



NANODENTISTRY: A PROMISING TOOL FOR DENTISTRY

Oral Medicine

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ABSTRACT

Background: Nanotechnology is manipulating matter at a nanometre level. Application of nanotechnology for treatment, diagnosis, monitoring and control of biological systems has recently been referred to as 'Nano-Medicine' by the National Institute of Health. It holds promise for advanced diagnosis, targeted drug delivery and biosensors. In the long term, medical Nano-Robots will allow instant pathogen detection and elimination as well as individual cell surgery in vivo. Dentistry is in no way exempted from this revolutionary technical advance in science.

KEYWORDS

Nano-Dentistry, Oral Medicine and Radiology.

Clinical implications:

New treatment opportunities may include dentition denaturalization, permanent hypersensitivity cure, complete orthodontic realignments during a single office visit, covalently bonded diamondized enamel and continuous oral health maintenance through the use of mechanical dentifrobots.

Nanotechnology is the use of matter on an atomic, molecular, and supramolecular scale for industrial purposes. The earliest, widespread description of nanotechnology referred to the particular technological goal of precisely manipulating atoms and molecules for fabrication of macro scale products, also now referred to as molecular nanotechnology.¹

Nanotechnology as defined by size is naturally broad, including fields of science as diverse as surface science, organic chemistry, molecular biology, semiconductor physics, energy storage^{2,3}. The associated research and applications are equally diverse, ranging from extensions of conventional device physics to completely new approaches based upon molecular self-assembly⁴ "Self-Assembled Wiggling Nano-Structures and the Principle of Maximum Entropy Production from developing new materials with dimensions on the nano scale to direct control of matter on the atomic scale⁴."

History of nanotechnology

Nanotechnology were used by artisans as far back as the 9th century in Mesopotamia for generating a glittering effect on the surface of pots.⁵ The concepts that seeded nanotechnology were first discussed in 1959 by renowned physicist Richard Feynman in his talk, 'There Plenty of Room at the Bottom' in which he described the possibility of synthesis via direct manipulation of atoms.

The term 'nanotechnology' was first used by Norio Taniguchi in 1974, through it was not widely known.⁶ In the 1980s, two inventions which enabled the imaging of individual atoms or molecules as well as their manipulation led to significant progress in the field of nanotechnology. Gerd Binnig invented scanning tunnelling microscopy (STM) while Heinrich Rohrer invented atomic force microscopy. Inspired by Feynman's concepts, K. Eric Drexler independently used the term "nanotechnology" in his 1986 book *Engines of Creation*:

The Coming Era of Nanotechnology. In 1991, Sumio Iijima discovered carbon nanotubes and by 2000, the United States government launched the National Nanotechnology Initiative (NNI – a Federal visionary research and development programme for nanotechnology-based investments through the coordination of 16 various US departments and independent agencies) and these paved way for the progress in research and development in the field of nanotechnology⁷

Approaches to Nanodentistry

In the top-down technique, larger devices are used to assemble smaller devices. Milling, machining, and lithography are a few examples of this technique.^{8,9} The bottom-up technique refers to the use of smaller components into a more complex assembly. It involves the process of designing custom-made molecules that reorganize to higher scale structures. This method is most widely used as it proves to be more economical and cost effective.

Nanotechnology in dentistry

Because of the growing interest in the future of dental application of nanotechnology, a new field called nanodentistry is emerging. The development of nanodentistry will allow nearly perfect oral health by the use of nanomaterials and biotechnologies including tissue engineering and nanorobots¹⁰

Clinical Categories:

General dentistry
Restorative
Endodontics
Implantology
Oral surgery
Orthodontics
Pediatric dentistry
Periodontics
Prosthodontics
Specialty care

Preventive dentistry

Researchers developed a nano-toothbrush, by incorporating nanogold or nanosilver colloidal particles between toothbrush bristles¹¹

In addition to its ability to improve upon mechanical plaque removal, researchers reported an antibacterial effect of the added gold or silver which could ultimately lead to a significant reduction in periodontal disease.

Oral hygiene products such as toothpastes and mouthwash solutions were also nano-modified according to recent reports. Nano-calcium fluoride, for instance, was added to mouthwash products to reduce caries activity, reduce dentine permeability, and increase labile fluoride concentration in oral fluid¹² Toothpastes containing calcium carbonate nanoparticles and 3% nanosized sodium trimetaphosphate have been reported to promote remineralisation of early carious lesions in comparison to a conventional toothpaste with no nano-additives¹³

Prosthodontics

Incorporating 0.4% TiO₂ nanoparticles into a 3D printed polymethylmethacrylate (PMMA) denture base was investigated in 2017, in an attempt to improve its antibacterial characteristics and mechanical properties¹⁴. According to measurements using Fourier Transform Infrared Spectroscopy (FTIR), Scanning Electron

Microscopy, and tests for antimicrobial efficacy against *Candida* species, improvements in the chemical and structural properties was reported, and the antibacterial effects specifically against *Candida* species was significant.

Researchers also investigated the tribological behaviour of a 7 wt% nano-zirconium oxide modified heat cured PMMA¹⁵. The addition of zirconium oxide nanoparticles significantly improved hardness levels, flexural strength, and fracture toughness of the heat cured PMMA denture base. Nano sized fillers were used due to their superior dispersion properties, less aggregation potential, and biocompatibility with the organic polymer. Nano zirconium not only improved physical properties of denture bases during the construction phase, they were reported to improve the transverse strength of a repaired denture base as well.¹⁶

Endodontics

Applications of nanotechnology in endodontics include the incorporation of bio-ceramic nanoparticles such as bioglass, zirconia, and glass ceramics in endodontic sealers. It has been found that the use of nano-particles enhances the adaptation of the adhesive to nano-irregularities, in addition to its fast setting time in comparison to conventional sealers, its dimensional stability, insolubility in tissue fluid, chemical bond to tooth tissue, and). This was corroborated by a recent study, testing the antibacterial effects against endodontic biofilm, bond strength to dentine, and the ionic release of calcium and phosphate when a novel bioactive endodontic sealer was used. The sealer was a mix of dimethylaminohexadecyl methacrylate (DMAHDM), 2-methacryloyloxyethyl phosphorylcholine (MPC), and amorphous calcium phosphate nanoparticles (NACP). The sealer was able to inhibit the formation of endodontic strains, while the nanoparticles were particularly useful in accelerating the remineralization process and in increasing bonding strength to dentine.

Conservative and aesthetic dentistry

The new development of a rechargeable nano-amorphous calcium phosphate (nACP) filled composite resin has been recently reported. The nanoparticles were able to not only improve composites' remineralising properties, it also maintained the same level of Ca and P release through recharge and release¹⁸. Researchers described it as a "smart" material through its constant ability to rapidly neutralise bacterial acids released along the restoration/tooth margins through the release of Ca and P, therefore was able to inhibit the initiation of secondary caries. This was corroborated by Wu et al., reporting a significant remineralising ability of nACP and its effectiveness in inhibiting the initiation of secondary caries. Researchers also reported that their results create a possibility for integrating nACP in other dental materials such as luting cements and bonding agents. This was corroborated by another study, showing a significant demineralizing ability in a dental bonding agent with nACP through the recharge and release of Ca and P ions for up to 3 week, without altering the bonding strength to dentine.¹⁹

Periodontics, Implantology, and regenerative dentistry

Scientists were able to create a novel drug delivery system for the treatment of periodontal disease, through triclosan or tetracycline loaded nanoparticles. These nanoparticles are uniformly dispersed within a matrix, which gradually biodegrades, releasing loaded drugs in increments to provide a longer contact duration with the diseased site²⁰. Niosomes, for instance, are chemically stable non-ionic vesicles, which offer a controlled and targeted drug delivery with enhanced penetration through biological tissue especially when the particles are less than 100 nm in size²¹. Furthermore, fullerenes have been heavily studied for their many potential applications, one of which is its effectiveness in drug delivery. Fullerenes are hollow carbon molecules which come in different shapes (spheres, tubes, and ellipsoids). The buckminsterfullerene (C60) was the first and most stable fullerene discovered in the 1980s, which resembled the geodesic domes designed by Buckminster Fuller, hence, named after him. These fullerenes can be constructed by either a bottom up approach, building it atom by atom, or by a top down approach from larger atoms, which according to the literature proved to produce a more stable fullerene structure.²² It was additionally used for other purposes in the medical field, such as radical scavenging and as antioxidants.

The literature also reports the benefits of combining a light curable, methacrylate resin matrix, with nACP as a bone grafting agent. This injectable material has the ability to strongly adhere to wet bone, and in recrystallizing nACP to hydroxyapatite in a matter of minutes²³.

It has been theorised that the osseointegration of implants within the jaw bone would be maximised if the implant surface was mimicking the surface topography of the extracellular matrix within natural tissue, which is typically between 10 and 100 nm in size

Nanotechnology in Oral medicine and radiology:

Nanodiagnosics:

Nano diagnostics is the use of nano devices for the early disease identification. In in-vitro diagnostics, nano medicine could increase the efficiency and reliability of the diagnostics using human fluids saliva or tissues samples by using selective nano devices, to make multiple analyses at sub cellular scale. In in-vivo diagnostics, nano medicine could develop devices able to work inside the human body in order to identify the early presence of a disease, to identify and quantify toxic molecules, tumor cells.²⁴ In an attempt to improve upon medical diagnostics, the concept of nano-biosensing was introduced. A biosensor is "an analytical device which incorporates a physically active element with an appropriate physical transducer to generate a measurable signal proportional to the concentration of chemical species in any type of sample". Biosensors were introduced in 1962 by Clark and Lyons (1962), followed by an ongoing extensive research and development of this promising technology by utilising various detection principles, leading to potential applications in public health, environmental monitoring, and food safety Table 1²⁵

Table 1. Detection principles in nano-biosensors.

Detection Principle	Definition
Piezoelectric	Piezoelectric biosensors have the ability to generate an electrical charge in response to mechanical stress, and the translation of mechanical energy to electrical energy is called the piezoelectric effect (Kumar, 2000)
Electrochemical	This detection principle starts with the analyte (target) chemically binding to the highly specific bioreceptor (e.g. a fixed enzyme), affecting the electronic properties of the sensor, and ultimately generating a readable signal (Hasanzadeh and Shadjou, 2016)
Optical	Optical nanosensors give quantitative measurements on an intracellular level. It converts the biorecognition of the analyte into an optical signal (Clark et al., 1999)
Calorimetric	Thermal biosensors or calorimetric biosensors rely on the rate of enzymatic exothermic reaction to measure the concentration of the analyte.

Diagnosis and treatment of oral cancer

Exosome is a membrane bound secretory vesicle containing a proteomic and genomic marker whose level is elevated in malignancy. This marker has been studied by using atomic force microscopy which employs nanoparticles. The nanoelectromechanical system, oral fluid nanosensor test, and optical nanobiosensor can also be used for diagnosing oral cancer. Nanoshells which are miniscale beads are specific tools in cancer therapeutics. Nanoshells have outer metallic layers that selectively destroy cancer cells while leaving normal cells intact. Undergoing trial are nanoparticle-coated, radioactive sources placed close to or within the tumor to destroy it²⁶

Digital dental imaging

Advances in digital dental imaging techniques are also expected with nanotechnology. The radiation dose obtained using digital radiography with nanophosphor scintillators is diminished and high quality images obtained²⁷

Future of Nanotechnology

Nanotechnology is foreseen to change health care in a fundamental way. It forms the basis of novel methods for disease diagnosis and prevention. It will be useful in therapeutic selection tailored to the patients profile and will come in handy in drug delivery and gene therapy.

CONCLUSION

The science and applications of nanotechnology are constantly evolving as we witness new products being introduced into the market. This comes with great responsibility to insure the safety, efficiency, and applicability of such new technologies. Their level of effectiveness as shown in the literature diverge, being more effective than some

materials and less effective than others. Although nanomaterials generally offer superior aesthetics and polishability, their mechanical properties fall short in comparison to microfilled resin composites for example. Therefore, the choice to use nanomaterials is dependent on the clinical scenario and tooth to be restored, paying close attention to aesthetic demand, loading, and the presence of any risk factors such as parafunctional habits. Research to improve upon existing nanomaterials is still ongoing, with future directions towards more efficient and cost effective nano-biosensing devices to diagnose in high accuracy oral cancer for example, in addition to new oral drug delivery systems to disrupt biofilm formation and reduce the incidence of caries and periodontal disease. Although the science behind nanotechnology is intriguing, the lack of long term clinical evidence addressing their clinical performance restricts their wide clinical use.

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