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Nanomaterials – The Modern Age Frontier in Implant Dentistry

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Abstract: Nanomaterials advent has contributed significantly in various lines of medicine and dentistry. This review article discusses about the various properties and the different nanomaterials indicated in periodontal regenerative medicine and implant dentistry. Various materials like chitosan, PLGA particles, Bioceramics etc have been introduced with unique properties like enhanced biocompatibility and osteogenic potential; along with newer additions of biomaterials with antimicrobial properties like Zinc oxide, Silver and Gold. This increasing interest in the field of nanomaterials has given rise to Nanotoxicology, a newer branch of science dealing with their associated toxicities in humans along with their environment. This gives us an opportunity for enhanced nanomaterials in the future with diverse advancements, for their direct application in clinical dentistry.

Keywords: Nanomaterials, Chitosan, Silk fibroin, Bioglass, Hydroxyapatite, PLGA nanoparticles, Dendrimers, Zinc oxide, Gold, Silver, Nanotoxicology.

INTRODUCTION

The advent of nanotechnology has significantly contributed to periodontal medicine and implant dentistry. One can analyze and manipulate to the level of atoms, giving rise to a variety of innovations like nanotubes, quantum dots, nanospheres, nanocapsules and dendrimers.

Currently nanomaterials are being employed in Periodontics as bio-membranes for correction of osseous defects, for osseous defects augmentation, as local drug delivery systems and selective differentiation and growth of epithelial cells during the complex periodontal surgeries (Sharan, J. *et al.*, 2017). The localized delivery of growth factors to the periodontium is an emerging and versatile therapeutic approach for which several controlled release technologies are being explored.

PROPERTIES OF NANO MATERIALS:

These nanomaterials depict some peculiar optoelectronic properties, which can be attributed to their small dimensions. This gives rise to an array of different electrical and mechanical properties, which in turn will alter their chemical and aggregation properties. Another unique property is their self assembly property -in which a randomly distributed system of pre-existing components generates structural organization among themselves spontaneously, incorporating functions and properties without additional complicated processing or modification steps.

This can be carried out by 2 means- intermolecular self-assembly and intramolecular self-assembly. Two methods exist for working with nanotechnology -Bottom-up methods, that use various processes to induce structures to self-assemble at the scale desired and Top-down methods, that build a structure at a scale easily worked to build another structure at a smaller, unreachable scale. (Mirsasaani, S. S. *et al.*, 2019) Various methods have been developed to produce these nanomaterials based scaffolds commercially -Freeze-drying, gas foaming, salt leaching, phase transformation, sponge replication, electrospinning etc. (Funda, G. *et al.*, 2020) At present, for enhanced commercial success by preventing the possible implant loss due to periimplantitis, surface modifications of implants are being suggested. The surface modification of these implants can be carried out by two processes-Additive (Surface coating with ceramic) and Subtractive (Surface machining, fluoride treatment, Acid etching, Laser etching etc) as nanotopography seems to influence cell interactions and cell behavior at surface of the material being used.

NANOMATERIALS IN PERIODONTICS AND IMPLANT DENTISTRY:

Various nanomaterials are being constantly researched to be used in the form of particles, drug delivery agents, barrier membranes or surface coatings.

They can be broadly classified as-

- Organic (eg: chitosan, silk fibroin, hydroxyapatite);
- Synthetic (eg: PLGA nanoparticles, dendrimers);
- Metals and metal oxides (eg: Zinc oxide, gold, silver).

1) **Chitosan**-

As a biomaterial, it displays better biocompatibility and mucus adhesion- along with being economical and exhibiting prominent antibacterial property in its nanoform. Composite chitosan has been developed by combining chitosan particles with different inorganic or organic substances to enhance its poor mechanical and processing properties. A study conducted by Cheng et al (2014) showed that bone regeneration could be assisted by PCL(poly-caprolactone) nanofibers scaffolds containing Chitosan Nanoparticles, leading to higher alkaline phosphatase (ALP) activity and mineralization of rat bone marrow-derived stromal cells (Cheng, Y. *et al.*, 2014).

2) **Bioceramics:**

- **Hydroxyapatite nanocrystals**-

  The Nanohydroxyapatite has a hierarchical architecture that mimics bone at multiple levels- from the macrostructure of cancellous and cortical bone, to the sub nanostructure of proteins and minerals. The presence of nanotubes or nanocrystals in the composite materials allows for enhancing the mechanical properties of the scaffolds. In a study conducted by Pan et al (2020), when Hydrogel/hydroxyapaptite material was injected into the mandibular incisors of rats following tooth extraction, the new bone area was enhanced more than 50%, while the alveolar ridge was promoted in excess of 60% after 4 weeks- leading to soft tissue wound healing within 1 week- hence displaying its potential in soft and hard tissue regeneration (Pan, Y. *et al.*, 2020).

- **Bioglass (BGC)**-

  Taking advantage of the good bioactivity and osseous bonding characteristics of BGC, a nanocomposite scaffold composed of chitin hydrogel and nBGC was developed using lyophilization technique by Sowmya et al (2011) (Sowmya, S. *et al.*, 2011). They showed enhanced porosity, swelling, bioactivity and degradation in comparison to the chitin-control scaffolds. BGC nanoparticles incorporated alginate composite scaffolds have also been developed and characterized; with following advantages -reduced swelling ability and degradation, enhanced biomineralization and protein adsorption (Sowmya, S. *et al.*, 2013).

3) **Poly (lactic co-glycolic Acid)** (**PLGA) nanoparticles**-

PLGA is highly compatible and has been approved by the U.S. Food and Drug Administration for use in drug delivery, diagnostics and other medical applications. Its clinical applications for bone regeneration are hindered by its poor osteoconductivity property, for which nanosized composite PLGA have been developed for osteogenic stem cell differentiation. (Bhuiyan, D. B. *et al.*, 2016) conducted a study in which they developed a multicomponent covalently-linked biodegradable biomaterial called n-HAp-PLGA collagen. Its properties are similar to cancellous bone, and maintain high mechanical strength, even in an aqueous environment (Bhuiyan, D. B. *et al.*, 2016).

4) **Silver nanoparticles**-

Among metallic nanoparticles, silver nanoparticles (AgNP) have stood out in scientific research for presenting antimicrobial properties and biological activity against bacteria, fungi, and enveloped viruses. By the release of cationic silver, they depict oxidative potential as their main mechanism of action. As the size of the silver nanoparticles decreases, its antimicrobial efficacy also increases. Choi et al (2019) conducted a study to show the antibacterial activity of titanium treated with two different silver and polyoxoxamine (PDA) concentrations, especially against *S. mutans* and *P. gingivalis* (Choi, S. H. *et al.*, 2019).

5) **Cerium oxide**-

CeO2 nanoparticles exhibit excellent biological properties, like- anti inflammatory and antibacterial potential. Ren et al (2021) have conducted a study where the in vitro data has proven that CeO2 NPs promote hPDLSCs (Human periodontal ligament stem cells) osteogenesis differentiation, whereas the in vivo study has demonstrated that PG-CeO2 (PCL/Gelatin composite alongwith cerium oxide) membranes accelerate bone regeneration (Ren, S. *et al.*, 2021).

LIMITATIONS AND TOXICITY OF NANOMATERIALS:

Nanotoxicology is a branch of bionanoscience which deals with the study and application of toxicity of nanomaterials. Because of their extremely small sizes, they are capable of entering the human body by inhalation, ingestion, skin penetration, intravenous injections and medical devices, and have the potential to interact with intracellular macromolecules. Once these nanoparticles are absorbed into the bloodstream, they can be easily distributed to various other organs like liver, kidney, lungs and in some cases- even brain. Out of the various mechanisms through which nanoparticles display toxicity, production of reactive oxygen species has been considered to be a significant one. One mechanism of Nanoparticles-induced oxidative stress occurs during the dissolution of iron-based Nanoparticles via the Fenton reaction. Also, some inert nanomaterials do not give rise to spontaneous ROS production; they are just capable of inducing ROS production under biological conditions, based on their ability of directly targeting the mitochondria intracellularly.

RECENT TRENDS IN NANOMATERIAL ASSOCIATED NANODENTISTRY:

Various developments are taking place in the field of nanodentistry, especially in the area of periodontal regeneration- for enhanced surgical outcomes. These include- Nanorobotic dentrifice, Dentifrobots, Quantum dots and Smart nanomaterials.

Nanorobotic dentifrice has been proposed to be delivered by mouthwash or toothpaste, which could perform continuous calculus debridement by inspecting the gingiva once in every 24 hours and also prevent early demineralization and carious progression. ***Dentifrobots***, or the nano-sized robots (size 1-10 micron), moving at a speed of 1-10 microns/sec, could identify and destroy the periodontopathic pathogens inside the oral cavity, along with fighting halitosis.

Recently, ***Quantum dots*** have been devised which is nothing but nano-sized semi-conductors, which when stimulated by UV radiation glow brightly. They are rather stable and also non toxic to the human tissues. These show promising effects in the healing of inflamed periodontal tissues and even in cancer. On stimulation by UV light, quantum dots attack the target cell whilst attached to the antibody which releases reactive oxygen species- destroying the target cell.

"Smart" nanomaterials can be incorporated into bone repair materials with various magnetic properties. Magnetic fields cause changes in cell physiological and biochemical processes that help in remotely controllable mechanotransduction- thus paving way for futuristic bone regenerative materials.

CONCLUSION:

Recent developments in nanomaterials and nanotechnology have provided a promising insight into the commercial applications of nanomaterials in the management of periodontal disease, taking us closer to the goal of complete regeneration of periodontal tissues for periodontal management. Nanomaterials have excellent physico-chemical properties, biomimetic features for promoting cell growth and stimulating tissue regeneration – suggesting great potential for enhancement of future treatment modalities. The better understanding of the properties of nanomaterials will pave a way for synthesis of new novel materials for future implant dentistry, thus exhibiting the potential of improving the quality of life.

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