**Ministry of High Education
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University of Baghdad
College of Dentistry**

Nanotechnology in Dentistry

A project submitted to the College of Dentistry, University of Baghdad, Department of Pediatric and Preventive Dentistry in partial fulfillment of the requirement for B.D.S degree

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Dedication

To the best mother ever to my lovely sister

To my hero my father

for their endless love and support

To my supervisor for her guidance and

help throughout the project.

Ruaa

Acknowledgment

We thank Allah for giving us the strength and patience to achieve this work, which I wish it, will be useful & objective.

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Symbol	Abbreviation
%	percentage
CNT	Carbon Nano tube
DNA	Deoxyribonucleic acid
RNA	Ribonucleic acid
GNP	Global Nano product
CaP	Current applied physics
CS NPs	Chitosan nanoparticles
GIC	Glass ionomer cement
EQUIA	Easy quick unique intelligent aesthetic

Introduction

A new revolution in the field of dentistry is the use of nanotechnology. This technology has got remarkable potential that can bring considerable improvements to human health in the form of nanomaterial, nano diagnostics and nano robotics. Nano dentistry will make possible the maintenance of comprehensive oral health by employing nano tissue devices which will allow precisely controlled oral analgesia, dentine replacement therapy, permanent hypersensitivity cure and complete orthodontic realignment etc., all in single office visit. However, like two sides of a coin, though nanotechnology possesses tremendous potential, it has its share of limitations including social issues of public acceptance, ethics, regulation and human safety (Feynman,1966;West *et al*,2000).

Nanotechnology is emerging as an interdisciplinary field that is undergoing rapid development and has brought about enormous changes in medicine and dentistry. Nanomaterial-based design is able to mimic some of the mechanical and structural properties of native tissue and can promote biointegration. A range of synthetic nanoparticles such as hydroxyapatite, bioglass, titanium, zirconia and silver nanoparticles are proposed for dental restoration. This review focuses on the developments in the field of nanomaterials in dentistry in the form of tissue regeneration materials, implantable devices, nanocomposites, endodontic sealers, etc, and issues of patient safety (Taniguchi,2000).

1. Nanotechnology

The art of manipulating the materials on an atomic or molecular scale especially to build microscopic devices.

United State government state that nanotechnology is research and technology development at atomic or molecular or macromolecular level in the length of scale approximately 1-100nm range, to provide a fundamental understanding of phenomena and materials at the nanoscale and to create and use structure, devices and systems that have novel properties and function because of their small and\or intermediate size(Kong *et al*, 2006;Mansoori , 2005).

The National Nanotechnology Initiative state that nanotechnology is the direct manipulation of materials at the nanoscale.This defines a technology that enables almost complete control of the structure of matter at nanoscale dimensions. Nanotechnology will give the ability to arrange atoms as desire and subsequently to achieve effective, complete control of the structure of matter (Kong *et al*, 2006;Mansoori , 2005).

The Japanese have come up with a more focused and succinct definition. "true nano"; as nanotechnology which is expected to cause scientific or technological jumps, or to provide great industrial applications by using phenomena and characteristic peculiar in nanolevel.

The aims of nanotechnology are to enable the analysis of structures at the nanoscale, to understand the physical properties of structures at the nanoscale dimension, to manufacture nanoscale structures, to develop devices with nano-precision and to establish a link between nanoscopic and macroscopic universes by inventing adequate methods (Ozbay , 2006).

Nanotechnology is based on the idea of creating functional structures by controlling atoms and molecules on a one-by-one basis (Freitas , 2000).

1.1. The concept of Nanotechnology

The word nano originates from the Greek word "dwarf". The concept of nanotechnology was first elaborated in 1959 by Richard Feynman, a nobel prize winning physicist, in a lecture titled, “There’s plenty of room at the bottom”. He ended the lecture concluding “this is a development which I think cannot be avoided” (Freitas , 2000).

1.2. Applications of Nanotechnology

Nanotechnology has applications in many fields

These flieds include:

- Medicine: Diagnostics, Drug delivery, Tissue engineering
- Chemistry and environment, Catalysis, Filtration
- Energy, reduction of energy consumption, increasing the efficiency of energy production
- Information and communication, novel semiconductor devices, novel optoelectronic devices, displays, quantum computers Heavy industry, aerospace, refineries, vehicle manufacturers, consumer goods, foods (Kanaparthy and Kanaparthy , 2011).

1.3. Approaches of Nanotechnology

Numerous approaches have been utilized successfully in nanotechnology and as the technology develops, further approaches may emerge, the approaches thus far have generally been dictated by the technology available and the background experience of the researchers involved. Nanotechnology is a truly multidisciplinary flied involving chemistry, physics, biology, engineering, electronics and social science which need to be integrated together in order to generate the next level of development in nanotechnology. Fuel cells, mechanically stronger materials nanobiological devices, molecular electronics, quantum devices, carbon nanotubes (CNTs), etc, have been made using nanotechnology.

The "top-down" approach involves fabrication of device structure via monolithic processing on the nanoscale and has been used with spectacular success in the semiconductor devices used in the consumer electronics. The "bottom-up" approach involve fabrication of device structure via systematic assembly of atoms, molecule, and other basic units of matter. This is the approach uses to repair cells, tissue, organ systems in living things and indeed for life processes such as protein synthesis. Tools are evolving which will give the scientists more control over the synthesis and characterization of novel nanostructures yielding a range of new products in the near future (Zhang *et al*,2009).

2. Nanomaterial

Nanomaterials are those materials with components less than 100 nm in at least one dimension. These may include atoms clusters, grains, fibers, films, nanoholes and composites from these combinations. Nanomaterials in one dimension are termed as sheets, in two dimensions as nanowires and nanotubes, and as quantum dots in three dimensions (Nagpal *et al*, 2011).

2.1. Nanomaterial Properties

Nanomaterial properties vary majorly from other materials due to two reasons: the increase in surface area and quantum effects. Nanoparticles due to their small size have a much increased surface area per unit mass compared to bigger particles. In addition to that, quantum effects become more dominant at the nano scale. All properties, including electrical, optical and magnetic ones, are altered (Drexler , 2006).

3. Nanomedicine

Nanaomedicine is the science of preventing, diagnosing and treating disease and preserving and improving human health by using nanosized particle this concept was first put forward in 1993 by Robert and Freitas. It was also defined as observing, controlling and treating the biological systems of the human body at the molecular level using nano-structures and nano-devices (Kubik T et al, 2005; Freitas R, 2008).

Nanomedicine includes various applications ranging from drug release with nanospheres to tissue scaffolds based on nanotechnologic design that realize tissue formation and even nanorobots for diagnostic and therapeutic purposes (Freitas R, 2005).

Drug molecules transported through the body by the circulatory system may cause undesirable adverse effects in untargeted regions. On the other hand, nanorobots can recognize unhealthy cells and can find and destroy them wherever they are located. Drug delivery to the exact target is of particular importance in cancer in order to destroy all of the cancer cells and at the same time avoid harming healthy cells (Freitas R, 2005).

Nanomedicine can overcome many important medical problems with basic nanodevices and nanomaterials, some of which can be manufactured . The results of many studies performed in the field of nanomedicine are very close to transformation into practice; therefore, it can be said that these successful developments are inevitable. Nanomedicine provides improvements in available techniques in addition to developing fully new techniques (Caruthers *et al*, 2007).

3.1. Types of Nanotechnologies in Nanomedicine

They can be generally divided into three potent molecular technologies:

i. Nanoscale materials and devices to be applied in advanced diagnostics and biosensors, targeted drug delivery and smart drugs.

ii. Molecular medicine through genomics, proteomics, artificial biobotics (microbial robots).

iii. Molecular machines and medical nanorobots aid inimmediate microbial diagnosis, treatment and enhancement of physiological functions (Kanaparthy and Kanaparthy , 2011).

4. Nanorobots

Nanorobots have a diameter of about 0.5–3 microns and made of components sized from 1–100 nanometers. Carbon will be the primary component in the form of diamond or fullerene. Nanorobots would respond to definite programs enabling clinicians to execute accurate procedures at the cellular and molecular level. Nanorobots may also use in the field of gerontology, with diverse applications in pharmaceutics, diagnostics, dental therapy, in reversal of atherosclerotic damage, enhancing lung function, aiding natural immunity, repairing brain injury, modifying cellular DNA sequences, and repairing cellular damage (Kanaparthy and Kanaparthy, 2011).

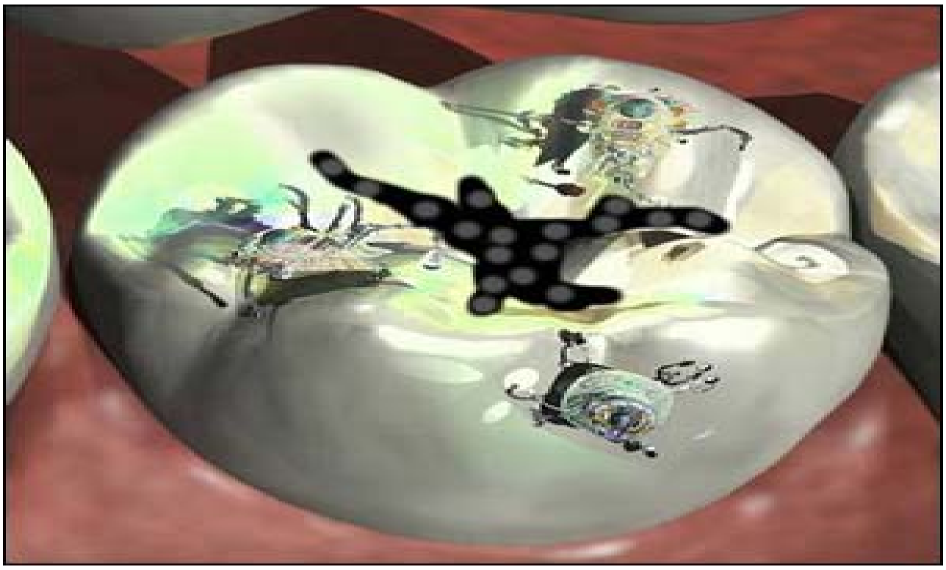


Figure (1): Nano robot (Kanaparthy and Kanaparthy, 2011)

5. Nanosensors

Nanosensors have been used for military application in identifying airborne harmful materials and weapons of chemical warfare and to identify drugs and other substances in expired air (Kanaparthy and Kanaparthy , 2011).

6. NanoDentistry

Similar to nanomedicine, the development of nanodentistry will allow nearly perfect oral health by the use of nanomaterials and biotechnologies, including tissue engineering and nanorobots (Freitas , 2000).

6.1. Fields of Nanotechnology in Dentistry

6.1.1. Local Nanoanaesthesia

A colloidal suspension containing millions of anesthetic dental nanorobots would be used to induce local anesthesia. Deposited on the gingival tissue, the nanorobots would reach the dentin and move toward the pulp via the 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 reestablish all sensations and to exit from the tooth. This technique is advantageous as it reduces apprehension and is fast and totally reversible .(Freitas, 2000).

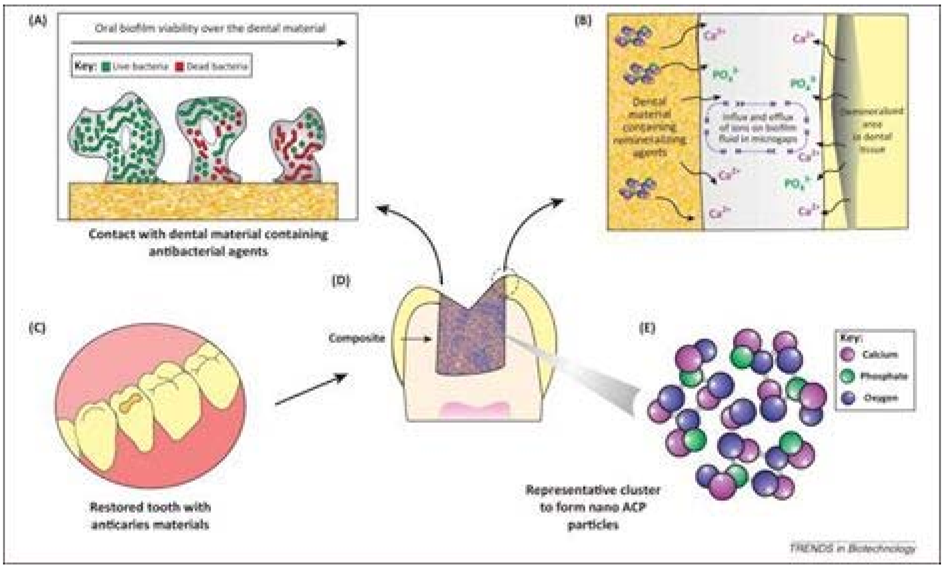
6.1.2. Management of Dentin Hypersensitivity

Dentin hypersensitivity is another area where dental nanorobots may find their use. Dentin is protected from external stimuli by enamel in the crown or by cementum in the root. The removal of this protective layer exposes the underlying dentinal tubules, changing the fluid pressure hydrodynamics of the fluid inside the dentinal tubules, and is believed to be responsible for dentin hypersensitivity.Global nano particals GNPs were found to be easily adsorbed on the inner dentinal tubule walls; the application of silver staining was then used to help to occlude the open tubules and reduce the dentin sensitivity. After brushing the opened tubules with highly concentrated GNPs, laser irradiation promoted the aggregation of nanoparticles to occlude the exposed tubules.

Furthermore, dental nanorobots offer a quick and permanent cure to dentin hypersensitivity by selectively and precisely occluding the tubules in minutes using biological materials. Nanorobots, using local organic materials, could result in effective occlusion of particular tubules, resulting in rapid and stable treatment (Freitas ,2000).

6.1.3. Prevention of Dental Caries

The use of a toothpaste containing nanosized calcium carbonate enabled remineralization of early enamel lesions. Furthermore, a study that investigated the bacteriostatic effects of silver, zinc oxide and gold nanoparticles on Streptococcus mutans, which causes dental caries, reported that compared to the other nanoparticles, silver nanoparticles had an antimicrobial effect in lower concentrations and with lower toxicity (Hernández-Sierra *et al*, 2008; Nakashima *et al*,2009).



Figure(2) :Role of nano technology in prevention of caries (Nakashima *et al*,2009).

6.1.3.1. Caries Vaccine

By blocking the surface protein antigen PAc or inactivation of glucosyltransferases enzyme. Both surface protein antigen PAc and glucosyltransferases are the virulent factors responsible for the adhesion of S. mutans to tooth surfaces. DNA vaccines, however, have poor immunogenicity in large animals and human beings. Nanotechnology has been employed to tailor delivery vehicles eg, anionic liposomes in chitosan/DNA nanoparticle Several attempts are currently underway in developing an effective anticaries vaccine as a new strategy of preventing the occurrence of dental caries. DNA vaccine was found to be an effective, safe, stable, and inexpensive immunogenic strategy in inducing both humoral and cellular immune responses. Many candidate anticaries DNA vaccines have been or are undergoing usage tests in animals or human beings. Examples of these vaccines include pcDNA3-Pac, pCIA-P, pGJGLU/VAX, and pGLUA-P (Talwar *et al*, 1999; Wang *et al*, 2014; Su *et al,* 2014).

Most of the anticaries vaccines work by preventing bacterial accumulation either complex was used as a delivery vehicle to enhance the immunogenicity of anticaries DNA vaccine. Furthermore, the surface charge of the delivery vehicle could be pH dependent to enable the release of the vaccine in a pH-dependent manner (Kt *et al*, 2013; Koga *et al*, 1990; Yamashita *et al*, 1993).

Despite the advances in nanotechnology, its clinical application for caries therapy is not yet feasible. Although, the Ca2+- and PO43−-releasing nanocomposites have load-bearing capability, their mechanical behavior as Ca2+ and PO43− ions being released is difficult to estimate and control under identical clinical situations. The profile of ions released under constrained conditions has not been investigated. A balance between the ion release and the rate of caries progression, which is unpredictable, must exist. The optimum particle size of nanofillers required for remineralization, the pattern in which the released ions are precipitated, and the orientation of precipitated nanocrystals in relation to collagen fibrils are important factors that require careful consideration in designing nanomaterials. Until now, all in vitro investigations indicated that nanotechnology could be effective in reversing lesion progression in the outer but not in the deeper part of early caries lesions. Controlling deep and large lesions, however, requires a thorough understanding of the caries progression process. Furthermore, incorporation of nanofillers within dental composites might be effective in preventing recurrent caries around restorations; the effect of these nanofillers, however, on bacteria left in affected dentin, which are sometimes left in deep cavities during conservation of tooth structures, has to be studied. Furthermore, regardless of the progress with anticaries vaccinations, their use in human beings has not been tried yet. Accordingly, there is no vaccine available on the market yet. The high diversity of oral flora, high salivary flow, difficult antigen delivery, enzymatic degradation of vaccine, and poor internalization could be limiting factors (Hannig *et al*, 2012).

6.1.4. Nanocomposite

The increasing interest in esthetic restorations in recent years has led to further development of materials that have the same color as that of teeth (Türkün L et al, 2007).

The latest advance in composite resins is the implementation of nanoparticle technology into restorative materials. (Papadogiannis D et al, 2008).

Nanotechnology has enabled the production of nano-dimensional filler particles, which are added either singly or as nanoclusters into composite resins. Nanofillers are different from traditional fillers. When the filler for traditional composites is produced, large particles are minified by pinning; however, these methods cannot reduce the size of a filler that is smaller than 100 nm, Nanotechnology allows the production of nano-sized filler particles that are compatible with dental composites; therefore, a greater amount of filler can be added into the composite resin matrix (Jung M et al, 2007; Mitra S et al, 2003).

Nanoparticles allow the production of composites with a smooth surface after the polishing process and confer superior esthetic features to the material. Composite resins containing such particles are easy to shape and have a high degree of strength and resistance to abrasion. Therefore, the area of use of resins containing nanoparticles is wider than that of composites containing hybrid and microfill fillers (Yesil Z et al, 2008).

In contrast to hybrid composites in which large particles can be separated from the matrix, only poorly attached nanoclusters are separated during abrasion in nanocomposites; thus, a well-polished restoration surface can retain its smoothness for a long time (Türkün L et al, 2007).

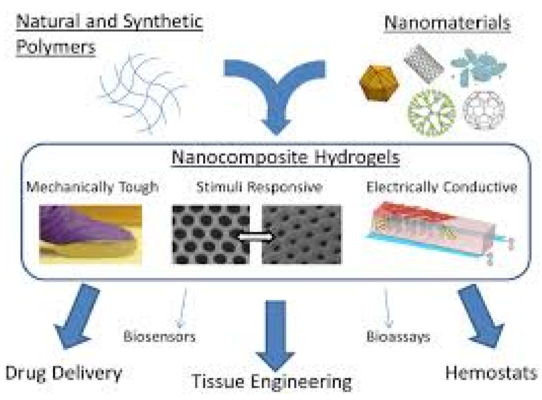


Figure (3) : Nano composite hydrogels. (Yesil Z et al, 2008).

6.1.4.1. Advantages of Nanocomposite

Increased hardness, Improved flexural strength, toughness and translucency, Decreased polymerization shrinkage (50%), Exceptional handling properties, High polish retention and Higher translucency giving it more lifelike appearance (Nagpal *et al*, 2011; Kanaparthy and Kanaparthy , 2011; Chandki *et al*, 2012).

6.1.5. Chitosan Nanoparticle

Chitosan (poly (1, 4), β-d glucopyranosamine), a derivative of chitin, the second most abundant natural biopolymer, has received significant interest in biomedicine . The industrial extraction of chitin is generally obtained from crustaceans such as crabs, lobsters, and shrimps, making up to 1013 kg in the biosphere . The structure of chitin closely resembles that of cellulose, and both act as a structural support and defense material in living organisms. Chitin has two reactive groups: primary (C-6) and secondary (C-3) hydroxyl groups allowing for various chemical modifications. Chitosan has an additional amino (C-2) group on each deacetylated unit. (Yesil Z et al, 2008).

Chitosan is known as a versatile biopolymer that could be synthesized in various forms such as powder (micro- and nanoparticles), capsules, films, scaffolds, hydrogels, beads, and bandages . Chitosan has a structure similar to extracellular matrix components and hence is used to reinforce the collagen constructs . This hydrophilic polymer with large numbers of hydroxyl and free amino groups can be subjected to numerous chemical modifications and grafting . Nanoparticles of chitosan have been developed mainly for drug/gene delivery applications.(Freitas ,2000).

Nanoparticles of chitosan could be synthesized or assembled using different methods depending on the end application or the physical characteristics required in the nanoparticles. Chitosan nanoparticles (CS NPs), by virtue of their charge and size, are expected to possess enhanced antibacterial activity. In addition, chitosan possesses several characteristics such as being nontoxic toward mammalian cells, color compatibility to tooth structure, cost effectiveness, availability, and ease of chemical modification. CS NPs can be delivered within the anatomical complexities and dentinal tubules of an infected root canal to enhance root canal disinfection.(Freitas ,2000).

Antibacterial Properties which include :

Chitosan and its derivatives such as carboxymethylated chitosan showed a broad range of antimicrobial activity, biocompatibility, and biodegradability. The exact mechanisms of antibacterial action of chitosan and its derivatives are still not vivid. However, a more commonly proposed mechanism is contact-mediated killing that involves the electrostatic attraction of positively charged chitosan with the negatively charged bacterial cell membranes. This might lead to the altered cell wall permeability, eventually resulting in rupture of cells and leakage of the proteinaceous and other intracellular components. Rabea et al. proposed that chitosan, due to its chelating property, sequesters trace metals/essential nutrients and inhibits enzyme activities essential for bacterial cell survival . Under transmission electron microscopy, the bacterial cells were seen to be completely enveloped in the chitosan forming an impermeable layer. This could have resulted in the prevention of transport of essential solutes leading to cell death. In case of fungi, chitosan was hypothesized to enter cells and reach nuclei, bind with DNA, and inhibit RNA and protein synthesis. (Yesil Z et al, 2008).

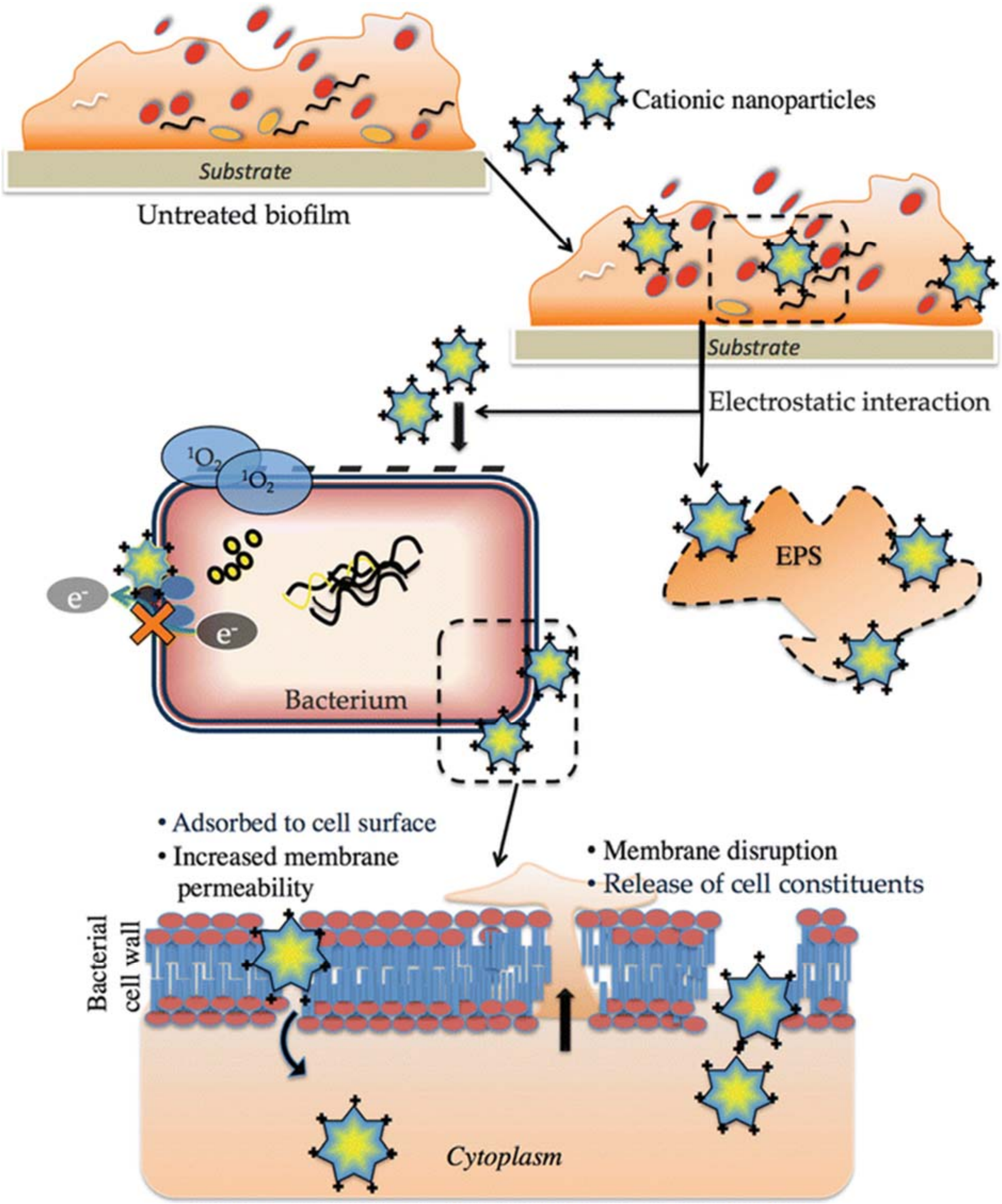


Figure (4): Chitosan Nanoparticle(Kanaparthy and Kanaparthy , 2011).

6.1.6. Nanorobotic Dentifrice (Dentifrobots)

Toothpastes or mouthwashes could contain the dentifrobots which would then survey all gingival surfaces regularly. They would also break down harmful materials into harmless substances and undertake constant calculus removal (Freitas R, 2000).

6.1.7. Nanosolution (Nanoadhesives)

Nanosolutions are constituted by dispersible nanoparticles, which are then used as a component in bonding agents. They lead to a homogenous and perfectly mixed adhesive consistently (Patil M et al, 2008).The advantages of nanosolution are: Higher dentine and enamel bond strength, High stress absorption, Longer shelf life, Durable marginal seal, No separate etching required, Fluoride release (Jhaveri H and Balaji P, 2005).

6.1.8. Nano Light Curing Glass Ionomer Restorative

Application of nanotechnology to glass-ionomer cement (GIC) was first developed for Ketac Nano with fluor aluminum-silicate technology having nanoparticles in the range of 1 μm. The addition of nanoparticles resulted in improved esthetics and polishability of the restoration. Another nanofilled light-cured varnish is applied onto the surface of viscous GIC (Fuji IX GP® Extra, GC Europe). This commercial product is the EQUIA (Easy-Quick-Unique-Intelligent-Aesthetic) system, which contains inorganic silica nanofillers (15 wt. % and 40-nm size) dispersed in a liquid. Nanofillers resulted in improved wear resistance by avoiding initial water intake and dehydration and decreased initial setting time (Friedl K et al, 2011 ;Chandki R et al, 2012).

in a retrospective study of nanomodified GICs evaluated their performance over conventional GICs and concluded EQUIA restorations to be superior. Earlier study of antimicrobial property of silver nanoparticles in

GIC against Streptococcus mutans has shown to be highly effective in reducing the bacterial load (Moshaverinia *et al*, 2008;Magalhães *et al,* 2012).

The **advantages** of nanolight curing GIC are : Excellent polish, Superb esthetics, Enhanced wear resistance.

The **Clinical Indications** of nano light curing GIC are: primary teeth restoration, Transitional restoration, Small Class I restoration, Sandwich restoration, Class III and V restoration, Core build-up.

6.1.9. Impression Material

Traditional vinylpolysiloxanes have incorporated nanofillers, which produce a distinctive material with improved flow, enhanced hydrophilic properties and superior detail precision.

6.1.10. Prosthetic Implants

Nanotechnology would aid in the development of surfaces with definite topography and chemical composition leading to predictable tissue-integration. Tissue differentiation into definite lineage will accurately determine the nature of peri-implant tissues. In addition to that, antibiotics or growth factors may be incorporated as CaP coating is placed on Ti implants as: Nanotite™ Nano-Coated Implant Several studies have suggested that materials with nanopatterened surface produced from various chemistries, such as metal polymers, composites and ceramics, exhibit better osseointegration when compared to conventional materials. Nano-patterned surface provided a higher effective surface area and nanocavities when compared to the conventional micro-rough surfaces. These properties are crucial for the initial protein adsorption that is very important in regulating the cellular interactions on the implant surface(Webster *et al* , 2004; Khang *et al* , 2008;Le Guéhennec *et al*, 2007)

The natural bone surface has a roughness of approximately 100 nm, and such nano details are therefore important on the surfaces of implants. Osteoblast proliferation has been induced through the creation of nano-size particles on the implant surface.it has been found that Roughing the implant surface at the nanoscale level is important for the cellular response that occurs in the tissue (Braceras *et al*, 2009; Ellingsen *et al*, 2006).

Among all engineering based implant surface modifications the CaP, coating has received significant attention. This material has chemical similarity to the natural bone. Biomimetic CaP coatings improve the osseoconductivity of implants and show promising slow delivery systems for growth factors and other bioactive molecules (Barrere, 1999; Yang *et al*, 2005).

The goal of nanotechnology is to build active and intelligent implants and structures that will interact with their surroundings, respond to environmental changes, deliver appropriate molecules or drugs and actively direct cellular events. However, the extrapolation of the techniques used for the fabrication of dental implants, to ensure that these features are robust enough to survive implantation, the reliability of test performed in vivo effect of nanoscale manipulation are still open technological challenges (Tomsia , 2011).

Titanium implants treated with a nanostructured calcium surface coat were inserted into rabbit tibias, and their effect on osteogenesis was investigated; the nanostructured calcium coat increased the responsiveness of the bone around the implant. Many in-vitro studies have shown that the nanotopography of the implant surface considerably affects osteogenic cells and that the nanoscale surface morphology enhances osteoblast adhesion. Moreover, the nanoscale surface morphology augments the surface area and thus provides an increased implant surface area that can react to the biologic environment (Suh J et al, 2007; Park J et al, 2009).

6.1.11. Tooth Repositioning

All the periodontal tissues, namely the gingiva, periodontal ligament, cementum and alveolar bone, may be directed by orthodontic nanorobots leading to swift and pain free corrective movements (Chandki R et al, 2012).

6.1.12. Antibacterial Nanoparticles

Metallic nanoparticles of copper, gold, titanium, and zinc have attracted particular attention, with each of them having different physical properties and spectra of antimicrobial activity. It is known that magnesium oxide (MgO) and calcium oxide (CaO) slurries acted upon both gram-positive and gram-negative bacteria in a bactericidal manner, while zinc oxide (ZnO) slurry acted in a bacteriostatic manner and exhibited stronger antibacterial activity against gram-positive than gram-negative bacteria. The antibacterial powders of magnesium oxide (MgO), calcium oxide (CaO) and ZnO generated active oxygen species, such as hydrogen peroxide and superoxide radical, which is responsible for their antibacterial effect. These NPs of metallic oxides with their high surface area and charge density exhibited greater interaction with bacteria and subsequently produced markedly high antibacterial efficacy. Furthermore, it is apparent that bacteria are far less likely to acquire resistance against metallic nanoparticles than other conventional antibiotics (Saravana K et al, 2006).

Heavy metal ions are known to have different cytotoxic effects on bacterial cell functions. Copper ions may induce oxidative stresses and affect the redox cycling, resulting in cell membrane and DNA damages. Zinc ions applied above the essential threshold level inhibit bacterial enzymes including dehydrogenase, which in turn impede the metabolic activity. Silver ions inactivate proteins and inhibit the ability of DNA to replicate.

NPs synthesized from the powders of Ag, CuO, and ZnO are currently used for their antimicrobial activities. The electrostatic interaction between positively charged NPs and negatively charged bacterial cells and the accumulation of large numbers of NPs on the bacterial cell membrane have been associated with the loss of membrane permeability and cell death.

6.1.13. Endodontic Sealer

Application of nanotechnology has been extended to the field of endodontics as well. Bioceramic-based sealer EndoSequence BC Sealer containing calcium silicate, calcium phosphate, calcium hydroxide, zirconia, and a thickening agent, has been developed. The addition of nanoparticles resulted in improved handling and physical properties. When introduced into root canals, a hydration reaction occurs where a nanocomposite structure of calcium. Water is essential for the setting reaction (Koch K and Brave D, 2009).

Thus, in over-dried canals, setting time is prolonged. The addition of nanoparticles also facilitates delivery of material from 0.012 capillary needles and its adaption to irregular dentin surfaces. It sets hard in few hours and has good sealing ability along with dimensional stability. Its alkaline pH of (12.8) gives antimicrobial properties as well (Koch K and Brave D, 2009; Zoufan K et al; Jiang J, 2011).

Silicon-based sealer containing gutta-percha powder and silver nanoparticles less than 30 µm in size has been introduced as well It is available as capsules that can be mixed and injected as a cold flowable filling system (Koch K and Brave D , 2009).

It has good biocompatibility and dimensional stability with good sealing ability and is resistant to bacterial penetration. Recently, antibacterial quaternary ammonium polyethylenamine (QPEI) nanoparticles have been incorporated into other sealers which are relatively stable, have good biocompatibility, and resulted in good antibacterial activity without affecting mechanical properties (Abramovitz I et al, 2012; Beyth N et al, 2008).

6.1.14. Dental durability & cosmetics

Changing the superficial enamel layer with materials like sapphire or diamond may enhance the toughness and appearance of teeth as these materials have 20-100 times the hardness of enamel. However, diamond and sapphire are brittle, but can be made tougher by their inclusion as part of a nanostructured composite (Fartash et al, 1996; Yunshin S et al, 2005).

6.1.15. Oral fluid nanosensor test (OFNASET)

This technology helps detect salivary biomarkers for oral cancers. It incorporates self-assembled monolayers (SAM), bionanotechnology, cyclic enzymatic amplification, and microfluidics for detection of salivary biomarkers. it had been demonstrated that a combination of two salivary proteomic biomarkers (thioredoxin and IL-8) and four salivary mRNA biomarkers (SAT, ODZ, IL-8, and IL-1b) provided high sensitivity and specificity in detection of oral cancer (Gau V and Wong D, 2007).

6.1.16. Orthodontic wires:

They may be drawn from a novel stainless steel material, Sandirk Nanoflex. This has the advantage of very high strength along with excellent deformability, corrosion resistance and fine surface finish. (Robert A and Freitas J, 2010).

6.1.17. Tissue engineering and dentistry

Potential applications of tissue engineering and stem cell research in dentistry include the treatment of orofacial fractures, bone augmentation, cartilage regeneration of the temporomandibular joint, pulp repair, periodontal ligament regeneration, and implant osseointegration. Tissue engineering enables the placement of implants that eliminate a prolonged recovery period, are biologically and physiologically more stable than previously used implants, and can safely support early loading (Bayne S, 2005; Roberson M et al, 2006).

Studies related to the regeneration of bone tissue constitute a major part of the studies in the tissue-engineering field. Nanoscale fibers are similar in shape to the arrangement between collagen fibrils and hydroxyapatite crystals in bone. The biodegradable polymers or ceramic materials that are often preferred in bone tissue engineering may not have sufficient mechanical endurance despite their osteoconductive and biocompatible properties. Studies performed in recent years indicate that nanoparticles can be used to enhance the mechanical properties of these materials. The main reason for preferring nanoparticles is that the range of dimension of these structures is the same as that of cellular and molecular components (Gumusderelioglu M et al, 2007; Ashammakhi N et al, 2007).

6.1.18. Diagnosis and treatment of cancer

Patients with head and neck cancer require staging assessments, invasive treatments and post-treatment monitoring with physical examination, and routine imaging. Nanotechnology appears balanced to provide devices, capable of sensitive and specific anatomic, molecular and biologic imaging; selective therapy of tumors; and low toxicity, resulting in a significant improvement over the current standard of care (El-Sayed I, 2010).

Multi-functionality is the key advantage of Nanoparticles over traditional approaches. Targeting ligands, imaging labels, therapeutic drugs, and many other functional modalities can be integrated into the Nanoparticles to allow for targeted molecular imaging and molecular therapy of cancer (Cai W et al, 2008).

The nanomaterials have the inherent advantage of possessing unique functional properties for cancer detection and treatment. Nanomaterial is classified in the size domain of proteins and cells. Hence, they have been used as biological tags by interfacing the Nanoparticles with biocompatible molecules (biological, small organic molecules or bioinorganic interface) (Salata O, 2004).

Different kinds of Nanoparticles suitable for drug and gene delivery probing DNA structures, etc., exist. They include liposomes, polymeric Nanoparticles (Nanoshperes and nanocapsules, solid lipid particles, nanocrystals, polymer therapeutics such as dendrimers, fullerenes and inorganic Nanoparticles, e.g., gold and magnetic Nanoparticles). Dendritic polymeric nano devices can detect cancer cells, identify cancer signature, and provide targeted delivery of anti-cancer therapeutics (Ravindran R, 2011).

Carbon nanotubes scan down DNA, and look for single nucleotide polymorphism. Nanowires having the unique properties of selectivity and specificity, can be designed to sense molecular markers of malignant cells. Nanoparticles contrast agents are being developed for tumor detection purposes

such as nuclear magnetic resonance imaging (Ravindran R, 2011).

Whereas several Nanoparticles have been developed, plasmonic gold Nanoparticles appear interesting because of their facile surface chemistry, relatively limited toxicity, and novel optimal properties useful for concurrent imaging and therapy. Gold nanotechnology brings forth ultra-sensitive optical imaging and multiple therapeutic options that may be used in unison. Gold Nanoparticles can be applied therapeutically for photo-thermal therapy, (Huang

X et al, 2007). Intra-vascular drug/gene delivery (Paciotti G et al, 2004).and ionizing radiation enhancement (Hainfield J et al, 2004).

Nanotech based cancer therapeutics and diagnosis, over the past decade, has evolved from nano-sized drug particle to functional nanomaterials that are capable of delivering heat, ionizing radiation and chemotherapeutic agents. By incorporating multidisciplinary engineering innovation in nanotechnology, an avenue for development of enhanced, miniaturized and low cost diagnostic/imaging instruments and treatment machines are opened (Hede S, Huilgol N, 2006). The future possibility of tackling “pain the bitter side of cancer therapy,” through nanotechnology would be considered one of the biggest breaks through achievement (Kam N et al, 2005).

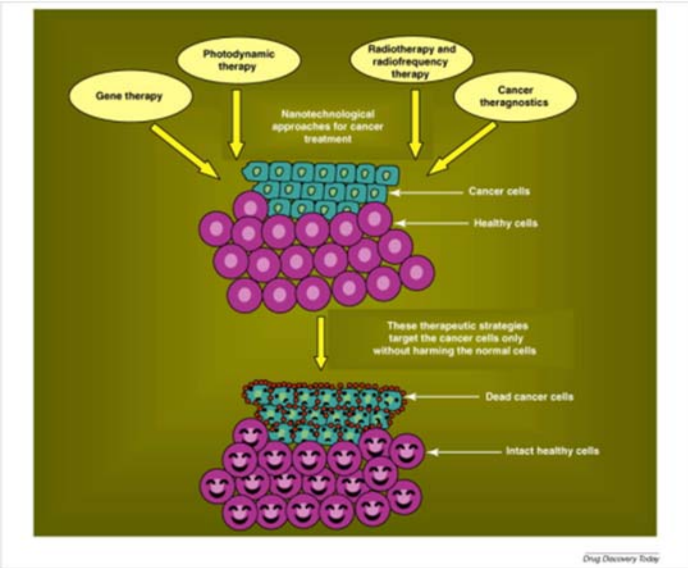


Figure (5): Treatment of cancer (Kam N et al, 2005)

6.1.19. Nanotechnology in preventive dentistry

The purpose of modern dentistry is the prevention of tooth decay rather than invasive restorative therapy however , despite tremendous efforts in promoting oral hygiene and fluoridation , the prevention and biomimetic treatment of early carious lesions are still challenges for dental researchers and public health , particularly for individuals with a high risk for developing caries, which is the most widespread oral disease. Recent studies indicate that nanotechnology might provide novel strategies in preventive dentistry, specifically in the control and management of bacterial biofilm or remineralization of micrometer-sized tooth decay (Selwitz R et al, 2007; Filoche S et al, 2010).

Dental caries caused by bacterial biofilm on tooth surface, and the process of cares formation is modulated by complex interaction between acid producing bacteria and host factor including teeth and saliva. On exposure to oral fluids protein aceos surface coating termed pellicle is formed immediately on all solid substrate (Webster T, 2007).

This conditioning layer which defines the surface charge and the nature of chemical groups exposed at the surface, changes of the properties of the surface (Hannig C, 2009).

Bacteria colonize the surface by adhering to the pellicle through adhesion – receptor interaction and form bioflm, known as dental plaque maturation of the plaque is characterized by bacterial interactions (coaggregation quorum sensing) and increasingly diverse bacterial population, each human host harbors bacterial population.

6.1.20. Nanoneedles

Nano-structured stainless steel crystals have been used to manufacture suture needles furthermore , Plans to make nanotweezers are also under way, which may enable cell surgery feasible (Kanaparthy R and Kanaparthy A, 2011; Chandki R et al, 2012).

6.1.21. Digital dental imaging

Advances in digital dental imaging techniques are also expected with nanotechnology. In digital radiographies obtained by nanophosphor scintillators, the radiation dose is diminished and high-quality images are obtained (Mupparapu M, 2006).

7. Challenges faced by Nanotechnology

It had been found that nanotechnology faced by challenges as Precise positioning and manufacture of nanoscale parts , Cost-effective nanorobot mass manufacturing methods , Synchronization of numerous independent nanorobots , Biocompatibility concern , Financing and tactical concerns , Inadequate assimilation of clinical research , Social issues of public acceptance, ethics, regulation and human safety (Kanaparthy R and Kanaparthy A, 2011; Chandki R et al, 2012).

Conclusion

Advances in nanotechnology are paving the future of healthcare management ,nanodevices cannot be seen by the naked eye yet possess powerful capabilities ,they have the potential to bring about significant benefits, such as improved health, better use of natural resources, and reduced environmental pollution. However, these nanodevices are also associated with significant potential misuse and abuse.

Nanodentistry aims to ensure comprehensive oral healthcare of the patient and emphasizes the primary prevention of oral diseases. With the availability of advanced and accurate diagnostic methods, a number of oral diseases can be prevented or treated at early signs, Challenges in terms of basic molecular engineering methods, mass production techniques, and simultaneous coordination of a large number of nanorobots must be addressed prior to any large-scale application of nanotechnology.

Though the science of nanotechnology may appear as fiction in the present scenario, the future holds strong promise for utilizing and maximizing this technology for the benefit of mankind. Nanotechnology will change dentistry, healthcare, and human life profoundly. However, at the same time, social issues of public acceptance, ethics, regulation, and human safety will need to be addressed before molecular nanotechnology can enter the modern medical and dental armamentarium.

Referances

- **Abramovitz I, Beyth N, Weinberg G, et al**. In Vitro biocompatibility of endodonticsealers incorporating antibacterial nanoparticles. J Nanomater. ;2012**.**23(7).
- **Ashammakhi N, Ndreu A, Yang Y, Ylikauppila H, Nikkola L, Hasirci V** Tissue engineering: a new take-off using nanofiber-based scaffolds.2009;45(7).
- **Bayne S .**Dental biomaterials: where are we and where are we going? **J** Dent Educ.2005; 69(5).
- **Beyth N, Houri-Haddad Y, Baraness-Hadar L, et al**. Surface antimicrobial activity and biocompatibility of incorporated polyethyleneimine nanoparticles. Biomaterials.2008; 29(31).
- **Braceras I, De Maeztu M, Alava J, Gay-Escoda C**. In vivo low-density apposition on different implant surface materials. Int J Oral Maxillofac Surg.2009; 38(4).
- **Cai W, Gao T, Hong H, Sun J.** Applications of gold nanoparticles in cancer nanotechnology. Nanotechnol Sci Appl. 2008;1(2).
- **Caruthers S, Wickline S, Lanza G.** Nanotechnological applications in medicine.Curr Opin Biotechnol. 2007; 18(1).
- **Chandki R, Kala M, Kumar K, Brigit B, Banthia P, Banthia R** Dent MaterJ. 2007; 23(7).
- **Ellingsen J, Thomsen P, Lyngstadaas P**. Advances in dental implant materials and tissue regeneration. Periodontol. 2006; 41(6).

- **El-Sayed I.**Nanotechnology in head and neck cancer: The race is on. Curr Oncol Rep. 2010;12(4).
- **Fartash B, Tangerud T, Silness J, Arvidson K.** Rehabilitation of mandibular edentulism by single crystal sapphire implants and overdentures: 3-12 year results in 86 patients. A dual center international study. Clin Oral Implants Res. 1996; 7(3).
- **Freitas R**. Nanodentistry. J Am Dent Assoc. 2000; 131(11).
- **Freitas R.** Nanotechnology, nanomedicine and nanosurgery. Int J Surg. 2005; 3(4).
- **Freitas R.** What is nanomedicine? Nanomedicine. 2005; 1(1).
- **Friedl K, Hiller K, Friedl K**. Clinical performance of a new glass ionomer based restoration system: A retrospective cohort study. Dent Mater. 2011; 27(10).
- **Gau V, Wong D**. Oral fluid nanosensor test (OFNASET) with advanced electrochemical-based molecular analysis platform. Ann N Y Acad Sci. 2007;1098(7).
- **Gumusderelioglu M, Mavis B, Karakecli A, Kahraman A, Cakmak S, Tigli S, Demirtas T, Aday S**. Doku mühendisliğinde nanoteknoloji. Bilim ve Teknik. 2007; 479(8).
- **Hainfield J, Slatkin D, Smilowitz H**. The use of gold nanoparticles to enhance radiotherapy in mice. Phys Med Biol. 2004;49(6).
- **Hede S, Huilgol N**. "Nano": The new nemesis of cancer. J Cancer Res Ther. 2006;2(5).
- **Hernández-Sierra J, Ruiz F, Pena DC, Martínez-Gutiérrez F, Martínez A, Guillén A, Tapia-Pérez H, Castañón G** The antimicrobial sensitivity of Streptococcus mutans to nanoparticles of silver, zinc oxide, and gold. Nanomedicine. 2008;4(3).

- **Huang X, Jain P, EL-Sayeed I, El-Sayeed M**. Gold nanoparticles: Interesting optical properties and recent applications in cancer diagnostics and therapy. Nanomedicine (Lond) 2007;2(6).
- **Jhaveri H, Balaji P**. Nanotechnology: Furure of Dentistry. J Indian Prosthodont Soc. 2005(4).
- **Jung M, Sehr K, Klimek J.** Surface texture of four nanofilled and one hybrid composite after finishing. Oper DentJ . 2007; 32(1).
- **Kam N, O'Connell M, Wisdom J, Dai H.** Carbon nanotubes as multifunctional biological transporters and near-infrared agents for selective cancer cell destruction. Proc Natl Acad Sci USA. 2005;102(7).
- **Kanaparthy R, Kanaparthy A.** The changing face of dentistry: nanotechnology. Int J Nanomedicine. 2011; 6(9).
- **KE Drexler**. Nanosystems: Molecular Machinery Manufacturing and Computation. New York:John Wiley and Sons. 2006;34(6).
- **Koch K, Brave D**. A new day has dawned: the increased use of bioceramics in endodontics. Dentaltown. 2009;10(4).
- **Kong L, Peng Z, Li SD, Bartold P.** Nanotechnology and its role in the management of periodontal diseases Periodontol. 2006;40(8).
- **Koga T, Okahashi N, Takahashi I, Kanamoto T, Asakawa H, Iwaki M.** Surface hydrophobicity, adherence, and aggregation of cell surface protein antigen mutants of Streptococcus mutans Serotype c. Infect Immun. 1990;58(2).

- **Kubik T, Bogunia-Kubik K, Sugisaka M.** Curr Pharm Biotechnol Nanotechnology on duty in medical applications.2005; 6(1).
- **Kt S, Kmk M, N B, Jimson S, R S.** Dental caries vaccine – a possible option? J Clin Diagn Res. 2013;7(6).
- **Le Guéhennec L, Soueidan A, Layrolle P, Amouriq Y**. Surface treatments of titanium dental implants for rapid osseointegration Dent MaterJ. 2007; 23(7)
- **Magalhães A, Santos L, Lopes L, et al**. Nanosilver application in dental cements. ISRN Nanotechnol. 2012;12(4).
- **Mansoori G**. Advances in atomic and molecular nanotechnology. Principles of Nanotechnology. 1st ed. Singapore: World Scientific Publishing.2005;45(7).
- **Mitra S, Wu D, Holmes B**. J Am Dent Assoc. An application of nanotechnology in advanced dental materials. 2003;134(10).
- **Moshaverinia A, Ansari S, Moshaverinia M, et al**. Effects of incorporation of hydroxyapatite and fluoroapatite nanobioceramics into conventional glass ionomer cements (GIC). Acta BiomaterJ. 2008; 4(2).
- **Mupparapu M.** New nanophosphor scintillators for solid-state digital dental imagers. Dentomaxillofac Radiol. 2006; 35(6).
- **N Gordon, U Sagman, P Borm.** The Potential Risks of Nanomaterials: A Review Carried Out Canadian Nano Business Alliance. Toronto, Canada. Nanotechnology Research and Development in Ca. 2008;34(6).
- **Nagpal A , Kaur J, Sharma S, Bansal A, Sachdev P**. Nanotechnology-the Era Of Molecular Dentistry. Indian J Dent Sci.2011;3(6).

- **Nakashima S, Yoshie M, Sano H, Bahar A.** Effect of a test dentifrice containing nano-sized calcium carbonate on remineralization of enamel lesions in vitro. J Oral Sci. 2009; 51(1). 'Nanodentistry': Exploring the beauty of miniature. J Clin Exp Dent. 2012;18(1).
- **Ozbay E**. İşe yarar nanoteknoloji. Seminer, Bilkent Üniv. Nanoteknoloji Araştırma Merkezi. 2006;23(7).
- **Paciotti G, Myer L, Weinreich D, Goia D, Pavel N, McLaughlin R,** et al. Colloidal gold: A novel nanoparticle vector for tumor directed drug delivery. Drug Deliv. 2004;11(8).
- **Papadogiannis DY, Lakes RS, Papadogiannis Y, Palaghias G, Helvatjoglu-Antoniades M.** The effect of temperature on the viscoelastic properties of nano-hybrid composites. Dent Mater. 2008 ; 24(2).
- **Park J, Kim H, Kim Y, An C, Hanawa T**. Enhanced osteoconductivity of micro-structured titanium implants (XiVE S CELLplus) by addition of surface calcium chemistry: a histomorphometric study in the rabbit femur. Clin Oral Implants Res.2009;20(2).
- **Patil M, Mehta DS, Guvva S** Future impact of nanotechnology on medicine and dentistry.J Indian Soc Periodontol. 2008; 12(2).
- **Ravindran R**. Nano technology in cancer diagnosis and treatment: An overview. Oral and Maxillofac Pathol J. 2011;2.
- **Roberson MT, Heymann O, Swift E** . Biomaterials Sturdevant's Art and Science of Operative Dentistry. 5th ed. Mosby Co. 2006;45(9).
- **Robert A,Freitas J**. Nanodentistry. Cover Story. J Indian Prosthodont Soc. 2010 ;131(4).

- **Salata O**. Applications of nanoparticles in biology and medicine. J Nanobiotechnology. 2004;2:3(9).
- **Su L, Yu F, Li Z, Zeng C, Xu Q, Fan M.** Intranasal co-delivery of IL-6 gene enhances the immunogenicity of anti-caries DNA vaccine. Acta Pharmacol Sin. 2014;35(5).
- **Suh J, Jeung O, Choi B, Park J.** Effects of a novel calcium titanate coating on the osseointegration of blasted endosseous implants in rabbit tibiae. Clin Oral Impl Res. 2007;18(3).
- **Türkün L, Uzer , Çelik E**. Antibakteriyal adeziv ile uygulanan kompomer ve nanofil kompozit restorasyonların bir yıllık klinik performansı Gazi Üniv Diş Hek Fak Derg. 2007;24.
- **Talwar G, Diwan M, Razvi F, Malhotra R.** The impact of new technologies on vaccines. Natl Med J India. 1999;12(6).
- **Wang J, Liu J, Jiang J, Wang W, Bai G, Guan X.** Study on gene vaccine pcDNA3-PAc against dental caries by intranasal immunization in rabbits. Shanghai Kou Qiang Yi Xue. 2014;23(2).
- **Yesil ZD, Alapati S, Johnston W, Seghi RR.** Evaluation of the wear resistance of new nanocomposite resin restorative materials. J Prosthet Dent. 2008; 99(6).
- **Yunshin S, Park H, Kim K**. Biologic evaluation of Chitosan Nanofiber Membrane for guided bone regeneration. J Periodontol. 2005;76(4).
- **Zoufan K, Jiang J, Komabayashi T**. Cytotoxicity evaluation of Gutta Flow and Endo Sequence BC sealers. Oral Surg Oral Med Oral Pathol Oral Radiol. Endodontol. 2011;112(5).

- **Khang D, Lu J, Yao C, Haberstroh K, Webster T**. The role of nanometer and sub-micron surface features on vascular and bone cell adhesion on titanium. Biomaterials. 2008;29:970(9).
- **Webster T, Ejiofor J**. Increased osteoblast adhesion on nanophase metals: Ti, Ti6A14V, and CoCrMO. Biomaterials. 2004;25(5).
- **Yang Y, Kim K, Ong J**. A review on calcium phosphate coatings produced using a sputtering process-An alternative to plasma spraying. Biomaterials. 2005;26(9).
- **Yamashita Y, Bowen W, Burne R, Kuramitsu H.** Role of the Streptococcus mutans gtf genes in caries induction in the specific-pathogen-free rat model. Infect Immun. 1993;61(9).
- **Barrere F, Layrolle P, van Blitterswijk C, de Groot K**. Biomimetic calcium phosphate coatings on Ti6A14V: A crystal growth study of ostacalcium phosphate and inhibition by Mg2+ and HCO3- Bone. 1999;25(4).
- **Tomsia A, Launey M, Lee J, Mankani M, Wegst Ulrike G, Saiz E**. Nanotechnology approaches for Better Dental Implants. Int Oral Maxillofac Implants. 2011;26(9).