Small Things Have a Big Impact-Nanotechnology in Periodontics

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Abstract: ***Small things have a big impact and so is nanotechnology. Nanotechnology refers to the control and manipulation of matter at nanometer dimension.It is extreme diverse,ranging from extensions of conventional device physics to completely new approaches based upon molecular assembly ,from developing new materials with dimensions on nanoscale to investigating whether we can directly control matter on atomic scale. Nanotechnology and its application in periodontics have improved the diagnosis, treatment, prognosis and prevention of the periodontal diseases. It utilizes nanobiotechnology, nanomaterials, and nanorobots for the treatment and maintenance of periodontal health. When we gain access to hold the nanorobots, we will be able to treat very rapidly a number of diseases that are a continuous threat for mankind today. Although the achievement of the goal of complete regeneration of the periodontal tissues could not be possible for many years. Recent developments in nanomaterials and nanotechnology have provided a promising insight into the commercial applications of nanomaterials in the management of periodontal diseases. Various materials structured in nanoscales and nanomaterials are developed to form an ideal scaffold interfaces with the tissues which provide new horizon in periodontal therapy. The present article aims to provide an early glimpse on the impact and future implication ,potential use and phenomenon of nanotechnology as applied to periodontics.***

Keywords: Nanotechnology, nanomaterials, nanorobots, periodontics, nanoparticles, nanodentistry

1. Introduction

Nanoscience or nanotechnology refers to the development and research of an applied science at the atomic or molecular level. Nanotechnology can be defined as science and engineering involved in the design, synthesis, characterization and application of materials and devices whose smallest functional organization in atleast one dimensions is on the nanometer scale. The word „"Nano"" means „"dwarf"" and in greek prefix signifies a „"billionth""[1,2] **.** Nanotechnology is developing fast in recent years and like other medical fields it is also set to transform dentistry in a huge way. It is now considered as a multidisciplinary field of scientific research. From the definition provided by the National Nanotechnology Initiative, nanotechnology exploits specific phenomena and direct manipulation of materials on the nanoscale[2] . It symbolizes inexpensive control of the structure of matter based on molecule-molecule control of products and byproducts[3] .A widely used definition for nanotechnology is " the creation and utilization of materials ,devices and systems through the control of matter on nanometer scale(1-100nm),i.e.at the level of atoms, molecules, and supra molecular structures". However nanotechnology is much more than the study of smaller things; it is the exploration and advancement of materials ,devices, and systems showing physical, chemical, and biological properties that are divergent from those found on a larger scale.

2. Historical Background

In 1959 Noble Physicist Richard.P. Feynman(Father of Nanotechnology) proposed using machine tools, which, in turn, would be used to make still smaller tools, and so on all the way down to the molecular level[4] .In this historical lecture ,he said "this is a development which I think cannot be avoided". He suggested that such nanomachines, nanorobots and nanodevices could ultimately be used to develop a wide range atomically precise microscopic instrumentation and manufacturing tools.The term „"nanotechnology"" was coined by Nario Taniguchi in 1975.In 1979,Eric Drexler encountered Freynman"s 1959 talk "There"s Plenty of room at the bottom".In 1986 Drexler[5] recoined the term „"Nanotechnology"" and wrote "Engines of Creation"":The Coming Era of Nanotechnology, a book to popularize the potentials of molecular nanotechnology. In 2000s begin the commercial applications of nanotechnology.[27,30]

3. How are Nanoproducts Made?

Two main approaches used in nanotechnology:

- **Top- Down Approach:** From top(larger) to bottom (smaller).These seek to create smaller devices by using larger ones to direct their assembly.Nano objects are constructed from larger entities without atomic level control.[8]
- **Bottom-Up Approach:** From bottom (smaller) to top(larger).These seek to begin with a nanometric structure(molecule) and creating a mechanism larger than original structure. Components are built from molecular components which assemble themselves chemically by principles of molecular recognition.[6,7]

4. Properties of Nanomaterials

Nanomaterials are those materials with components less than 100 nm in atleast one dimension, including clusters of atoms, grains less than 100nm diameter, films less than 100nm in thickness, nanoholes and composites that are combination of these.[14] At the nanoscale, properties of materials behave differently, governed by atomic and molecular rules. Researchers are using the unique properties of materials at this small scale to create new and exciting tools and products in all areas of science and engineering. Nanotechnology combines solid state physics, chemistry, electrical engineering, chemical engineering, biochemistry, biophysics, and materials science. It is thus a highly interdisciplinary area – integrating ideas and techniques from a wide array of traditional disciplines. They exhibit

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much better performance properties than traditional materials which include

- Stiffness,
- Enhanced toughness,
- Increased scratch,
- Improved transparency,
- Abrasion, solvent and heat resistance,
- Decreased gas permeability .

In addition. nanoparticles have special properties, including

- Magnetic,
- Optical,
- Chemical, and
- Electro-optical properties, which differ from those of either individual molecules or bulk species.
- Nanoparticles have a greater surface area per unit mass than compared with larger particles .

Various Nanoparticles are as Follows: [10,12,15]

Nanopores,Nanotubes,Quantumdots,Nanoshells,Dendrimers, Liposomes,Fullerenes,Nanospheres,Nanowires,Nanobelts,Nanorings,Nanocapsules.

Self Assembly:

Self-assembly is an important feature of nanostructured materials. Here, an autonomous organization of components into patterns or structures without human intervention occurs [13] . The whole process can be manipulated and facilitated through the correct setting of conditions. Self assembly can be classified into static and dynamic processes[13].The most commonly used in self assembly are the polyelectrolyte materials, cationic polyelectrolytes and anionic polyelectrolytes. The most universal driving forces for establishing self-assembly are electrostatic attractive interactions between positive and negative charges.

Inorganic Nanomaterials either Currently in Use or Under Development

- Semiconductor nanoparticles
- Metal nanoparticles
- Metal oxide nanoparticles
- Silica nanoparticles
- Polyoxometalates
- Gold nanocrystals

5. Applications in Periodontics

Nanomaterials For Periodontal Drug Delivery

Nano particles owing to their small size, penetrate regions that may be inaccessible to other delivery systems such as periodontal pocket subgingivally. Pinon-Segundo et al produced and characterized triclosan loaded nanoparticles by the emulsification-diffusion process, in an attempt to obtain a novel delivery system adequate for the treatment of periodontal disease[17] .These triclosan-nanoparticles behave as homogenous polymer matrix-delivery system, with the drug molecularly dispersed. It was concluded that triclosan nanoparticles were able to effect a reduction of the inflammation of the experimental sites. Timed release of drugs may occur from biodegradable nanospheres. This also allows for site specific drug delivery. A good example is Arestin in which tetracycline is incorporated into microspheres for drug delivery by local means to a periodontal pocket[19] .

Nanomaterials For Periodontal Tissue Engineering

Nanotechnology has got the potential to produce nonbiologic self-assembling systems for tissue engineering purposes[20].Currently tissue engineering concepts for periodontal regeneration are focused on the utilization of synthetic scaffolds for cell delivery purposes [3] .Non biologic self assembling nanosystems will automatically undergo pre-specified assemblies much in line with known biologic systems associated with cells and tissues. It is possible to create polymer scaffolds in the future for cell seeding, growth factor delivery and tissue engineering via nanodevices implanted to sites of tissue damage. It metabolizes trapped organic matter into harmless and odourless vapours and performing continuous calculus debridement. These invisibly small dentifrobots (1-10microns),would safely deactivate themselves if swallowed. Further the devices would identify particles of food, plaque and lift them from teeth to be rinsed away. Being suspended in liquid and able to swim about, devices would be able to reach surfaces beyond reach of toothbrush bristles or the fibres of floss.

Scaffolds and Nanotechnology

Scaffolds play a pivotal role in tissue engineering. Scaffolds may be populated by cells before implantation or, if they are information rich or permissive constructs, they may mobilize host cells, or cells may simply migrate into them, after implantation. Scaffolds are known as artificial extracellular matrix and help in accommodating the cells and guide them to grow, proliferate, migrate, and differentiate, leading to the formation of a specific tissue while secreting the extracellular matrix that is required for tissue regeneration. Several in vitro and in vivo_experiments have shown that nanostructured materials, which mimic the nanometer topography of the native tissues, improve biocompatible responses, and result in better tissue integration [21] . Nanostructured materials have unique surface properties (such as energy, wettability, topography, etc.) that make them intriguing for applications involving interactions with proteins and subsequently cells [22] **.**

Bone Replacement Materials

Nanotechnology aims to emulate bone for dental applications and more particularly for development of nanobone. Nanocrystals show a loose microstructure, with nanopores situated between the crystals. The surfaces of the pores are modified such that they adsorb protein,due to addition of silica molecules. Bone defects can be treated by using these hydroxyapatite nanoparticles. These can be used in osseous defect in periodontal surgeries. Nanohydroxyapatite (nHA) is more biodegradable and highly biocompatible as compared to hydroxyapatite.The material also adapts itself well to the size and shape characteristics of healthy bones.Due to increased initial cellular attachment ,calcium ions help in osteoblast differentiation.Degradation of nHA alters Ca/P metabolism and activates osteoblast via specific Ca ion channel(Webster 1999).Increased osteoblast attachment leads to higher Ca release than conventional[26] .Chitsazi MT et al 2011

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evaluated the efficacy of autogenus bone graft and nanocystalline hydroxyapatite in the management of human intrabony periodontal defects .Complete resorption of the nanohydroxyapatite had taken place after 12 weeks. Osseous defects in periodontal surgeries can be treated by using HA nanoparticles.[23]

Trade Names[27]

- OSTIM(Oscartis GmbH,Obernburg-Germany)HA
- NanoOSSTM(Angstrom Medica,USA)HA
- VITOSSO (Orthovita,Inc.,Great Valley Parkway Malvern USA)HA+TCP

Nanotechnology in Periodontal Biofilms

Nanotechnology has been used to study dynamics of demineralisation and mineralisation process in dental caries by use of atomic force microscopy.It detects bacterial induced demineralisation at ultrastructural level[31] .To determine effect of biofilm culture on cell envelope,proteome of P.gingivalis cell surface proteins like RgpA were increased in biofilm cells.Old culture techniques might have been gold standard till date but are slow and detects only cultivable bacteria.Nanotechnology selectively removes periodontal and cariogenic bacteria while preserving normal flora in a more targeted and protective approach.

Tooth Repair

Nanorobotic manufacture and installation of a biologically autologous whole replacement tooth that includes both mineral and cellular components, that is, „complete dentition replacement therapy‟should become feasible within the time and economic constraints of a typical office visit through the use of an affordable desktop manufacturing facility, which would fabricate the new tooth in the dentist‟s office[9] .Chen et al[33] made use of nanotechnology to simulate the natural biomineralisation process to create the hardest tissue in the body,the enamel by using highly organized microarchitectural units of nanorod like calcium HA crystals arranged parallel to each other.

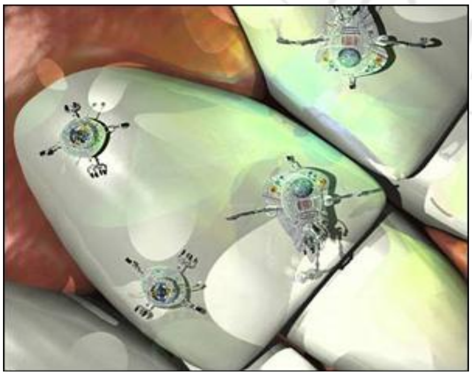

Figure 1: Dentifrobots cleaning the teeth

Atomic Force Microscopy(AFM)

Botelho,Martins2010[35] conducted a study using 8.5 % doxycycline gel containg nanospheres,prepared using carbopol 940,% w/v for preventing bone loss.AFM images analysed the topographical and roughness surface aspects,that has increased the prediction of periodontal therapy evaluation.[34,35,36]

Implants

Bone growth and implant success can be accelerated by the use of nanotechnology.Besides surface contact area and surface topography, bone bonding, and stability play a major role in implant success and osseointegration. Osteoblast formation on a more complex implant surface is formed by the addition of nanoscale deposits of hydroxyapatite and calcium phosphate particles[37] .Material engineering, and hence implant dentistry, has advanced extensively on the basis of researches conducted on the effects and subsequent optimization of micro topography and surface chemistry. These new implants constructed on the basis of this technology are more acceptable as they enhance the integration of nano coatings resembling biological materials to the periodontal tissues[38] .In addition, implant surfaces coated with titanium oxide nanotubes and laced with silver nanoparticles serve the purpose of fighting infection thus increases the shelf life of the implants[39] .These implants use nanometer scale calcium phosphate to create a more complex topography on the implant surface,which as proven to expedite osseointegration by 150% thereby decreasing the length of treatment by one to three months.Ostman et al.2008[24] in a 1 year clinical and radiographic study concluded that immediate loading of NanoTite Prevail implants seems to be a viable option in implant rehabilItation,at least when a good initial fixation is achieved. Further periimplantitis surface conditioning with citric acid improves nanoparticle sized hydroxyaopatite blended clot adhesion to titanium implant surfaces[25] .Surface modifications of dental implants can be done by nanotechnology as surfaces properties such as roughness and chemistry play a determinant role in achieving and maintaining their long-term stability in bone tissue[2,40] .The most common reason for failure of dental implant is the deficient formation of bone around the biomaterial immediately after the implantation. With the use of coating of nano particles over the dental implants, adhesion and integration of surrounding tissues is improved[41] .

Growth Factors

Growth factors such as platelet-derived growth factor (PDGF) have significantly enhanced periodontal therapy outcomes with a high degree of variability, mostly due to the lack of continual supply for a required period of time. One method to overcome this barrier is gene therapy. PDGF-B gene delivery in fibroblasts using nano-sized calcium phosphate particles (NCaPP) as vectors has found to significantly enhance fibroblast proliferation[42] .

Laser Plasma Application for Periodontia

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:

1) Shock waves
2) Microabrasion of hard tissues
3) Stimulus to produce collagen[44]

Clinical applications of this laser plasma application in periodontia are Periodontal therapy, melanin removal and soft tissue incision (without anesthesia)[43] **.**

Challenges Faced by Nanodentistry[27]

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a)Engineering challenges

- Precise positioning and assembly of molecular scale part
- Feasibility of mass production technique
- Manipulating and coordinating activities of large numbers of independent microscale robots simultaneously

b) Biological challenges

- Ensuring compatibility with all intricate of human body
- Developing biofriendly nanomaterial

c) Social challenges

- Ethics
- Regulation and human safety
- Public acceptance

Nanorobots

Nanorobotics is the technology of creating machines or robots at or close to the microscopic scale of nanometers [45] .A nanorobot can be defined as an „an artificially fabricated objects able to freely diffuse in the human body and interact with specific cell at the molecular level by itself. These miniature robots are so small that they can be introduced into the body either through the vascular system or through the catheters, and with external guidance and monitoring by the surgeon they can perform precise intracellular surgery, which would not be possible with the human hand.

Composition of Nanorobots

Diameter of about 0.5 to 3 microns and will be constructed out of parts with dimensions in range of 1-100nms.Carbon is the principle element in the form of diamond. Other light elements like hydrogen,Sulfur,Oxygen,Nitrogen,Fluorine,Silicon are used for special purposes in nanoscale gears and other components[46] .

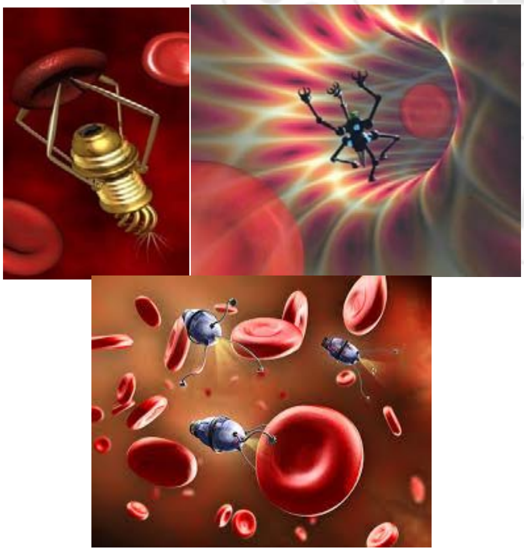

Figure 2: Dental nanorobots

The exterior of a nanorobot will likely be constructed of carbon atoms because of its inert properties and strength.Supersmooth surfaces will lessen the likelihood of triggering the body‟s immune system ,allowing the nanorobots to go about their business unimpeded.Glucose or natural body sugars and oxygen might be a source for propulsion and the nanorobot will have other biochemical or molecular parts depending on its task[48] .

6. Mechanism of Action of Nanorobots

The powering of nanorobots can be done by metabolizing local glucose and oxygen for energy and externally supplied acoustic energy.Other sources of energy within the body can also be used to supply the necessary energy for the devices[47] .

Communication

Is an important fundamental capability of nanorobots. They must be able to communicate with each other in order to monitor collective task progress and pass along relevant sensory, messaging,navigational and other operational data[49] .Nanorobots function will be controlled by simple onboard computers capable of performing about 1000 or fewer computations per second. Communication with the device can be achieved by broadcast-type acoustic signaling. Navigational network may be installed in the body providing accuracy to all passing nanorobots that interrogate them, wanting to know their location. This will help to keep track of various devices in the body. Nanorobots are able to distinguish different cell types by checking their surface antigens. They are accomplished by use of chemotactic sensors keyed to the specific antigens on the target cells. When the task of nanorobot is completed they can be retrieved by allowing them to exfuse themselves via the human excretory channels. These can also be removed by active scavenger systems[47] .It is Freitas(1999) who described how medical nanorobots might use specific motility mechanisms to crawl or swim through human tissues with navigational recession, cytopenetration and use any of a multitude of techniques to monitor, interrupt or alter nervecells.Nanorobots act similar way in dentistry too[15,50] .

Are These Nanorobots Safe?

The non pyrogenic nanorobots used in vivo are bulk Teflon, carbon powder and monocystal sapphire.Pyrogenic nanorobots are alumina ,silica,copper,zinc.Nanorobots may release inhibitors,antagonists or down regulators for the pyrogenic pathway in a targeted fashion to selectively absorb the endogenous pyrogens,chemically modify them and then release them back into the body in a harmless inactivated form[51] .

Application of Nanorobots

Medical Applications: Nanorobots are complex molecular machines used for diagnosing,treating and preventing disease,relieving pain,preserving and improving human health. The first useful application in nanomedicine was to identify cancer cells and destroy them.

An interesting utilization of nanorobots may be their attachment to transmigrating inflammatory cells or white blood cells ,to reach inflamed tissues and assist in their healing process thus medical nanorobots augment the immune system by finding and disabling unwanted bacteria and viruses, protecting the body against harmful pathogens.

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Medical nanorobots monitor diabetes by controlling nutrients concentrations in the human body including blood glucose levels in diabetic patients.Also useful in preventing myocardial infarction,breaking kidney stones and in curing skin diseases[46] .

7. Application of Nanorobots in Periodontics

The growing interest in the future of dental applications of nanotechnology is leading to the emergence of a new field called nanodentistry.Nanorobots induce oral ananlgesia,desensitize tooth,manipulate the tissues to realign and straighten irregular set of teeth,and also used in preventive,restorative,curative procedures and major tooth repair[47] .

a) Oral anaesthesia induction
b) Oral hygiene and halitosis
c) Dental Hypersenstivity

Oral Anaesthetic Induction

To induce oral anaesthesia in the era of nanodentistry, dental professional will instill a colloidal suspension containing millions of active analgesic micrometer sized dental nanorobots on the patients gingiva. Nanorobotic analgesics offer greater patient comfort, reduced anxiety ,no-needle, greater selectivity, control ability of the analgesic effect, fast and completely reversible action ,avoidance of most of side effects and complications[53] .

Mouthwashes (Oral Hygiene And Halitosis)

Subocclusally dwelling nanorobotic dentrifice(dentifrobots) delivered by mouthwash or toothpaste could patrol all supragingival and subgingival surfaces at least once a day and destroy pathogenic bacteria residing in plaque and elsewhere,while allowing harmless oral microflora to fluorish in health ecosystem.It metabolizes trapped organic matter into harmless and odourless vapours and performing continuous calculus debridement.These invisibly small dentifrobots would safely deactivate themselves if swallowed.Further the device would identify particles of food,plaque and lift them from teeth to be rinsed away.Being suspended in liquid and able to swim about,devices would be able to reach surfaces beyond reach of toothbrush bristles or the fibers of floss[47] .

Dental Hypersenstivity

Natural hypersensitive teeth have eight times higher surface density of dentinal tubules and diameter with twice as large as nonsensitive teeth. Reconstructive dental nanorobots, using native biological materials,could selectively and precisely occlude specific tubules within minutes,offering patients a quick and permanent cure as the nanorobots pass through the journey of enamel -dentin reaches pulp[16] .Once installed in the pulp,having established control over nerve impulse traffic,dental nanorobots may be commanded by the dentist to shut down the sensitivity in the selected tooth that requires treatment[51] .Nanorobots selectively and accurately block these dentinal tubules using native materials, thus offering quick and permanent relief to the patient[52] .

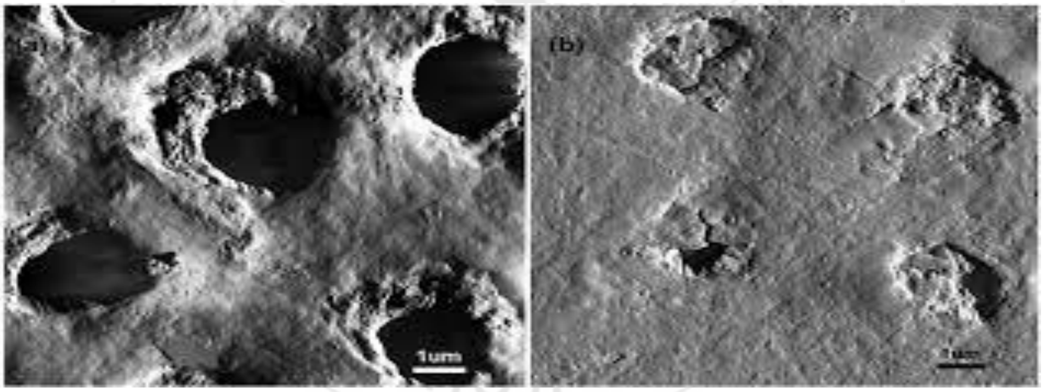

Figure 3: Nanomaterials occluding dentinal tubules.

Disadvantages of Nanorobots :[47]

1) Design Cost is high
2) Installation cost is high
3) Maintenance is difficult
4) Hard to interface,customize, and design,complex.
5) Social challenges of ethics,public acceptance,regulation and human safety.
6) Precise positioning and assembly of molecular scale parts.
7) Biocompatibility.

Advantages of Nanorobots:[46]

1) Build up artificial immunity
2) Treat and fight disease and restore lost tissue at the cellular level.
3) No harm with their use
4) Bloodless surgery.

8. Conclusion

Nanomaterials and nanoparticles are likely to be cornerstones of innovative nanodental devices to be used for drug discovery and delivery, discovery of biomarkers and molecular diagnostics. Nanotechnology seems to be where the world is headed if technology keeps advancing ,and competition practically guarantees that advances will continue.It will open a huge range of opportunities of benefit for both the dentist and the patient. Although the achievement of the goal of complete regeneration of the periodontal tissues for periodontal management may not be possible for many years,recent developments in nanomaterials and nanotechnology have provided a promising insight into the commercial applications of nanomaterials in the management of periodontal diseases. A large number of materials scientists have devoted their

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efforts to the development of new nanomaterials; however, a need exists for them to collaborate more closely with dentists and dental scientists.Current work is focused on the recent developments, particularly of nanoparticles and nanotubes for periodontal management, the materials developed from such as the hollow nanospheres, core shell structures, nanocomposites, nanoporous materials, and nanomembranes will play a growing role in materials development for the dental industry.Programmable and controllable microscale robots comprised of nanoscale parts fabricated to nanometer precision will allow medical doctors to execute curative and reconstructive procedures in the human body at the cellular and molecular levels. A longer-term hope is that self-replicating nanomachines could repair and rebuild damaged teeth and oral tissue completely.The multidisciplinary field of nanotechnology is bringing the science of almost incomprehensibly small device closer and closer to reality. Nanotechnology can become a predicted future in which dentistry, including periodontal practice and periodontal therapies may become more high-tech and more effective. However comprehensive research facility must be made available to meet the rigorous requirements for the development of nanotechnologies.

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