Small is the new big; nanotechnology in periodontics: A review

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Abstract
With the ever-growing advancement in the field of dentistry, one of the major breakthroughs is the use of nanotechnology. Nanotechnology is a relatively recent development in scientific research. To use this gem of the technology to its full potential, basic and adequate knowledge about its functioning and science behind it is necessary. The use of nanotechnology in periodontics is relatively untouched. This paper aims to compile the basic principles, uses and benefits of nanotechnology in the field of periodontics, and help the reader in unleashing its potential in the non-surgical as well as surgical aspects, local drug delivery and a plethora of other aspects. Simultaneously, focusing on the problems that are faced for its practical usage and the safety concerns.

Keywords: nanodentistry, nanoparticles, nanorobotics, nanotechnology

1. Introduction
Nanotechnology is the science that deals with the manipulation of materials and technology at the atomic or molecular level, with at least one dimensions less than 100 nm. The word nano originates from the classical Latin “nanus” or its ancient Greek etymon “nanos” (νάνος), meaning “dwarf”. Nanotechnology which is a relatively newer development in the scientific research, its origin dates back to 1959, when Richard Feynman first introduced the concept of nanotechnology [1,2]. The fusion of nanotechnology in the treatment modalities for periodontal diseases can be considered as one of the major breakthroughs in the field of periodontics. Periodontal disease is one of the most prevalent disease globally, and can affect about 90% of the population [3], and the prevalence in developing countries like India, is as high as 96.30% [4]. Majority of the periodontal diseases are a sequel of untreated inflammatory process [5], taking place in the various periodontal structures, viz, gingiva, bone, periodontal ligaments and cementum. The major challenge faced in the treatment of these periodontal diseases is the accessibility to the area of inflammation. With the advent of newer procedures and more precise instruments the accessibility to space constricted areas has been a lot more better, introduction of nanotechnology in the treatment of periodontal disease and its collaboration with the existing modalities will not only add to better treatment protocol, but will also increase the precision and make treatments more site specific. This review article aims to summarize and simplify the current research trends revolving around nanotechnology in periodontics, their uses, benefits, various treatment options, use of dental nanorobots, at the same time addressing the hurdles faced in their usage in routine procedures, the safety concerns and potential biohazards. Also, this article puts a step forward in the direction of translation of nanodentistry to a more specific, nano-periodontics approach for periodontal diseases.

2. Generations of nanotechnology
Nanotechnology is currently housed under four generations, which is categorized as follows: [6]
- First generation (From 2000): Passive (steady function nanostructures): E.g., Nanostructured coatings invasive; noninvasive diagnostics for rapid patient monitoring.
- Second generation (From 2005): Active (evolving function nanostructures): E.g. Reactive...
3. Applications of nanotechnology in periodontics
Nanotechnology in periodontics has touched every aspect of treatment modality, ranging from non-surgical therapy to implant procedures, including regenerative methodologies. Understanding their mechanism plays a pivotal role if more efficient usage of nanotechnology and better treatment procedure and eventually better outcome.

3.1 Nanorobotic Dentifrice (Dentifrobots)
Nanorobots (dentifrobots) released by mouthwash or toothpaste on the occlusal surfaces of teeth can clean organic residues by moving throughout the supragingival and subgingival surfaces, continuously preventing the accumulation of calculus. These nanorobots, which are as small as 1-10 microns, can move as fast as 1-10 microns/second, are safely deactivated when swallowed. Properly configured dentifrobots can identify and destroy pathogenic bacteria residing in the plaque [7].

3.2 Nanofibers
Nanofibers are fibers whose diameter is in the nanometer range. Nanofibers including nanorods, nanoplatelets, nanotubes, nanofibrils and quantum wires are various nanomaterials that are being extensively researched for various applications, significantly focusing on their applications in periodontal regeneration.

This article focuses on nanofibers in the following aspects of periodontal disease management:

3.2.1 Bone and cartilage tissue engineering
Scaffolds play an important role in tissue regeneration, it provides a suitable environment for differentiation, proliferation of the cells and hence aids in regeneration. Nanofibers play a vital role in acting as a scaffold for alveolar bone and cartilage regeneration, it aids in target specified delivery of drugs, growth factors and genetic materials [8, 9]. Since nanoparticles have a larger surface area, due to smaller particle size, the scaffold becomes more porous and allows better infiltration of drugs and growth factor, leading to better regenerative properties [9]. The application of novel methodologies in nanotechnology such as 3-D fiber deposition and electro-spinning has led to the enhancement of nanoscaffold quality [10].

3.2.2 Ligament tissue engineering
Tissue engineering methods involving nanofibers have been experimented (Lin et al 1999) to overcome the challenge of incomplete or improper healing of ligaments after an injury, by means of natural tendencies or conventional techniques. In particular, aligned nanofibers enhanced cell response and hence were explored as scaffolds for ligament tissue engineering.

3.2.3 Tissue engineering and graft material
A graft with nano-structured PLGA-Poly(lactic-co-glycolic acid) on the exterior (promoting smooth muscle cell function) and conventional PLGA on the interior (promoting endothelial cell function) could be utilized to enhance integration into vascular tissue and thus increase implant efficacy [12].

3.3 Treatment of Dental hypersensitivity
Dentin sensitivity is another pathology that is suitable for nanodental treatment. Many therapeutic agents provide only a temporary effect for this common, painful condition. However, dental nanorobots can seal specific tubules by using natural biomaterials within a few minutes and provide a quick and permanent recovery from this condition. [13] Tian and co-authors theorized that due to excessive dispersion of nanomaterials, it can easily enter the dentinal tubules, of 2-3 um, and block the sensation leading to relief from dental hypersensitivity [14].

3.4 Nano anesthesia
Anesthesia is an inseparable part of periodontal surgery, along with conventional anesthesia technique, injection, comes long waiting period and multiple injections for longer duration procedures. With the aid of nanotechnology, it becomes possible to encapsulate various anesthetic drugs in form of liposomes, with high clinical acceptance [16]. Liposomes are spherical, nanovesicles consisting of a phospholipid bilayer, [15] and hydrophilic part; thus, enabling encapsulation of various drugs without being distorted [16]. Nanorobotic local anesthetics are composed of a colloidal solution of activated nanosized local anesthetic molecules. When applied to the gingival or the oral mucosa and signaled, the anesthetic travels via the epithelial and connective tissues of the gingiva to reach the pulp, thus providing selective anesthesia, which is under the control of the clinician [17]. The advent of this technology offers greater patient comfort with minimal patient anxiety, precise selectivity, and controllability of the analgesic effect, as well as complete reversibility of the analgesic [18].

3.5 Local drug delivery
Local drug delivery refers to disease site targeted application of drugs which helps in the treatment being more site specific, rather than a systemic approach. In a study, triclosan particles were applied to the inflamed site, which helped in reduction of the inflammation. Also, it expressed future use of nanotechnology, a procedure called as Arestin®, in which microspheres containing tetracycline are placed into periodontal pockets and tetracycline is administered locally [19].

4. Applications of nanotechnology in dental implants
Many reports have shown that nanometer-controlled surfaces have a great effect on early events such as the adsorption of proteins, blood clot formation, and cell behaviours occurring upon implantation of dental implants. These early events have an effective impact on the migration, adhesion, and differentiation of Mesenchymal stem cells (MSCs). Nanostructured surfaces may control the differentiation pathways into specific lineages and ultimately direct the nature of peri-implant tissues. Despite an active research in dental implants, the ideal surface for predictable tissue integration remains a challenge [20].

5. Barriers in nanotechnology

5.1 Engineering: Feasibility of mass production technique

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Nanoscale genetic therapies; targeted cancer therapies.
- Third generation (From 2010): Integrated nanosystems: E.g. Artificial organs built from nanoscales; evolutionary biosystems.
- Fourth generation (From 2015/2020): Heterogenous nanosystems: E.g. Nanoscale genetic therapies; molecules intended to self-assemble themselves.

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Feasibility of mass production technique

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Precise positioning and assembly of molecular scale parts
Manipulating and coordinating activities of various microscale robots

5.2 Biological: Development of biofriendly nanomaterial
Biocompatibility with all intricate of the human body

5.3 Social: Ethics Public acceptance Regulation and human safety

6. Future prospects
Computer controlled nanorobots are the main stay in the
future of nanotechnology in periodontal therapy. Nanorobots promises
play a vital role in various treatment and preventive modalities, including dentifrice
(dental hypersensitivity [14], local drug release [19]). These nanorobots tend to move up to the desired site of action, by means of the
commands provided by the dentist, exert their pre-programmed action at the site, and are later on deactivated and retrieved by onboard computer held by the dentist (The movement of nanorobots via dentinal tubules into the pulp
guided by combination of chemical and thermal gradients can be controlled by an on board computer held by the dentist)

7. Conclusion
The future of periodontics looks incomplete without the
inclusion of nanotechnology in the routine periodontal therapy,
be it surgical or non-surgical; however, it will take extensive research in terms of development of biomaterials of the
nanoscale, which can be instilled safely in the human body.
Nanotechnology promises to play a vital role in
minimizing patient discomfort, at the same time maximizing the effects of a particular periodontal therapy. The research revolving around nanotechnology in dentistry and periodontics in particular, is extensive and promises an exciting and enticing future, which will lead to a much efficient growth and development of periodontics and oral
implantology.

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