Graphne in Periodontology

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Abstract
Purpose: Nanotechnology has made significant advancement in recent years in various fields of medicine including dentistry. Graphene, one of the nanomaterials posses distinctive properties due to small size, larger surface area and interaction with various biological tissues and cells. It possess antibacterial properties also due to which it is being explored in Periodontal disease management also. **Approach:** This review includes studies published in the English language on graphene and graphene derivatives and its uses in periodontology. **Findings and conclusion:** This review addressed recent research on the biocompatibility, cytotoxicity, and antibacterial activity of nanomaterials based on graphene as well as graphene's potential for promoting osteogenic differentiation of stem cells, which is essential for its prospective use in periodontal treatment.

1. Introduction

Periodontitis and peri-implantitis are chronic inflammatory conditions that affect the tissues surrounding teeth and dental implants. These conditions arise from an immune response triggered by periodontal pathogens. The continuous invasion of these pathogens compromises the innate and acquired immune responses of the host, resulting in the destruction of periodontal tissues including the alveolar bone. Therefore, the main objectives in the treatment of periodontitis and peri-implantitis involve controlling the infection, prevent destruction of the tissues, and eliminating pathogens and biofilms from the tooth or implant surface.[1]

In recent years, nanotechnology has made significant progress, leading to advancements in various fields, including dentistry. Nanomaterials such as graphene and its derivatives, possess distinctive characteristics owing to their small size, expansive surface area, and ability to interact with cells. This interaction promotes migration and proliferation of cells, adhesion, and differentiation. Numerous graphene derivatives, including Few-Layered Graphene (FLG), ultrathin graphite, Graphene Oxide (GO), reduced Graphene Oxide (rGO), and graphene nanosheets, are included in the graphene family of nanomaterials. Their sizes, number of layers, and surface characteristics vary from one another.[2]

Graphene is utilized in the management of periodontal disease due to its antibacterial properties, regenerative abilities, and its capacity to promote the regeneration of periodontal tissue and bones. The application of graphene coated surfaces has demonstrated an improvement in osteogenic potential.[3] Several research groups have focused on investigating graphene oxide (GO) as a coating material for titanium (Ti) implants to enhance osseointegration. Additionally, graphene oxide has been found to enhance the adhesion, proliferation, osteogenic differentiation, and interaction of bone marrow stem cells with implants. A study employing graphene oxide coating on implant surfaces observed the formation of new bone and a close proximity between the implants and bone tissue.[4] Furthermore,it has been reported that graphene has the ability to promote the differentiation of different types of stem cells into osteoblasts.[1]Therefore, this review provides a concise discussion on the potential applications of graphene and its derivatives in the field of periodontology.

2. Materials and Methods

This review includes studies published in the English language on graphene and graphene derivatives and its uses in periodontology. The Google Scholar and PubMed databases were systematically searched. In the search, the keywords consisting of “graphene”, “graphene in periodontology” and “periodontal regeneration” were employed. These keywords would cover information about graphene and its derivatives in periodontal disease management.

3. Discussion

3.1. Graphene Derivatives in Management of Periodontal Disease

The physicochemical, mechanical, and morphological features of graphene and its derivatives are favourable. Materials derived from graphene, such as graphene oxide, suppress the periodontal bacteria responsible for periodontitis. Additionally, the regeneration of bone and periodontal tissue was extensively explored using these materials. The biocompatibility, bioactivity, and potential to improve cell proliferation features in periodontal ligament stem cells have been highlighted as promising characteristics of graphene oxide-based materials, particularly graphene oxide-fibroin, in tissue engineering.Furthermore, graphene has demonstrated the ability to stimulate the osteogenic differentiation of various cells, which includes osteogenic cells, stem cells from bone marrow, and periodontal ligament stem cells.[2,3]

3.1.1*Application against Periodontal Pathogens*

The application of graphene and its derivatives against periodontal pathogens has shown promising results in inhibiting their growth and biofilm formation. Researchers have investigated various forms of graphene, such as graphene-reinforced titanium and graphene oxide nanosheets, and their effectiveness against pathogens like Porphyromonasgingivalis (P. gingivalis), Streptococcus mutans, and Fusobacterium nucleatum.[5]

Studies have demonstrated that graphene materials can penetrate the cell walls and membranes of these pathogens, leading to cell death through plasma leakage. Graphene oxide nanosheets, in particular, have shown efficacy in destroying the cell walls and membranes of P. gingivalisand F. nucleatum.[6] In addition to graphene, other carbon-based materials like carbon quantum dots have also been studied for their ability to inhibit P. gingivalis biofilm formation. Furthermore, a composite of graphene oxide quantum dots and curcumin has been found to effectively inhibit the formation of polymicrobial biofilms, including periodontal pathogens such as Aggregatibacteractinomycetemcomitans, P. gingivalis, Prevotella intermedia, Prevotellanigrescens, Escherichia coli, and Staphylococcus aureus.[7,8]

These findings suggest that graphene and its derivatives have the potential to be utilized as effective agents against periodontal pathogens. However, it is important to note that further research and clinical investigations are necessary to fully understand their potential and ensure their safe and effective application in treating periodontal diseases.

3.1.2*Application for Periodontal Tissue Regeneration*

Regenerative periodontal therapy has emerged as a promising area of research, aiming to restore lost periodontal tissue even after successful prevention or reduction of periodontal disease. Numerous studies have explored different approaches, such as the utilization of stem cells, scaffolds, biomaterials,or their combination.[9,10]In general, scaffolds or other nanocarriers are used in regenerative dentistry to transfer stem cells, growth-promoting factors, or their combinations to the diseased location. The combination of graphene oxide and silk fibroin has been identified as a highly promising option for tissue engineering in regenerative medicine. In a research study, the composite material composed of graphene oxide-silk fibroin was examined for its ability to promote cell adhesion, proliferation, viability, and the expression of mesenchymal phenotype in periodontal stem cells. The study concluded that this composite holds great potential for therapeutic applications in regenerative periodontal therapy.[11]

In another investigation, the bioactivity of human periodontal ligament stem cells was evaluated on a titanium substrate coated with graphene oxide. The results indicated several positive outcomes, including a higher rate of cell proliferation and increased alkaline phosphatase activity. Moreover, the study observed the upregulation of genes associated with osteogenesis, such as alkaline phosphatase, bone sialoprotein, collagen type I, and osteocalcin.[12] Additionally, a separate study demonstrated that a scaffold made of graphene oxide exhibited biocompatibility and the capacity to facilitate the formation of new bone and periodontal tissue.[13]Significant progress has been made in the field of tissue regeneration through the utilization of graphene derivatives. However, further research is necessary to validate their effectiveness in clinical practice.

3.1.3. Application for Periodontal Bone Regeneration

Several factors, including tooth extraction, infection and local or systemic changes in the host response frequently contribute to periodontal bone loss.[14]To replace the lost bone different types of artificial bone are used, including bone grafts (autograft, allograft, and xenograft), ceramics (hydroxyapatite, tricalcium phosphate, and calcium sulphate), and growth factors (demineralized bone matrix, platelet-rich plasma, and bone morphogenic proteins).

Implants are commonly used for replacing missing teeth, and their success depends on bone regeneration and osseointegration.Therefore, surface modifications of implant materials are necessary, and graphene derivatives, such as graphene oxide and its functional conjugates showed favourable results regarding improved bioactivity and osseointegration.[15]

Studies have demonstrated that graphene can stimulate the differentiation of different cell types involved in bone formation, including osteogenic and periodontal ligament stem cells.[16] A study using titanium coated with graphene showed that this combination can suppress a variety of oral pathogens and promote the proliferation of human gingival fibroblasts.[17] Another study discovered that human bone marrow mesenchymal stem cells and gingival fibroblasts adhered to single-layer graphene sheets on titanium with good proliferative, osteogenic differentiation, and adhesion properties. It also showed improved antimicrobial qualities.[18] In another study, new bone formation employing reduced graphene oxide was reported.[19]

3.1.4 *Application in implants*

In a study conducted on a peri-implantitis model, researchers investigated the effects of combining minocycline hydrochloride with graphene oxide and applying it to titanium surfaces. The results showed that the groups treated with minocycline hydrochloride-graphene oxide-titanium exhibited minimal bone loss compared to those treated with titanium alone or minocycline hydrochloride-conjugated titanium, or graphene oxide-titanium. Additionally, there was a notable absence of neutrophils in the graphene oxide-titanium and minocycline hydrochloride-graphene oxide-titanium groups, while an accumulation of osteocyte cells was observed. Consequently, it was suggested that minocycline hydrochloride-conjugated graphene oxide could serve as an effective therapeutic coating to prevent peri-implantitis.[20]

Studies with graphene oxide coatings on implant surfaces observed new bone formation in proximity between implants and bone tissue.[21]

4. Conclusion

The study of applications for nanomaterials based on graphene has made remarkable progress in recent years. This review focuses on the latest advancements in periodontology that involve the use of graphene and related nanomaterials. The properties of graphene are quite impressive. Graphene seems particularly appealing since it can be functionalized and combined with a variety of biomaterials and biomolecules in addition to having remarkable mechanical strength, electrical conductivity, and thermal stability.This enables the creation of nanocomposites with enhanced characteristics and the imparting of new properties to existing materials. This review addressed recent research on the biocompatibility, cytotoxicity, and antibacterial activity of nanomaterials based on graphene as well as graphene's potential for promoting osteogenic differentiation of stem cells, which is essential for its prospective use in periodontal treatment. The adhesion, proliferation, as well as differentiation of stem cells were then examined in relation to the effect of nanomaterials based on graphene.The review further presents recent research where graphene and related nanomaterials are used for modifying the surfaces of dental implants and other scaffold materials such as membranes.

Overall, it is strongly emphasized that further investigation into the use of graphene-based nanomaterials in periodontal treatment is necessary. This exploration has the potential to greatly enhance and advance treatments in the near future.

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