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Nanotechnology and its Diverse Applications in Periodontia

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Abstract
Nanotechnology is the science that deals with the tiniest particles at the molecular level. Also called as molecular manufacturing, it has brought about revolution in a number of fields such as material science, medicine, information technology and engineering, among others. The first to utilize nanotechnology in the periodontal management was Kong et al. The concepts regarding tissue engineering in periodontal regeneration was based on their researches. This review focuses on the versatile applications of this ground breaking technology in Periodontics.

Keywords: *nanotechnology, periodontics, nanomaterials, local drug delivery*

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I. Introduction

"There's plenty of room at the bottom," said the noble prize-winning physicist Richard Feynman in his lecture, [1] creating the foundation of nanotechnology around 1959. In the latter half of 20th century, as science was evolving with its diversified additives, so did the concept of nano-technology and by the year 2000, R.A. Freitas Jr. coined the term "nano dentistry" and defined it as the science and technology that would make possible the maintenance of near perfect oral health through the use of nanomaterial and biotechnology, including tissue engineering and nanorobotics [2].The term 'Nanotechnology' has emanated from the Greek word 'nano,' which means dwarf. The medical applications of nanotechnology and nanorobots were first described by the scientist Robert Freitas Jr. [2]. He visualized the probable applications and developments of nanoscience in various areas of dentistry, such as nanorobotics in inducing aesthesia, tooth repair, treatment of dental hypersensitivity, tooth repositioning, and periodontal diseases [2]. The study of nanoscience involves a scale within a range of 1-100 nm [3]. The widespread applications of nanotechnology in dentistry are owing to the fact that the wide range of nanomaterials are capable of producing a large surface area, which have the capacity to develop unique physical and chemical properties [4-6].

II. Discussion

VARIOUS NANOSTRUCTURES FOR DENTAL APPLICATION

Molecular units having diameters in the range of 0.1 to 100 nm are known as nanoparticles and demonstrate the extensive use of nanoscale units in dentistry. Resin- based composite restorations (RBC) are one such type of nanoparticles that are currently in use. The main focus of research now-a-days is to make newer types of silane bonding agents for maximum use with nanoparticles in RBC. Organosilanes, such as allyltrimethoxysilane, show good compatibility with nanoparticle fillers like TiO2.A considerable record of clinical utility and widespread use has been demonstrated by RBC with nanoparticles and associated modifications [7].

Next comes nanorods and nanospheres. Nanorods are particularly important in a restorative context. Chen et al. synthesized the self- assembly properties of enamel prism- like hydroxyapatite (HA) nanorods. Being similar to the enamel rods that form up the basic crystalline structure of dental enamel, nanorods could strikingly mimic the naturally occurring structure [8]. In association with calcium phosphate deposition and amelogenin nanochain assembly, nanospheres are being researched as restorative systems, to imitate the nano processes that are so far inherent in natural tooth development [9]. Various types of nanotubes have been investigated for use in dentistry. Titanium oxide nanotubes have shown in-vitro, the acceleration of the kinetics of HA formation. The modified single- walled carbon nanotubes (SWCNT) demonstrate the improved flexural strength of RBC [10].

Polymer nanofibers with diameters in the nanometre range, allow an easier addition of surface functionalities, since they have a larger surface area per unit mass when compared to polymer microfibers [11]. Polymer nanofiber materials as drug- delivery systems, filters and scaffolds for tissue engineering, have been extensively researched. Ceramics containing fluor- HA and HA have been recently produced using nanofibers. Nanofibers have shown to improve the physical properties of composites when added in precise proportions and with uniform distribution of the crystals [12].

AN OVERVIEW OF THE BASIC NANOPARTICLES AND ITS USAGE IN DENTISTRY

Nanoparticle (Major element)	**Uses in dentistry**
Carbon nanotubes	Cavity restoration
Graphene	As a coating on implants, acrylic teeth (for its action against biofilm)
Hydroxyapatite	Decreases dentinal hypersensitivity, used in toothpastes, mouth rinses For coating on implants- facilitates osseointegration
Iron oxide	Controls microbial infections, used in implants
Zirconia	Crowns, dental implants, nano-composites, polishing agent (active against enterococcus faecalis)
Silica	Filler particles, polishing agent, for dentinal hypersensitivity
Silver	Antibacterial properties, used in tooth pastes, mouth rinses
Titanium	Drug releasing implants
Biosensors like SPR, Quartz crystal biosensor for ATPase H + transporting, lysosomal accessory protein (ATP6AP1),	For cancer detection. Also, Diabetes, CVS diseases, obesity, sexual hormonal diseases, drug abuse via salivary markers

FABRICATION TECHNIQUES OF NANOMATERIALS

The fabrication techniques of nano structures can be divided into 2 approaches: “top-down” and “bottom-up” [10,13]. In the top- down approach, the larger devices are used to direct the assembly to produce smaller devices. It is synthesized by grinding and milling. Some of the examples are, nanoneedles, nano- based bone replacement cement, nanoimpression material, nanocomposites, nanoencapsulation, andnanocoatings on implant [10,13]. The least expensive ways to produce nanomaterials in bulk are offered by mechanical methods. The simplest of them is ball milling. In ball milling, nanomaterials are produced by mechanical attrition.In this method, kinetic energy is transferred to a material undergoing reduction from a grinding medium. In case of compaction and consolidation, which are industrial scale process, nanomaterials are "put back together" to form materials with enhanced properties. This method can be employed for making metallic alloys. Several top-down mechanical methods are utilized by industry. In case of thermal methods, those that provide heat to a fabrication process are considered more important. Of these, nano thread materials can be formed by electrospinning. An excessive input of energy– whether in the form of heat, electricity or solar energy, are required by high energy methods. The first controlled means of making carbon nanotubes was arc discharge. Laser ablation and solar flux are other methods which work well. The only problem encountered is control of quality and potential upscale. Plasma methods are also included in this category. Plasmas require high-energy situations (high potential bias, etc.). With the exception of solar flux methods, where sunlight is easily available, the problem with other high energy methods is-upscale potential. Top-down chemical fabrication methods are always easy to upscale and many are widespread industrial processes, such as anodizing [10,13].

In bottom-up methods, atoms or molecules combine to form nanomaterials. Reactive constituents react over a catalyst or pre-templated surface to form nanostructure materials, in a gas-phase process known as chemical vapor deposition (CVD). CVD helps in the economical synthesis of carbon nanotubes. Precursors such as methane or acetylene or other carbon source gases are passed over Co, Fe or Ni catalyst. When these precursors finally decompose into carbon, the catalyst particles form the nanotubes. An industrial process, atomic layer deposition is capable of coating any material, regardless of size, with a monolayer or more of a thin film. Other bottom-up industrialized processes are molecular beam epitaxy and MOCVD. All of self-assembly and synthesis occurs within the liquid phase. The advantages ofliquid phase methods are, they are up scalable and low cost. Electro deposition and electroless deposition are very simple ways to make nanomaterials[10,13].

NANOTECHNOLOGY IN PERIODONTICS

With the advancement of dentistry, its practice has become increasingly complex with the evolvement of many specialties within the profession. The different specialities are Oral Medicine &Radiology, Oral Maxillofacial Surgery, Conservative Dentistry & Endodontics, Pedodontics, Public Health Dentistry, Oral Pathology, Orthodontics, Prosthodontics and Periodontics.

Periodontics is the branch of dental science that aims exclusively on the tooth supporting structures such as gingiva, periodontal ligament, cementum, alveolar bone and mucosa, as well as diseases that affect them.

Periodontal diseases affecting the hard and soft tissues around the teeth lead to gum diseases, bone loss, and in severe conditions tooth loss. Various treatments are available for the management of periodontal diseases; some of them include both medicinal treatment and surgical interventions. Medicinal treatments include drug molecules which are naturally macro-sized particles that find it challenging to penetrate the periodontal pockets. Conversely, the nanoscale sizes of nanoparticles make it easier for them to reach subgingival regions. For instance, drug delivery by inclusion of nanoparticles for treatment of periodontal treatment with Triclosan (TCS) has served as a good example [14,15].

The numerous studies of Kong et al., who put forward the application of nanotechnology in the periodontal management, helped in formulating many concepts with regards to tissue engineering in periodontal regeneration [11].

Nanorobotic dentifrices, also known as dentifrobots, metabolize trapped organic matter into harmless and odorless vapors. These nanorobots in the dentifrices which scans, recognize, and destroys pathogenic bacteria that are present in the plaque and oral cavity, are called dentifrobots [12]. Dentifrobots in the size range of 1–10 μ are invisibly small, and they crawl at the speed of 1–10 μ/s,and provide advantages of being economical and timid as they are purely mechanical devices that would safely deactivate themselves if swallowed[11].

Nanotechnology has also helped in periodontal drug delivery. With the advent of nano pharmaceuticals, nano sensors, nano switches, and nano delivery systems, the science of periodontics has witnessed considerable development. Developed by Pinon Segundo et al., triclosan- loaded nanoparticles have emerged as a new delivery system for the treatment of periodontal disease [16]. A preliminary in vivo study performed in dogs, concluded that triclosan nanoparticles were able to reduce the inflammation of the experimental sites [7]. Drugs are incorporated into nanospheres, which are composed of a biodegradable polymer [17]. This enables timely release of the drug as the nanospheres degrade and in turn helps in specific site drug delivery [12].

Nanotechnology has been effectively utilized in the treatment of dentinal hypersensitivity and in laser plasma. Change in the pressure transmitted to the pulp hydrodynamically is the main cause of dentinal hypersensitivity. Studies have shown that the dentinal tubules of a hypertensive tooth have twice the diameter and eight times the surface density, when compared to the non-sensitive teeth. Nanorobots precisely and particularly block the dentinal tubule by using native materials, thus providing swift and enduring comfort to the patient [11]. Use of nano-sized titania particle emulsion on human skin followed by laser irradiation, leads to the disintegration of the particles along with other results like: Shock waves, micro abrasion of hard tissues and stimulus to produce collagen. Clinical applications of laser plasma in periodontia are periodontal therapy, melanin removal and soft tissue incision [8].

A major role in implant success and osseointegration, is determined by bone bonding and stability, besides surface contact area and surface topography. The use of nanotechnology can accelerate bone growth and hence overall implant success [7]. Researches conducted on the effects and subsequent optimization of microtopography and surface chemistry, show that material engineering and implant dentistry have advanced extensively [16].Acceptability of these implants constructed on the basis of nanotechnology increases as they enhance the integration of nano coatings resembling biological materials to the periodontal tissues. Another advantage of implant surfaces coated with titanium oxide nanotubes and laced with silver nanoparticles is that, they serve the purpose of fighting infection, thus increasing the shelf life of the implants [10].

One of the most commonly performed procedures worldwide are bone transplants. Scaffolds that are porous three- dimensional structures, are needed by these transplants, which guide bone formation and provide cell support. We are still facing with numerous challenges to fully harness bone's capability to regenerate itself, despite the numerous investigations to develop such porous materials. The essential elements that are required for bone regeneration are- (i)osteoconductive matrix (scaffold), (ii)osteoconductive signals, (iii)osteogenic cells that can respond to these signals, and (iv) an adequate blood supply. The first and foremost step that hold prime importance in the whole process, is the fabrication of strong and porous scaffolds. The tools delivered by nanotechnology, aids in engineering the scaffold's internal surfaces and to create devices used in drug delivery with carefully controlled spatial release patterns. The osteogenic differentiation of the appropriate progenitor cell, is favoured by the presence of calcium in the matrix [11].

A natural nanostructure, as a bone is said to be, is composed of organic compounds, collagen forming its main constituent. This natural structure, is imitated by nanotechnology, for the formation of nano bone, which finds its diverse applications in dentistry. Situated between these crystals, lies a loose microstructure with nanopores, known as nanocrystal. The properties displayed by bone are consistently far more superior to their individual constituent phases. The macroscale orientation of the bones ranges from being compact/cortical (dense material found at the surface of bones) to spongy/cancellous (foam- like material). Osteon surrounds and shields the blood vessels. They form the basic constituent of compact bone. Osteons have a lamellar pattern, with each individual lamella having fibres arranged in geometrical patterns. Several collagen fibrils collectively form the fibres. These collagen fibrils, which are mineralized, are the basic building blocks of bone. The bone is composed of collagen protein called tropocollagen.Silicon molecules helps in the adsorption of protein, hence added onto the surface of the pores. For the treatment of bone defects in periodontal diseases, these HA nanoparticles can be used [11].

III. Conclusion

Nanotechnology is foreseen to revolutionize health care by providing novel methods for disease diagnosis and prevention, therapeutic selection tailored to the patient's profile and, through drug delivery and gene therapy. Though the current pace of development is impressive, clinical application of nanotechnology is far away, since most of the research is at the basic science level[18]. There is an increasing need for awareness about the futuristic and advanced forms of treatment provided today. Despite the numerous benefits and versatile applications, every technology carries with itself certain drawbacks. Some of the basic engineering problems that might be encountered are- biocompatibility, precise positioning, assembly of molecules, economical mass production, and coordination of the activities of the microrobots [10,18]. Social issues of public acceptance, ethics, regulation and human safety are other challenges that need to be addressed.

Needless to say, the benefits of nanotechnology far outweigh the risks. Nanomedicine offers an opportunity for dentists to incorporate more biomimetic substances in dental treatment so that there is greater coordination between the nanostructures replacing the parts of the teeth with our body's regenerative processes [19]. Hence, it can be concluded that nano dentistry will give a new vision to comprehensive oral health care, as trends of oral health have been changing to more preventive intervention than a curative and restorative procedure [10,18].

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