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REVIEW ARTICLE

Emerging nanotechnology in periodontitis and coronavirus disease 19-An overview

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Abstract

Nanotechnology, the greatest of all inventions humans have ever made till date. Here nanoparticles are used as a medium for the diagnostic and therapeutic purposes. There are higher chances of the emergence of nanodevices and nanorobots of biologic material to succeed nearly impossible results in the near future. Nanotechnology has laid its path in every field of science, giving rise to nanodentistry. Invention of dental nanorobots in the near future will help in precise diagnosis and may lead us to new treatment opportunities. This article will focus mainly on applications of nanotechnology in the field of Periodontics.

Introduction

Nanotechnology - "This is a development which I think cannot be avoided" said Richard Feynman, noble prize-winning physicist, in 1959, in his lecture.[1]

In mid-1980's, Engineer K Eric Drexler published his book "Engines of creation," to popularize nanotechnology[2] and later in 1986 re-coined the term nanotechnology.

Nanodentistry

The term "Nanodentistry" was first introduced by scientist Freitas in 2000.[1] Nanodentistry is defined as the science and technology of diagnosing, treating and preventing oral and dental diseases, relieving pain, preserving and improving dental health using nanostructured material.[3]

Nanodentistry involves

1. Nanorobotics- used in oral analgesia, dentin hypersensitivity, tooth renaturalization, dental biometrics, and dentirobots.
2. Nanodiagnostics - Nanoscale cantilevers, nanopores, nanotubes, quantum dots, oral fluid nanosensor test for diagnosing tumor cells and its gene sequencing, Lab-on-a-chip for periodontitis.[4]
3. Nanomaterials - Nanocomposites, nano solution,[5] materials to induce bone growth such as Ostim, VITOSS, and NanOSS™.

Nanorobots

These computer-controlled robotic devices are formulated of nanometer-scale components to provide molecular precision.[6] The ideology for injecting nanorobots into the human body was introduced by Drexlerwhch was later designed and dissembled by Freitas.[2]

Payload holds a small dose of drug; the micro camera helps in visualizing the field; electrodes act as battery using the electrolytes in the blood and also kill the cancer cells by generating an electric current and a swimming tail for propulsion to get into the body as they travel against the flow of blood in the body.[7]

Nanotechnology in Periodontics

With increasing prevalence of periodontal disease with respect to age, an additional postoperative care has always been a paramount despite the traditional periodontal treatment procedures for the maintenance of periodontium.[8] To overcome this difficulty a study was carried out by Bartold *et al.* by applying tissue engineering in periodontal regeneration.[9]

Harunganamadagascariensis leaf extract

Investigated by Moulari *et al*., is used to treat gingival infections and dental caries.

Chitosan loaded-tripolypeptide (TPP)

Chitosan/oligonucleotide loaded TPP has reported continuous release of oligonucleotides that can be used in localized treatment of periodontal diseases.[10]

Triclosan loaded nanoparticles

These are homogenous polymer matrix-type delivery where the depletion zone moves to the midway of the device as the drug is released suggesting controlled release of the drug. In *in-vivo* experiment done in dogs, gingival index and bleeding on probing were recorded and the study was carried out with tricolsannanoparticle. The study concluded that triclosannanoparticle efficiently reduced gingival inflammation.[11]

Antibiotic free delivery systems

With increase in antibiotic resistance, the use of antigen nanoparticles can be applied as microbial growth inhibitors in the treatment of periodontal diseases.

Bone replacement materials

Nanohydroxyapaptite (NHA) is a highly biodegradable and biocompatible material. During initial cellular attachment, calcium enhances the differentiation of osteoblast. On degradation of NHA alters calcium phosphate metabolism activating osteoblast producing calcium ions.

Synthetic NHA is prepared by chemical precipitation of calcium nitrate tetrahydrate and ammonium dihydrogen phosphate under hydrothermal treatment.[12] NHA helps in the proliferation and osteogenic differentiation of periodontal ligament cells and as a bioresorbable agent in osseous restoration.[13]

NHA used for osseous defects is: Ostim (Osartis GmbH, Germany) HA, VITOSS (Orthovita, Inc, USA) HA + Tricalcium Phosphate (TCP), and NanOSS™ (Angstrom Medica, USA) HA.

Ostim (Ostaris GmbH, Germany)

Available as paste composed of 65% water and 35%. Ostim is synthetically manufactured, osteoconductive, and facilitates bone growth. Ostim is initially osseously interweaved, resorbed as it heals, and finally replaced by natural bone.

In a study by Chitsazi *et al*., involving autogenous bone graft (ABG) and Ostim in the management of human intra-bony periodontal defects there was complete resorption of the NHA after 12th week.[14]

NanOss (Angstrom Medica, USA)

NanOss Bioactive is an advanced bone graft combining an engineered extracellular matrix that mimics the composition, structure, and size of bone,[15] providing induction of natural bone [Table 1].

VITOSS® (Orthovita, Inc., USA)

An Improved Form of β-TCP with 39% calcium and 20% phosphorus. It is a highly porous material resembling human cancellous bone with almost 90% pore space. These pores are sizedbetween1 mm and 1000 mm. In canine studies, new cancellous bone reached density and structure of existing cancellous bone by 12 weeks.

GTR Membrane

Chitosan is a copolymer of N-acetyl- glucosamine and N-glucosamine units, a natural biopolymer, and is biocompatible. The wide biologic feature of chitosan is under study for its use as bone substitute in periodontal surgeries.[16]

Carbon fiber, a type of nanofiber has shown enhanced osteoblastic cell adhesion which is vital for orthopedic and dental implants.[17]

Biofilm

Nanotechnology uses reverse proteolytic labeling method to obtain the effect of oral microbes in the biofilm. It is found that cell-surface C-terminal proteins(R gp A, Hag A, CPG 70, PG99), transport proteins (Hmu Y, Iht B), metabolic enzymes (Frd AB), and immunogenic proteins are in abundance. In a recent study, ionic plasma disposition silver nanoparticles is found to be effective against oral bio-films microbes such as *Escherichia coli*, *Staphylococcus aureus* and *Aspergillus niger*.[18]

Dentin Hypersensitivity

Dentin hypersensitivity is a result of exposure of dentinal tubules. The use of dental nanorobots is an instant and permanent treatment where the nanorobots under chemical gradient and temperature variation move from the dentin, occluding the exposed tubule, and reach the pulp. The entire movement of these nanorobots is guided by the dentist on a nanocomputer.[1]

Dentifrobots

Dentifrobots are small nanorobots (1–10 micon) from toothpaste or mouthwash that reside subocclusally and get deactivated on swallowing.

Nano toothpaste contains nanoxyd, calcium peroxide, enzymes (papain, bromelain), fluoride combination, Co-enzyme Q10, and Vitamin E.[1] They ensure uninterrupted debridement of supra and subgingival calculus resulting extended ditch to halitosis and also teeth whitening.[19]

Mouthwashes contain nano calcium fluoride. Because of its high solubility, they increase the fluoride release in the oral cavity complementing the mineralization of the tooth. They are used as an anticaries agent and reduces dentinal permeability.[20]

Atomic force microscopy (AFM)

In a study by Botelho, Martins 2010 with 8.5% doxycycline nanosphere gel prepared from 2% w/v carbopol 940, the AFM images analysis on topography and surface roughness has shown increased periodontal healing by preventing bone loss.[21]

Gene therapy

Gene delivery system includes viral, nonviral vectors, and gene guns(injecting genetic materials directly into tissues). Nanotechnology employs nanosize gene carriers instead of viral vectors that are less immunogenic in the process of substituting the repaired gene.[22]

In *in-vitro* study, calcium phosphate nanoparticles, a nanovector serves to deliver fibroblast, its target gene for periodontal regeneration.[23]

Implants

Dental implants despite its success rate, need a continuous improvisation in its limitations that are consequences of infection, accelerated bone loss, or bad osseo-integration resulting in unsatisfactory bone formation around the implant material soon after implantation causing implant failure.[24]

Using nanotechnology, the chemistry and surface roughness of dental implants are modified that provides the necessary desired bone-to-implant contact instead of fibrous tissue encapsulation.[25]

Methods of Synthesis of Implant Nanomaterials

Mainly they can be processed by two methods:

Top-down

Here the large structure is ground using ultrafine grinders, lasers, vaporized, and then cooled to form nanoparticles.

Bottom-up

In this method, molecules are arranged to build a complex structure with novel and effective properties.

Surface modification for dental implants

At present, surface of the implants is modified by coating nanostructured diamond, nanostructured processing applied to hydroxyapatite coatings and Nanostructured metallo-ceramic coatings. These coatings are aimed at providing better mechanical properties and surface reactivity that helps the osteoblastic cells to adhere, proliferate and mineralize along the implant-bone interface.[26]

Micro- and Nanopatterning of Dental Implants

It is always convincing when the topography of implant surface simulates to that of natural tissue's ECM (<500 nm) provides better adhesion of implant to the bone.[27] A stand-in for surface coating is the use of nanopatterning with molecular peptide grafts or chemically treated implant surface. Once the implant is placed, these surface treatments have shown to produce cell-matrix and protein marker, improved fibrin clot adhesion, and thus, the osteogenic cells migrate towards the implant surface.[28] However, more studies are needed to differentiate the edges between the surface topography of nanopatterning and micropatterning, respectively.

Table 1: Comparison of human bone, NanOss, traditional calcium phosphate

Properties	Human bone	NanOss bioactive	Traditional calcium phosphate
Surface area	100 m^2/g	70 m^2/g	<1 m^2/g
Crystal size	25–500 nm	15–100 nm	1000–10,000 nm

Advances in implant dentistry

Nanostructure metalloceramic coatings are in the initial phase of evolution.

Coating multiple layers of Cr/CrTi/CrTiNnanocrystals over Co-Cr-Mo substrate has been shown to produce better adhesion and scratch resistance at the interface.

Nanoporous ceramic coatings work by annodizing aluminum ion over the titanium plant's surface.[29]

Nanotechnologyin coronavirus disease (COVID)-19

Nanoparticles incorporated in PPE, mouth masks have antibacterial activity and have shown increased protection.

Medical instruments and many other highly infective surfaces being coated with nanoparticles are applied in the control of Covid-19 spread.

Nanotechnology in diagnostic kits makes it portable with higher efficacy, sensitivity, and specificity portable. The use of nanoplasmonic sensors in the diagnostic kits helps in rapid detection of even live viruses using its respective antibody. This has been of major importance in this Covid-19 pandemic.[30]

Conclusion

Nanotechnology - a foreseen future in the field of dentistry is inevitable in the management of an individual's oral health under microscopic level. Despite its overwhelming potential, the need of ethical considerations, social acceptance, human safety is mandatory to provide the world's 80% population with a high standard of dental treatments. Even though this vision sounds unseen, unheard or untouched, theoretical and applied advancements are under progress.

As sensibly said – "It is best to intervent than intervene;" the 21st century nanomedical physicians will be able to use the goodness of one's body's natural healing power. The end of this article quotes the words of Richard P Feynman who said "This is a development which cannot be avoided."

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