in the introduction of a new biomedical material is biocompatibility of the material. For graphene-based nanomaterial to be applied in clinical use, it is necessary tounderstand the interaction of graphene and their derivatives with living systems and their toxicity both in vivo and in vitro. The cytotoxicity of GFNs depends on various factors including their morphology (size, shape, and sharp edges), surface charge, surface functionalization, dispensability, state of aggregation, number of layers, purity, and methods of synthesis [7].

The concentration of GFNs is directly proportional to its toxicity, 50ug/ml might be a toxicity threshold for GO on normal mammalian cells. Many studies suggested that Oxidative Stress is the main cause, as the elevated ROS level may oxidize various molecules including DNA, lipids, and proteins inducing apoptosis or necrosis [8]. However, studies on the cytotoxicity of GFNs in oral setting are very limited.

Antibacterial effects-

As we know, oral cavity is a complex ecosystem, forming structurally and functionally organized dental biofilm embedded in a matrix of polymers of host and bacterial origins. A thorough understanding of the antimicrobial mechanism is still in its infancy. Many studies and investigations have suggested three different predominate mechanisms regarding its antibacterial mechanism.

Physical damage is induced by blade like graphene materials piercing through the microbial cellular membrane causing leakage of intracellular substance leading to cell death.

Chemical effect is primary Oxidative Stress mediated with production of ROS, as increase in intracellular ROS accumulation could cause intracellular protein inactivation, lipid peroxidation, and dysfunction of the mitochondria, which ultimately lead to gradual disintegration of cell membrane and eventual cell death [9].

Streptococcus mutans is the primary gram-positive facultative anaerobic bacteria involved in caries formation while **Porphyromonasgingivalis** and **Fusobacteriumnucleatum**are Gram-negative anaerobic bacteria associated with periodontitis and root canal infection. A study conducted by Heetal. evaluated the antibacterial activity of GO nanosheets against these three common types of bacteria and found that GO nanosheets were highly effective against the growth of dental pathogens. At GO concentration of 40μg/mL, bacterial growth of P.gingivalis and F. nucleatum were inhibited, while, at concentration of 80 μg/mL, GO absolutely killed all S. mutans [10]. This could be explained by the difference of resistance toward oxidative stress generated by GO between anaerobic and facultative anaerobic bacteria, in which GO nanosheets were more bactericidal against obligate anaerobic bacteria.

PROMISING APPLICATIONS OF GRAPHENE IN RESTORATIVE DENTISTRY, ENDODONTICS & TISSUE ENGINEERING

Restorative Dentistry-

Despite the developments in Glass Ionomer cement constituents with addition of various filler types including fibers, metallic powders, and hydroxyapatite powders, its poor physio mechanical properties remains to be a concern. In recent years, attempts has also been made to incorporate graphene derived nanomaterial into commercially available glass ionomer for reinforcement. Graphene, when combined with glass ionomer prepared with poly(acrylicacid), has significantly enhanced physio-mechanical properties of Glass Ionomers. Fluoride graphene when prepared by hydrothermal reaction of graphene oxide and mechanically blend with glass ionomer could produce a GICs/FG composites matrix, which could significantly enhance the mechanical, anti-bacterial properties of glass ionomer. With the increase of FG content in glass ionomer, there is a decrease of pore sand microcracks in the internal structure of material and an increase in antibacterialability making it less susceptible to erosion disintegration and microbial invasion.

Reinforcing resin polymer matrices with graphene nanoparticles as fillers show improvement in physicochemical properties of dental nano composite. Due to the presence of microcavities between the healthy tissue and dental restoration causing bacteria invasion, there has been an increasing interest in development of anti-biofilm adhesives. One concern with dental adhesive monomers is its excessive ROS production which not only cause oxidative stress associated toxicity toward fibroblasts and pulp cell, but also affect saliva redox equilibrium and decreasing natural oral immune system defenses. Due to graphene's anti bacterial properties, Bregnocchi et al. proposed using GFNs as an antimicrobial and antibiofilm filler for dental adhesive. The study result showed that GFNs modified dental adhesive significantly inhibited the adhesion and growth of S. mutans without interfering its original mechanical performances and without producing excess of ROS.

Endodontics

The main cause of endodontic treatment failure is persisting infection in the root canal. Recently developed photodynamic therapy has gained attention for effective canal disinfection while preserving dentin structures. One of the material that plays a key role in this technique is nontoxic photosensor, such as indocyanine green (ICG), but its limitations like poor stability and concentration dependent aggregation cannot be ignored [11]. Modifying ICG with GO not only significantly reduced number of E. faecalis in the canals and S. mutans, but also improve the stability and bioavailability of ICG, preventing its degradation and aggregation[12].

Sodium hypochlorite is the most commonly use intracanal irrigants for its effective anti-bacterial and tissue-dissolving abilities. However, sodium hypochlorite accident such as apical extrusion during root canal treatment cause acute instant symptoms with serious potential sequelae including rapid hemolysis and ulceration of surrounding tissues, destruction of endothelial, fibroblast cells [13]. Incorporating graphene into silver nanoparticles showed strong antibacterial property, as efficacy as 3% sodium hypochlorite in canal disinfection, but with less cytotoxic effect to bone and soft tissues [14].

Bioactive cements have been widely used in endodontics for management of perforation, retrograde root filling, and pulp capping. Among them, Biodentine(BIO) and EndocemZr (ECZ) are considered as the safest cements that exhibits the least discoloration and calcification of tooth, however their limitations such as high pull-out bond strength, long setting time can be overcome by 3 wt % addition of graphene nanosheets which decreases the setting time of both cements significantly, and can be explained by the role of carbon based materials to act as a matrix for the development of C–S–H and calcium hydroxide, thereby reducing the induction period and accelerating the hydration process[15].

Tissue Engineering-

Dental pulp stem cells (DPSC) are self-renewing and multipotent cells which contain mesenchymal stem cells that can relatively easily obtained from the extracted teeth. They may undergo both osteoblastic and odontoblastic differentiation making it an interesting model for tissue regeneration.

Rosa et al. first confirmed the capability of GO to allow DPSC attachment and proliferation[16]. Xie et al. then tested the potential ability of graphene to induce DPSC's odontogenic and osteogenic differentiation. Without stimuli from bioactive factors, graphene produced by the chemical vapor deposition (CVD) method downregulated the expression of odontoblastic genes (MSX-1, PAX, and DMP), which implied that CVD grown graphene may not serve as a platform for endodontic and pulp regeneration**.**However, osteogenic genes and proteins including RUNX2, COL, and OCN were significantly upregulated on graphene. This is very likely that the osteogenic differentiation of stem cells presented higher potential as the rigidity of substrate increased

Nevertheless, graphene could be a potential material to be used for bone tissue engineering and regeneration.It could be speculated that graphene is one of the most promising biocompatible scaffolds for MSCs adhesion, proliferation, and differentiation, particularly toward the osteogenic lineage. Graphene alone with optimal concentration may spontaneously drive stem cells osteogenesis

II. Conclusion

Graphene and its derivatives are versatile materials that present unique characteristics such as large surface area, high mechanical properties and can be transferred onto different substrates to enhance their properties. As they can be functionalized and combined with several biomolecules and biomaterials, this carbonaceous material has great potential to design bio-composite with improved physicochemical and mechanical properties and to confer to existing biomaterials enhanced bioactivity and new capabilities providing new hope in the field of dentistry.

References

[1]. Ge Z, Yang L, Xiao F, Wu Y, Yu T, Chen J, Lin J, Zhang Y. Graphene Family Nanomaterials: Properties and Potential Applications in Dentistry. International journal of biomaterials. 2018;2018.

[2]. Xie H, Cao T, Rodríguez-Lozano FJ, Luong-Van EK, Rosa V. Graphene for the development of the next-generation of biocomposites for dental and medical applications. Dental Materials. 2017 Jul 1;33(7):765-74.

[3]. N. Chatterjee, H.-J. Eom, and J. Choi, "A systems toxicology approach to the surface functionality control of graphene-cell interactions,"Biomaterials,vol.35,no.4,pp.1109–1127,2014.

[4]. S. Y. Wu, S. S. A. An, and J. Hulme, "Current applications of graphene oxide in nanomedicine," International journal of nanomedicine,vol.10,no.9,2015.

[5]. H. Wang, W. Gu, N. Xiao, L. Ye, and Q. Xu, "Chlorotoxin conjugated graphene oxide for targeted delivery of an anticancer drug,"International Journal of Nanomedicine,vol.9,no. 1,pp.1433–1442,2014.

[6]. B. Gadgil, P. Damlin, and C. Kvarnstr¨om, "Graphene vs. reduced graphene oxide: A comparative study of graphene based nanoplatforms on electrochromic switching kinetics," Carbon,vol.96,pp.377–381,2016.

[7]. S. Malik, F. M. Ruddock, A. H. Dowling et al., "Graphene composites with dental and biomedical applicability," Beilstein Journal of Nanotechnology, vol.9,no.1,pp.801–808,2018.

[8]. A.Nel,T.Xia,L.M¨adler,andN.Li,"Toxic potential of materials at the nano level,"Science,vol.311,no.5761,pp.622–627,2006.

[9]. X. Zou, L. Zhang, Z. Wang, and Y. Luo, "Mechanisms of the Anti-microbial Activities of Graphene Materials,"Journal of the American Chemical Society,vol.138,no.7,pp.2064–2077,2016.

[10]. S. Panda, T. K. Rout, A. D. Prusty, P. M. Ajayan, and S. Nayak,"Electron Transfer Directed Antibacterial Properties of Graphene Oxide on Metals,"Advanced Materials,vol.30,no.

[11]. V.Chrepa, G.A.Kotsakis, T.C.Pagonis and K.M.Hargreaves, "The effect of photodynamictherapy in root canal disinfection: a systematic review,"Journal of Endodontics, vol. 40, no. 7, pp. 891–898,2014.

[12]. T. Akbari, M. Pourhajibagher, F. Hosseini et al., "The effect of indocyanine green loaded on a novel nano-graphene oxide for high performance of photodynamic therapy against Enterococcus faecalis, "Photo diagnosis and Photodynamic Therapy,vol.20, pp.148–153,2017.

[13]. S.A.Farook,V.Shah, D.Lenouvel, O.Sheikh, Z.Sadiq, and L. Cascarini,"Guidelines form and management of sodium hypochlorite extrusion injuries," British Dental Journal, vol. 217, no. 12, pp. 679–684,2014.

[14]. D.K.Sharma, M.Bhat, V.Kumar, D.Mazumder, S.V.Singh ,and M. Bansal, "Evaluation of Antimicrobial Efficacy of Graphene Silver Composite Nanoparticles against E. faecalis as Root CanalIrrigant:Anex-vivostudy,"Int.J.Pharm.Med.Res,vol.3, no.5,pp.267–272,2015.

[15]. N. Dubey, S. S. Rajan, Y. D. Bello, K.-S. Min, and V. Rosa, "Graphene nanosheets to improve physico-mechanical properties of bioactive calcium silicate cements,"Materials,vol.10,no. 6,2017.

[16]. V. Rosa, H. Xie, N. Dubey et al., "Graphene oxide-based substrate: physical and surface characterization, cytocompatibility and differentiation potential of dental pulp stem cells," Dental Materials,vol.32,no.8,pp.1019–1025,2016.

Dr. Rinky Hajong,etal. "GRAPHENE:- A Future Promising Biomaterial In Endodontics & Restorative Dentistry : A Review." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(4), 2020, pp. 21-24.