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APPLICATIONS OF NANOTECHNOLOGY IN INTERDISCIPLINARY DENTISTRY

Dental Science

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ABSTRACT

Nanotechnology has brought revolutionary changes in the fields of medicine and dentistry. The application of nanoparticles in dentistry is termed as nanodentistry. Researchers worldwide experiment and employ suitable nanoparticles to overcome the existing drawbacks associated with various materials and techniques used in dentistry. Dentistry is finely segregated into various disciplines, yet still closely interwoven and interdependent to achieve a successful treatment outcome. This approach forms the backbone of interdisciplinary dentistry. From combating infections caused by microbes to improving anchorage of implants, nanotechnology and nanomaterials find multitude of use in interdisciplinary dentistry. This review article summaries the plethora of nanoparticles and their application in interdisciplinary dentistry.

KEYWORDS

Interdisciplinary Dentistry, Nanomaterials, Nanoparticles, Nanotechnology.

INTRODUCTION

The word 'Nano' has its origin from the Greek word 'dwarf'. The theory of nanotechnology was first developed in 1959 by Richard Feynman, a Nobel Prize-winning physicist, in a lecture titled, "There's plenty of room at the bottom" presented at the American Physical Society meeting held at the California Institute of Technology (CalTech) on December 29, 1959 [1]. Feynman explained that the entire area on the head of a pin (1/16 in.), if amplified 25,000 times, would have an area capable of housing all the pages of the Encyclopedia Britannica. He aptly predicted that this would be the future of material science [2].

Particles, which measure less than 100 nm in at least one dimension, are called as nanoparticles. Nanoparticles have distinctive advantage over their microscale or 'bulk' counterpacts, on account of their numerous advantageous properties like smaller size, greater surface energy and higher proportion of surface atoms. These materials have revolutionized the fields of engineering and medicine. They are steadily gaining foothold into dental material science and transforming clinical dentistry for the better [3]. Interdisciplinary dentistry is the key to successful treatment outcome in today's practice. In this aspect, endodontic-periodontic, endodontic-prosthodontic and endodontic-periodontic-prosthodontic interrelationship assumes significant importance. Various nanomaterials are being extensively researched and used in interdisciplinary dental practice. This article presents an overview of such materials and their usage.

Nanomaterial

A material can be called as 'Nano' when it contains components which measure less than 100 nm in at least one dimension. These may consist of grains, atom clusters, fibres, films and composites [3]. Nanomaterials possess unique properties due to their increased surface area and quantum effects [4]. The following nanomaterials hold key to the future of nanoscience-fuelled interdisciplinary dentistry.

Materials Of Significance In Endodontic-periodontic Interdisciplinary Approach

Chitosan Nanoparticles (CS-NPs)

Chitosan nanoparticles (CS-NPs), due to their charge and size, possess enhanced antibacterial activity [5]. Rabea *et al.* proposed that chitosan exerts its antibacterial effect by inhibiting enzyme activities essential for bacterial cell survival [6]. Shrestha *et al.* studied the effectiveness and long-term potency of CS-NPs and zinc oxide NPs (ZnO-NPs) in eradicating biofilm bacteria. Both CS-NPs and ZnO-NPs were found to possess antibacterial properties even after aging for a period of 90 days. *Enterococcus faecalis* in planktonic and biofilm forms were tested in this study. While planktonic bacteria were completely eliminated, biofilms managed to survive even after 72 h of exposure to CS-NPs [7].

Sireesha *et al.* compared radicular dentinal tubular penetration and fracture resistance of micron- and nanoforms of chitosan and calcium hydroxide as intracanal medicaments. The authors observed that both the nanoforms exhibited superior antibacterial efficacy against *Enterococcus faecalis* and improved depth of penetration into the root dentin. The reduction in fracture resistance of teeth noticed with the nanoforms at 1-month interval was lesser than that observed with conventional calcium hydroxide. Hence, these nanoforms were recommended for endodontic disinfection [8]. Figures 1 and 2 show nanoforms of chitosan and calcium hydroxide with their respective scanning electron microscopic (SEM) images.

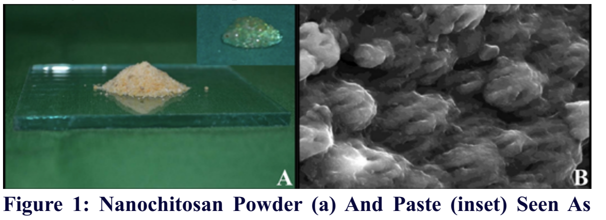

Figure 1: Nanochitosan Powder (a) And Paste (inset) Seen As Agglomerated Particles Under SEM (B).

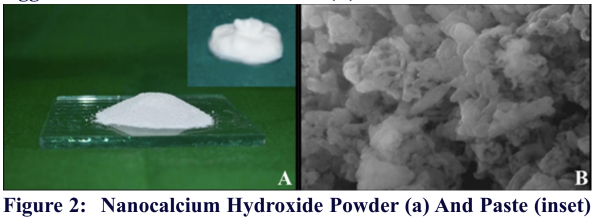

Figure 2: Nanocalcium Hydroxide Powder (a) And Paste (inset) Seen As Agglomerated Particles Under SEM (B).

Gonzalez *et al.* reported that copper nanoparticles/chitosan nanocomposites effectively inhibit the growth of *A. Actinomycetemcomitans*. This combination holds promise as a therapeutic agent in the augmentation of localized periodontal therapies [9]. Dung *et al.* investigated the suitability of chitosan nanoparticles as a matrix for the controlled release of antisense oligonucleotides aimed at the treatment of oral inflammatory disorders. The oligonucleotides (ONT) were mixed with chitosan, resulting in the formation of complex chitosan-oligonucleotide (CH-ONT) solution. Tripolyphosphate (TPP) was added as a cross linker either to chitosan or to CH-ONT complex. The results of this study showed that the low molecular weight chitosan nanoparticles promoted prolonged release of ONT. The authors suggested that chitosan could also prevent enzymatic degradation of ONT that would possibly occur in the oral mucosa and periodontal pockets [10].

Biosynthesized Silver Nanoparticles (Biosynthesized Ag-NPs)
Silver nanoparticles, isolated and biosynthesized from the leaves of fungi, *Withania somnifera* were evaluated for antimicrobial efficacy against *P. gingivalis, B. pumilus and E. faecalis*. The results showed that these particles had effective antibacterial efficacy and are applicable for treating diseases of endodontic, periodontal or combined origin [11].

Polydopamine Nanoparticles (PDA-NPs)
Oxidative stress plays a major role in the induction of periodontal diseases. Bao *et al.* developed biocompatible polydopamine nanoparticles that could serve as potent ROS scavengers. The results showed that PDA-NPs possess antioxidative activities against toxic ROS, highlighting their potential as efficient ROS scavengers which could protect human gingival epithelial cells against oxidative stress and inflammatory reaction [12]. Deng *et al.* synthesized PDA-NPs incorporated peptide-decorated polycaprolactone (PCL) hybrid fibrous membrane and checked for human mesenchymal stem cell (hMSCs) adhesion, proliferation and differentiation both *in vitro* and *in vivo* conditions using mouse calvarial critical size defect model. The authors observed that PDA-NPs-PCL hybrid fibrous membrane exhibited excellent hMSC differentiation, increased apatite deposition and osteo differentiation potential without any added growth factors. Interestingly, *in vivo* assessment of mouse defect model showed remarkable bone reconstruction and regeneration. This could potentially aid in guided tissue regeneration for bony defects [13].

Hydroxyapatite Nanoparticles (HAp-NPs)
Sun *et al.* reported that HAp-NPs (or nano-HA) promoted proliferation and osteogenic differentiation of periodontal ligament cells compared to dense HAp [14]. HAp-NPs possess striking similarity in structure and chemical composition to natural teeth. Hence, they are widely used in repairing damaged enamel [15]. Li *et al.* and Huang *et al.* demonstrated that HAp-NPs can effectively remineralize artificial enamel caries lesion. Their remineralizing potential was found to be comparable to that of fluoride [16]. HAp-NPs are found to be effective in the treatment of dentinal hypersensitivity (DH). Their smaller size enables easy penetration, accumulation and occlusion of the dentinal tubules, thereby reducing DH [17]. The effect of nano-HA on enamel remineralization and their influence on the sealing ability and shear bond strength of pit and fissure sealants was studied by Memarpour *et al*. The results of the study showed that nano-HA remineralized the demineralized enamel in pits and fissures and enhanced its bond to the sealant, without compromising the sealing ability of the latter [18]. HAp-NPs have also been used as a nanocarrier for antibiotic and anticancer drugs [19,20]. Figure 3 shows nanohydroxyapatite particles along with their SEM and transmission electron microscopic (TEM) images.

Figure 3: Nanohydroxyapatite powder (A) seen as agglomerated rods under SEM (B) and as rod shaped crystals under TEM (C).

Madhumati *et al.* reported that tetracycline loaded calcium deficient hydroxyapatite (TC-CDHA) nanocarriers were effective against *S. aureus* and *E. coli* bacteria. They proved the biocompatibility of these particles on human periodontal ligament cells. Augmented cellular proliferation and bone regeneration noted with this new material makes it an ideal drug delivery agent for use in periodontal therapy [21]. Similarly, Nagarathinam *et al.* reported that triple antibiotic paste (TAP) loaded apatitic nanocarriers (TAAN) exhibited significantly higher antibiofilm activity against *E. faecalis* compared to TAP. The authors observed an improved disinfection of dentinal tubules with TAAN and thus, recommended its use as an intracanal medicament for root canals [22].

Magnetic Nanoparticles
Chlorhexidine (CHX) finds use in endodontics as well as in the prevention and treatment of gingivitis and periodontitis [23,24]. The fact that CHX can be rendered inactive upon its interaction with body fluids resulting in loss of its antibacterial potential lead researchers to downsize the medicament to nanomeric form [25,26]. Tokajuk *et al.* developed nanosystems comprising of amino silane-coated magnetic nanoparticles functionalized with chlorhexidine (MNP-CHX) [27]. The drawbacks associated with the conventional CHX were overcome with the use of MNP-CHX NPs, which were found to be lethal to bacteria and fungi even in the presence of saliva. They had a profound antibacterial and antifungal effect and were found to be lethal to planktonic and biofilm-forming microorganisms. They were also capable of inhibiting the growth of multi-species biofilms.

Poly (d, l-lactide-co-glycolide) (PLG) nanoparticles
PLG nanoparticles (PLG-NPs) have been utilized to deliver antibacterial agents in the treatment of endodontic and periodontal infections. Moulari *et al.* investigated the antibacterial property of an ethyl acetate leaf extract of Harungana madagascariensis (HLE), a native African plant, by potentializing HLE with PLG nanoparticles. The *in vitro* bactericidal activity of HLE-PLG-NPs against bacteria implicated in dental caries and gingivitis were studied. The results showed that encapsulating HLE in PLG NPs enhanced the antibacterial effect of the former. This was attributed to the bio-adhesive nature of PLG particles that enables prolonged adhesion and effectiveness of the antibacterial substance against the pathogens [28].

Materials of significance in Endodontic-Prosthodontic interdisciplinary approach
Silver Nanoparticles (Ag-NPs)
Cheng *et al.* evaluated the effect of incorporating Ag-NPs on the mechanical properties and biofilm formation ability of composite resin [29]. The results showed that mechanical properties of Ag-NPs composite and control group (without Ag-NPs composite) were similar, but the counts of colony forming units were lesser in Ag-NPs composite than the control group. Melo *et al.* reported that incorporation of Ag-NPs in a dental adhesive disrupted the formation of biofilm, without compromising bond strength [30]. Sameiei *et al.* observed that addition of Ag-NPs to the commonly used endodontic repair material, MTA significantly improved the antimicrobial properties of the latter [31].

Acosta-Torres *et al.* reported that Ag-NPs incorporated polymethylmethacrylate (PMMA) resin showed significantly lesser adherence of candida albicans on it compared to unmodified PMMA [32]. Zhao *et al.* observed that bacterial adhesion was inhibited over Titanium-implants coated with Ag-NPs for a period of up to one month. This successfully prevented post-infection at early stages of implant placement [33].

Graphene Nanoparticles
A uniform crystal lattice without any vacancies makes graphene a nanoform. Thus, graphene is used to treat various bacterial biofilms [34]. Graphene/zinc oxide nanocomposite has the potential to counteract the biofilm caused by *S. mutans*. Acrylic teeth coated with graphene are used due to their cost-effectiveness, fracture resistance and low-density property [35].

Carbon Nanotubes
Carbon nanotubes (CNTs) exhibit remarkable properties owing to their unique structure such as the presence of C-C bond and sp^2 hybridization, which confers them with strong mechanical properties. Research has shown that CNTs when incorporated into commercially available implant materials such as titanium, zirconia and hydroxyapatite improve the surface charge and texture of the implants. The CNTs surface treated implants showed better cell differentiation and rapid cell adhesion between the implant surface and bone cells and also decreased the aging of the implants [36]. Akasaka *et al*. coated the dentin surface with CNTs solution aimed at prevention of recurrent caries under composite restoration. The authors observed that CNTs could serve as promising pre-treatment agents under composite restoration, since they were found to bond to the collagen of dentin, serves as nucleation sites for hydroxyapatite without interfering the bond strength of composite to tooth [37]. The strength and stiffness of

composite and epoxy resin were increased by incorporation of CNTs which acted as nanofillers [38]. Reduced polymerization shrinkage and enhanced mechanical properties were seen in CNTs incorporated heat cure monomer [39].

Zirconia Nanoparticles

Zirconia nanoparticles (ZrO_2-NPs) possess a significant antimicrobial property against *C. albicans and Aspergillus niger*. Gowri *et al.* explained that the ZrO_2-NPs produce active oxygen species, that will cause an interruption of the cell membrane of microorganism and ultimately result in increased cell membrane permeability [40]. Gad *et al.* observed that *Candida albicans* adhesion to cold-cure resin was significantly reduced by the addition of ZrO_2-NPs [41].

Materials Of Significance In Endodontic-periodontic-prosthodontic Multidisciplinary Approach

Local Nano Anaesthetic

A colloidal suspension containing millions of anaesthetic dental nanorobots would be used to induce local anaesthesia. When deposited on the gingival tissue, the nanorobots would reach the dentin and move towards the pulp via dentinal tubules, guided by chemical differentials, temperature gradients, and positional steering by a nanocomputer under the control of the dentist. On reaching the pulp, the analgesic robots may close down all sensation in the tooth. When the treatment procedure has been concluded, the nanorobots may be ordered to re-establish all sensations and to exit from the tooth. This technique will be advantageous as it would greatly reduce apprehension and be fast and totally reversible [42]. Suture needles incorporating nanosized stainless steel crystals have been developed. Nanotweezer was first created by Philip Kim and Charles Lieber at Harward University in 1999. Its working end is a pair of electrically controlled carbon nanotubes made from a bundle of multiwalled carbon nanotubes. To operate the tweezers, a voltage is applied across the electrode that develops a positive and negative electrostatic charge on the electrode [43].

CONCLUSION

Nanotechnology will bring even greater changes to the field of dentistry. Nanoparticle functionalization can result in higher drug efficacy as more bioactive molecules could be loaded onto one nanoparticle. Newer economic multifunctional nanoparticles and their modifications should be developed based on clinical requirements and human needs. The whole concept of nanotechnology in health care should be accepted with positive zeal and caution for future development.

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