Graphene family nanoderivatives: ameliorating prosthetic dental materials: A review.

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Abstract
Due to their improved aesthetic quality resin composites can be considered the most used class of materials in dental restorations. But resin materials have some limitations. Incorporation of different nanomaterials in the resin component helps to it's properties. The science of graphene-based engineered nanomaterials is developing as new dental materials in the field of dental medicine. Because of their superior mechanical, chemical, and biological properties, they have got appreciable attention for various biomedical applications. The aim of this review article is to present the state of the art of graphene nanoderivatives and their applications in the dental medicine.

Keywords: Graphene, biopolymers, carbon nanoderivatives, resins, fixed prosthesis.

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Introduction

Various metallic and non metallic nanoparticles are used in the field of dental materials to enhance the performance of the materials and thereby the prosthesis. Most dental materials are in intimate contact with oral tissue for a long time; they must be noncytotoxic and biocompatible and have a harmonious interaction with host while performing desired functions. Therefore, a lot of interest has been shown in continuous development of dental materials with enriched properties.

Acrylic resins are hard, fragile and crystalline polymers, which are most commonly used thermostable materials in dentistry, they have a low impact resistance and a low transverse and flexion resistance. To overcome these drawbacks graphene can be incorporated as a nanomaterial not only due to its high traction resistance, coefficient of thermal expansion, high capacity for absorption and lubrication, flexibility and large surface area, but also for its high weight to resistance ratio. The combination of nano reinforcements and the original polymer is one of the main aspects that explains the increase in mechanical properties in this type of compound material. The discovery of 4 free standing graphene by Andre Geim and Konstantin Novoselov at the University of Manchester in 2004. Since then, there´s been tremendous interest from academics, industries and government institutions in exploration of graphene properties, production methods and potential applications.

In the fields of science and technology, metallic nanoparticles of silver, copper, strontium are commonly used whereas in case of nonmetals carbon is most commonly used. Carbon is an abundant element that has many applications. various carbon allotropes can be synthesized by altering the combinations of sp, sp2 , and sp3 hybridization, and a variety of carbon structures and nanostructures have been introduced to date. Generally,sp2 hybridized carbon atoms arranged in a hexagonal lattice to form carbon structure, but there are many different potential structures, morphologies and properties. carbon nanostructure has 4 categories: zero, one, two and three-dimensional.[1-3]

Structure of graphene:

Being a carbon allotrope , graphene is the thinnest and strongest material in existence. Graphene sheets are made up of sp2 hybridized carbon atoms which are 2 dimensional and 10nm thick in honey comb lattice pattern.

Graphene and its derivatives have good electrical conductivity, transparency, biocompatibility, superior mechanical strength and high surface area[4-5]. Hence they are popular in the fields of science and technology. To enhance strength and mechanical properties of composite and nanocomposites graphene is used. It also has some potential applications in the field of medicine such as disease diagnosis, cancer therapy and targeting, bio-imaging, drug and gene delivery.

Graphene Family Nanomaterials:

They can be classified on the basis of surface properties, number of layers, and size.[6] (fig:1). graphene oxide (GO) is one of the most important chemical graphene derivatives Among other members which could be produced through energetic oxidation of graphite through Hummers method using oxidative agents (fig:2). GO possessed a variety of chemically reactive functional groups on its surface, which facilitate connection with various materials including polymers, biomolecules, DNA, and proteins.[7] reduction of graphene oxide can be done via 3 methods: chemical, thermal and microwave.

Biological properties:

An ideal material used for creating scaffolds must be able to maintain the natural environment of the oral cavity This material must also be able to allow stem cells to form, proliferate and differentiate into specific tissue lineages. One can conclude that the material has required excellent biocompatibility for tissue engineering only if desired tissue lineage obtained which ultimately result in stem cell differentiation.[8] The use of graphene-based nanomaterials to stimulate cellular mineralization and osteogenic differentiation based on these materials' ability of osseoconduction in dentistry has been tested and proven.[9] once graphene and its composites are administered, they immediately come into contact with the immune system, hence In vivo, the interaction of with the immune system is very important to consider. A small amount of graphene and a higher quantity of SF creates good environment for the proliferation of PDLSCs. In lymphocytes, GO have no cytotoxic effects on T lymphocytes in low doses, while doses over 100 µg/ mL can cause apoptosis stemming due to oxidative stress [10] Graphene nanocomposites show high antibacterial properties against both Gram-positive and Gram-negative bacteria. Graphene physically damage microorganisms by penetrating and cutting the cell membrane, wrapping cells inducing mechanical stress and extracting phospholipids from lipid membranes as result of general antibacterial activity. oxidative stress is then generated through ROS generation and charge transfer phenomena.

Fabrication Of Graphene:

Since graphene was discovered it's manufacturing and fabrication method is always a major challenge that can not only produce high quality graphene but also at large scale. (Table No.3). Utilization of graphene by various industries depends mostly on finding fabrication methods for large scale production.[11] The popular method for production of graphene is via the reduction of graphite oxide or graphene oxide (GO) to reduced graphene oxide (RGO).[12,13] The popularity of this method is due to low-cost, high scalability potential, excellent yield and ability to disperse functionalized graphene in various solvents.

Graphene/Polymer Composites :

Graphene enhances the mechanical, electrical and thermal properties of polymer materials. However, a number of barriers must be overcome in order to reach the full potential of the resulting composites with acceptable properties for wider applications. (Table:4). The interaction between graphene and the polymer as well as graphene dispersion in the polymer matrix ultimately affects composites properties.[14,15] In order to achieve significant improvement of the polymer properties, nanoscale homogenous dispersion of graphene in the polymer matrix is essential.[16] Homogeneous dispersion minimizes the formation of concentrated local stresses and promotes uniform load transfer throughout the matrix.

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Implants:

The graphene film being hydrophobic exhibited a self-cleaning effect on its surfaces. This helped in reducing the adhesion of microorganism including S. mutans and S. sanguinis when coated on titanium substrate. Additionally, compared to titanium alone, graphene possesses osteogenic property which enhances the expression of osteogenic related genes RUNX2, COL-I, and ALP, osteocalcin gene thereby increases the deposition of mineralized matrix.[25] GO-Ti substrate provided a suitable environment for the attachment, proliferation, and differentiation of PDLSCs.

Graphene oxide/chitosan/hydroxyapatite-titanium (GO/CS/HA-Ti) is produced by incorporating GO + chitosan (CS) into hydroxyapatite-titanium substrate through electrophoretic deposition. It improves the adhesion, proliferation, and differentiation of BMSC cells in vivo and possessed superior osseointegration in vitro.

Ren et al. further incorporated GO and rGO into a hydrothermally prepared porous titanium scaffold on Ti implants, constructing a delivery vehicle for dexamethasone, an osteoinductive synthetic glucocorticoid. Their study showed that DEX-GO-Ti and DEXrGO-Ti enhanced ALP activity of rBMSCs, confirming their osteopromotive ability to promote proliferation and to accelerate osteogenic differentiation of rBMSCs.[26] Titanium implants when coated with graphene and its derivatives have remarkable abilities to improve properties of titanium, enabling binding of biomolecules, and induce osseointegration. These characteristics place them under the spotlight for improved and modified implant materials.

Dentures:

PMMA resin is a material of choice in case of denture prosthesis. PMMA has a good adaptability over mucosal tissues, furthermore it is biocompatible, non cytotoxic and its colour resembles the mucosa. Being a denture base material it has less strength when compared with metallic frameworks. Incorporation of graphene family nanoparticles in denture base materials enhances it's tensile properties and makes it more tough. Graphene oxide nanoparticles in combination with titanium dioxide particles is the material of choice now a days to improve quality of denture base materials.

Fixed Partial Prosthesis:

Rehabilitation of a missing tooth/teeth needs proper diagnosis and planning which will ultimately meet patient's expectations, providing them a good functional and esthetic replacement. Zirconia, lithium disilicate are some materials of choice in these cases. When compared with graphene, zirconia crown prosthesis more tooth preparation plus the prosthesis bears a high weight whereas graphene crown prosthesis are light in weight and requires less reduction of tooth, thereby conserve natural tooth structure.

Lithium disilicate material has a glass crystalline phase which makes it brittle and less resistant to fractures. Graphene when in combination with PMMA resin more fracture resistant crown prosthesis especially in posterior regions where occlusal load is more. As far as esthetics areas are concern graphene has wide range of shades. Commercially available graphene includes monochrome and multichroma formats which provide a great range of shades and choices to the clinician.

Full Mouth Rehabilitation:

The addition of carbon nanotubes, such as GO, in acrylic resins may enhance the resin's mechanical properties and decrease the degree of contraction during polymerization. [27,28]. Lee et al.[29] reported that antimicrobial-adhesion effects are better after incorporation of GO in PMMA than those exhibited by pure PMMA via increased hydrophilicity.

Conclusion:

Compared with conventional polymer materials, polymers nanocomposed with graphene have a higher modulus and specific resistance. the distribution of tension between the structures, makes them capable of withstanding tensions practically without suffering deformations. Safety and potential risks of GFNs should be determined, research efforts should be made to ensure biocompatible use of graphene in oral environment.

The functional potential of graphene with various biomaterials and biomolecules make it a promising candidate for use, despite its other properties, such as mechanical strength, electrical conductivity and thermal stability.[30] One of the most essential future goals for the biomedical therapeutic application of graphene and its derivatives, are antibiotic and/or anti-cancer agents, which is related to conceptual understanding of their toxicity profile. Researches toward graphene in dental materials can be conducted in 2 ways where one is to prepare new dental materials of graphene, and the other is by modifying them with addition of different substrates.

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TABLES:

Table No.1: Properties of graphene and it's derivatives

Parameters	Graphene	Graphene Oxide	Reduced Graphene Oxide
C:O Ratio	0	2-4	8-246
Young's Modulus (Tpa)	1	0.2	0.25
Fabrication	Chemical vapour deposition	Oxidation and exfoliation of graphite	Reduction of graphene oxide
Production Cost	High	less	less

Table No. 2: Properties and applications

Properties	Applications
Strength	Composite materials and alloys
Flexibility	Coatings, adhesives
Thermal Conductivity	Composites, polymers
Impermeability	Fillers, purification
Optical Properties	Thinner, transparent coatings

Table No. 3: Different methods of graphene manufacturing

1.	Micromechanical cleavage
2.	Graphene via graphite oxide
3.	Liquid-phase exfoliation
4.	Mechanical milling of graphite
5.	Electrochemical exfoliation

Table No. 4: Graphene polymer composites[17]

1.	Graphene/epoxy composites
2.	Graphene/cellulose composites
3.	Graphene/ Polyaniline (PANI) composites
4.	PVA/graphene nanocomposites
5.	Polyurethane (PU)/graphene composites
6.	Poly (vinylidene fluoride) (PVDF)/graphene composites
7.	Graphene/Polyethylene terephthalate (PET) nanocomposites
8.	Polycarbonate (PC)/graphene nanocomposites
9.	Graphene/alginate composites
10.	Polystyrene (PS)/graphene nanocomposites

Table No. 5: Applications And Actions Of Graphene Nanoparticles [24]

Applications	Actions
Membranes	Collagen membranes + GO= affects Human Gingival Fibroblasts (HGFs) It promotes the process of osteoblastic differentiation, It is compatible with cell viability in a dose-dependent manner It also decrease inflammation.[18]
Polymers and cements	Zinc Oxide Nanorods (ZnO-NRs) + GO the antimicrobial quality the ZNO-NRs lightened the colour.
Teeth whitening	Cobalt Tetraphenylporphyrin (CoTPP) + GO being a catalyst for teeth bleaching.[19] photoactivating hydrogen peroxide + CoTPP/rGO together creates more reactions between stains molecules [20]
Dental bacteria detection	Fabricated graphene nanosensors could biotransfer on to the surface of a human tooth for recognition of the pathogenic bacteria
Inhibition of bacterial biofilm formation	GO film could inhibit the adhesion and activity of bacterial cells during the early stage of biofilm formation and GO was powerful in killing the S. mutans bacteria.

Tissue engineering	Graphene's aromatic scaffold nature allows it to promote cell attachment, growth, proliferation, and differentiation. GO scaffolds+ gelatinhydroxyapatite (GHA) matrix, improves overall mechanical strength and osteogenic differentiation [21,22] These G/HA hydrogels are strong, highly porous, electrically conductive and biocompatible. [23]

FIGURES

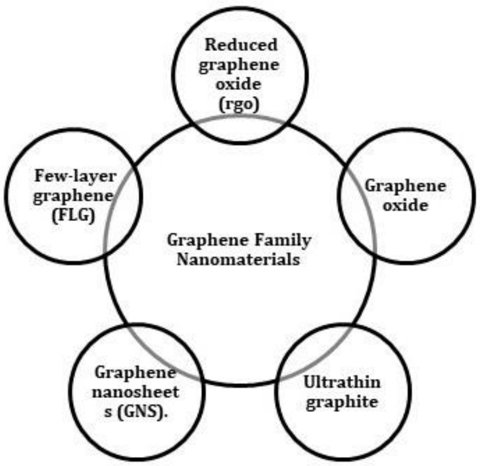

Figure No. 1

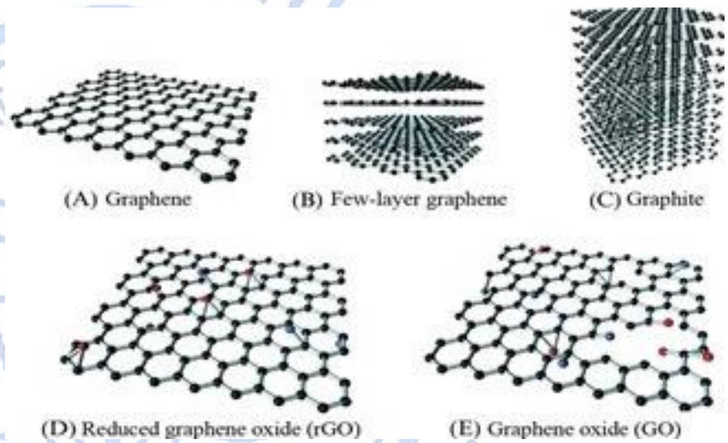

Figure No. 2

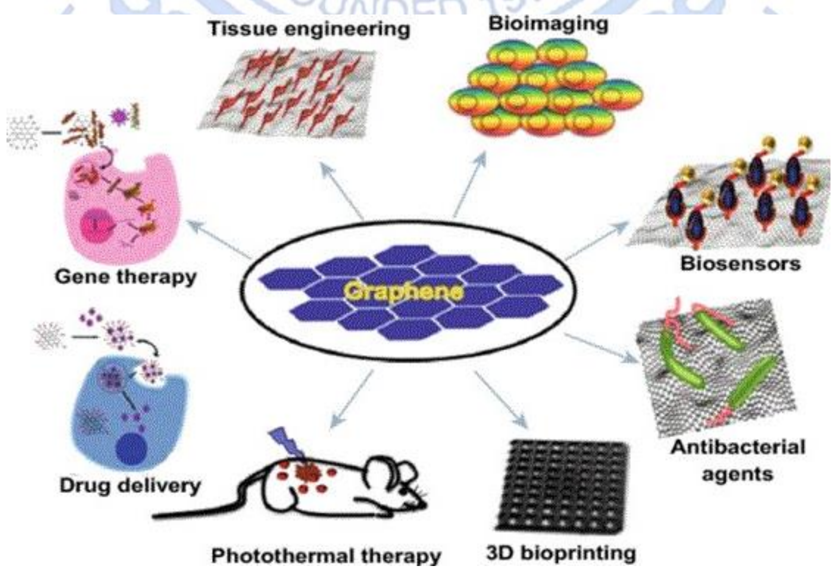

Figure No. 3