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Nanotechnology in Dentistry

A project submitted to
The College of Dentistry, University of Baghdad, Department of Pedodontics and Prevention in Partial Fulfilment for the Bachelor of Dental Surgery

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Certification of the Supervisor

I certify that this project entitled " **Nanotechnology in Dentistry**” was prepared by the fifth-year student **Laith Haider Mohammed Saied** under my supervision at the College of Dentistry/University of Baghdad in partial fulfilment of the graduation requirements for the Bachelor Degree in Dentistry.

Assist. Lec. Noor Mohammed Hassan

Date 25/5/2022

Dedication

At first, I would like to dedicate this project to God for the guidance, strength, power of mind, protection and skills.

To my beloved parents, who gave the little they had to ensure I would have the opportunity of education, they have been my source of inspiration and strength when I thought of giving up. They continually provide their moral, spiritual, emotional, and financial support.

To my brothers, sisters, relatives, friends, and colleagues who shared their words of advice and encouragement.

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First of all, I thank “Allah” almighty for granting me the will and strength to accomplish this project, and I pray that his blessings upon me may continue throughout my life.

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List of Abbreviations

Abbreviation	Description
Al_2O_3	Aluminium Oxide
API	Active Pharmaceutical Ingredients
Ca	Calcium
CVD	Chemical Vapor Deposition
DNA	Deoxyribonucleic Acid
FDA	Food and Drug Administration
GP	Gutta Percha
HA	Hydroxyapatite
HMP	Hexametaphosphate
nACP	Nano-amorphous Calcium Phosphate
nAg	Silver Nanoparticles
nHA	Nano-hydroxyapatite
nm	Nanometer
P	Phosphorus
PAc	Surface Protein Antigen
PFM	Porcelain Fused to Metal
PMMA	Poly-methylmethacrylate
RNA	Ribonucleic Acid
SEM	Scanning Electron Microscopy
TiO_2	Titanium Dioxide
TMP	Trimetaphosphate
TP	Triphosphate
ZnO	Zinc Oxide

Introduction

The term nanotechnology is derived from the Greek word nanos, meaning dwarf 'little old man'. It is about manipulating matter on atomic and molecular levels; just as robots assemble cars from a set of predefined parts, nano-robots will assemble things from atomic and molecular building blocks. Nanotechnology enables almost complete control of the structure of matter at nanoscale dimensions. It involves the research and technological developments, that are used to create structures, devices, and systems with novel properties and functions as a result of their small size; with the ability to control or manipulate matter on the atomic scale **(Mansooni, 2005; Kong et al., 2006).**

This technology has revolutionized medical and dental fields by improving mechanical and physical properties of materials, and helping to introduce new diagnostic modalities and nano-delivery systems; giving emergence to other fields such as nanomedicine and nanodentistry **(Kanaparthy and Kanaparthy, 2011)**.

Studying dental structures and surfaces from a nanoscale perspective may lead to better understanding about the structure, function and physiological relationship of dental surfaces. It encourages the concept of minimally invasive dentistry, creating a more dentist friendly atmosphere. However patient awareness and education is important to make them understand the developments in this field and treatment options **(Mantri and Mantri, 2013)**.

Aim of the Project

This project focuses on the developments in the field of nanomaterials in dentistry; in terms of clinical applications of nanotechnology in various dental fields; with a general overview of the classification and fabrication techniques of nanostructured materials.

Review of Literature

1. Nanotechnology

Nanotechnology is the art and science of material engineering in a scale of less than 100 nm, roughly the size of 2 or 3 atoms. A nanometer is 10^{-9} or one billionth of a meter **(Anisa *et al.*, 2003)**.

Nanomaterial is a material with at least one dimension in the nanoscale range **(Trotta and Mele, 2019)**.

Nanoparticle is an object where its all dimensions are in the nanoscale range **(Trotta and Mele, 2019)**.

Nanostructured materials are materials that have structural elements, molecules, crystallites, or clusters with dimensions in the nanoscale range **(Moriarty, 2001)**.

Nanocomposites are multicomponent materials with multiple different phase domains in which at least one of the phases has at least on dimension in the nanoscale range **(Chen *et al.*, 2008)**.

Nanotechnology has applications in many fields like **(Kanaparthy and Kanaparthy, 2011):**

- Medicine (diagnostics, drug delivery, and tissue engineering).
- Chemistry (catalysis and filtration).
- Energy (reduction of energy consumption).
- Heavy industry (consumer goods and foods).

2. Nanomedicine

Nanomedicine is the science and technology of diagnosing, treating and preventing diseases, in addition to preserving and improving overall human health, using nanoscale structured materials **(Kubik *et al.*, 2005)**.

Nanotechnologies in nanomedicine can be devided in three potent molecular technologies **(Kanaparthy and Kanaparthy, 2011)**:

- Nanoscale materials and devices to be applied in advanced diagnostics and biosensors, targeted drug delivery, and smart drugs
- Molecular medicine through genomics, proteomics, artificial biobotics (microbial robots)
- Molecular machines and medical nanorobots aid in immediate microbial diagnosis and treatment, and enhancement of physiological functions.

Nanorobots are machines with a diameter of about 0.5-3 microns and made of components sized from 1-100 nanometers, which would respond to definite programs enabling clinicians to execute accurate procedures at the cellular and molecular level **(Kanaparthy and Kanaparthy, 2011)**.

Nanosensors are chemical or mechanical sensors that have used in 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)**.

3. Nanomaterials

Nanomaterials are materials with at least one dimension in the nanoscale range of 1-100 nanometers **(Trotta and Mele, 2019)**. They may include atoms, clusters, grains, fibers, films, nanoholes and composites from these combinations They can be identified by variable classification systems into different material types, shapes, and dimensions (**Nagpal *et al.*, 2011)**.

3.1 Material-Based Classification of Nanomaterials

A. Organic Nanomaterials:

These include nanomaterials made mostly from organic matter. The utilization of noncovalent (weak) interactions for the self-assembly and design of molecules helps to transform the organic nanomaterials into desired structures such as dendrimers, micelles, liposomes and polymer naoparticles, which are biodegradable and non-toxic. A number of such particles, including micelles and liposomes, have a hollow core, termed as nanocapsules that have the sensitivity towards thermal and electro-magnetic radiations, including heat and light **(Harb *et al.*, 2018)**.

Such specific features render them a perfect option for drug delivery. Due to their stability, capacity, and delivery systems, the absorbed drug system determines the respective type of uses and efficacy, thus organic nanomaterials have widespread usage in biomedicine for targeted drug delivery **(Andre *et al.*, 2018; Broza *et al.*, 2018; Oveisi *et al.*, 2018; Palazzolo *et al.*, 2018; Yu *et al.*, 2018)**.

- **Polymeric nanomaterials**

Organic-based nanomaterials, which basically have nano-sphere or nano-capsule shapes and can be easily functionalized. Nanospheres are matrix particles with overall solid mass and other molecules are absorbed at the external surface of the spherical surfaces. Nanocapsules are solid masses thoroughly encapsulated into the particle **(Zhu *et al.*, 2018; Makvandi *et al.*, 2020)**.

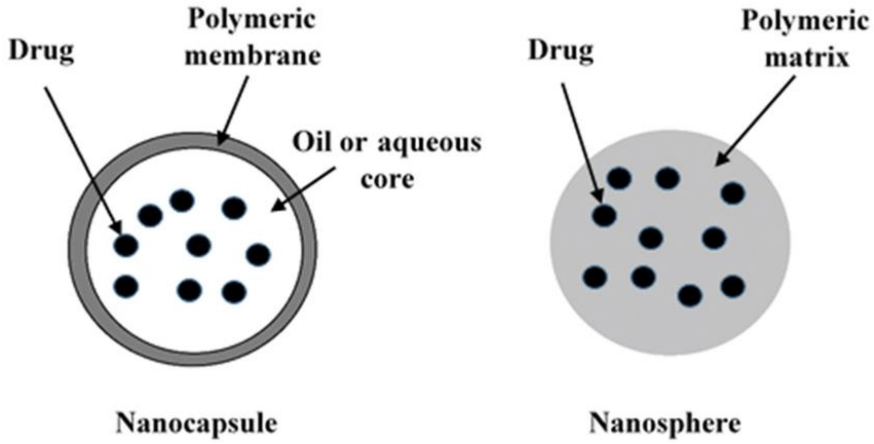

Figure 1: Nanospheres and Nanocapsules. They are small vesicles used to transport drugs. Nanospheres are typically solid polymers with drugs embedded in the polymer matrix. Nanocapsules are a shell with an inner space loaded with the drug of interest. Both systems are useful for controlling the release of a drug and protecting it from surrounding environment **(Khalil *et al.*, 2017)**.

- **Lipid-based nanomaterials**

Similar to polymeric nano-materials, they possess a solid core, which is made of a lipid and also a matrix containing lipophilic molecules while the emulsifiers or the surfactants stabilize the outer core. They have varied applications in medicine carriers, delivery, and RNA release for treating cancer **(Palazzolo *et al.*, 2018)**.

B. Inorganic Nanomaterials:

These nanomaterials include metal and metal oxide nanoparticles and nanostructured materials. These nanomaterials can be synthesized into metals such as gold or silver nanoparticles, metal oxides such as titanium dioxide (TiO_2), and zinc oxide (ZnO) nanoparticles, and semiconductors such as silicon and ceramics.

- **Metal nanomaterials**

They enjoy specific opto-electrical characteristics, for example nanomaterials of noble metals such as silver, gold, and copper. These metal nanomaterials are highly valued as cutting-edge advanced materials **(Chen *et al.*, 2018; Cheng *et al.*, 2018; Roach *et al.*, 2019)**.

- **Metal oxide nanomaterials**

Metal oxide nanomaterials are synthesized with high reactivity and effectiveness. Some examples are zinc oxide (ZnO), aluminium oxide (Al_2O_3), titanium oxide (TiO_2) **(Zhang *et al.*, 2018; Pires *et al.*, 2020)**.

- **Ceramic nanomaterials**

Inorganic non-metallic solids, which are used in catalysis, photo-degradation of dyes, and imaging applications **(Foster *et al.*, 2018; Jung *et al.*, 2018)**.

- **Semiconductor nanomaterials**

Semi-conductor materials have features between metals and non-metals. They are highly prominent materials in photo-catalysis, photo-optics, and electronic devices **(Singh *et al.*, 2018)**.

C. Carbon based Nanomaterials:

Carbon based nano-materials can be grouped into fullerenes, graphene, carbon nanotubes, carbon nanofibers, carbon black (figure 2) **(Cai *et al.*, 2019)**. Laser ablation, arc discharge, and chemical vapor deposition (CVD) are the important production methods for these carbon-based materials fabrication (except carbon black) **(Kumar, 2016)**.

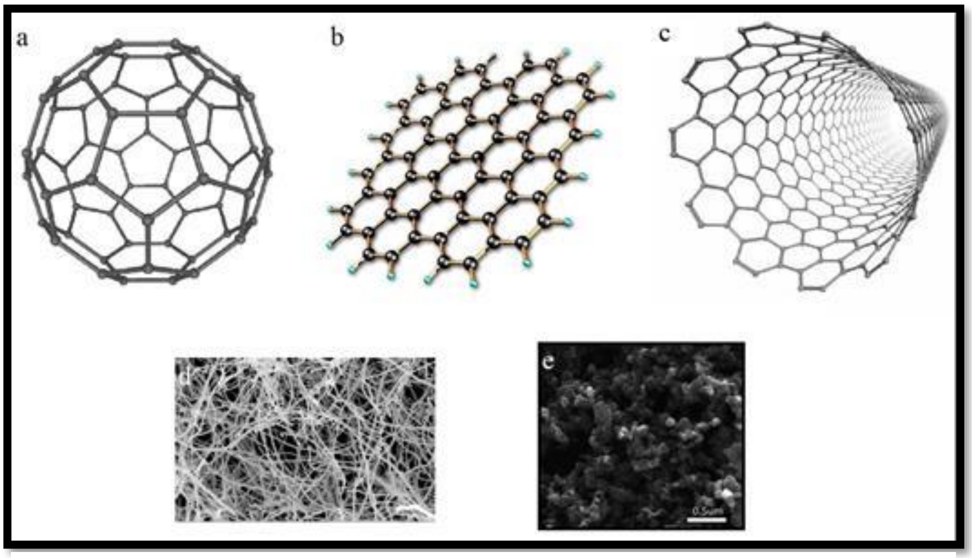

Figure 2: Carbon-based nanoparticles (a) fullerenes, (b) graphene, (c) carbon nanotubes, (d) carbon nanofibers and (e) carbon black **(Ealias and Saravanakumar 2017)**.

D. Composite Based Nanomaterials:

Composite nanomaterials are multi-phase nanoparticles and nanostructured materials with one phase on the nanoscale dimension that can either combine nanoparticles with other nanoparticles or nanoparticles combined with larger or with bulk-type materials (e.g., hybrid nanofibers) or more complicated structures, such as a metal organic framework. The composites may be any combinations of carbon-based, metal-based, or organic-based nanomaterials with any form of metal, ceramic, or polymer bulk materials **(Jeevanandam *et al.*, 2018)**.

3.2 Classification According to Dimension

Nanomaterials can be classified into different types including: one, two, and three-dimensional nanostructures; that can be utilized in medical and dental fields for diagnosing early stages of disease development. Those occurring in one-dimension are termed as sheets; the two-dimensional ones are nano-tubes and nano-wires, and quantum dots are used as three-dimensional nanostructures **(Arora and Kapoor, 2014; Okada and Matsumoto, 2015; Rasheed *et al.*, 2016)**.

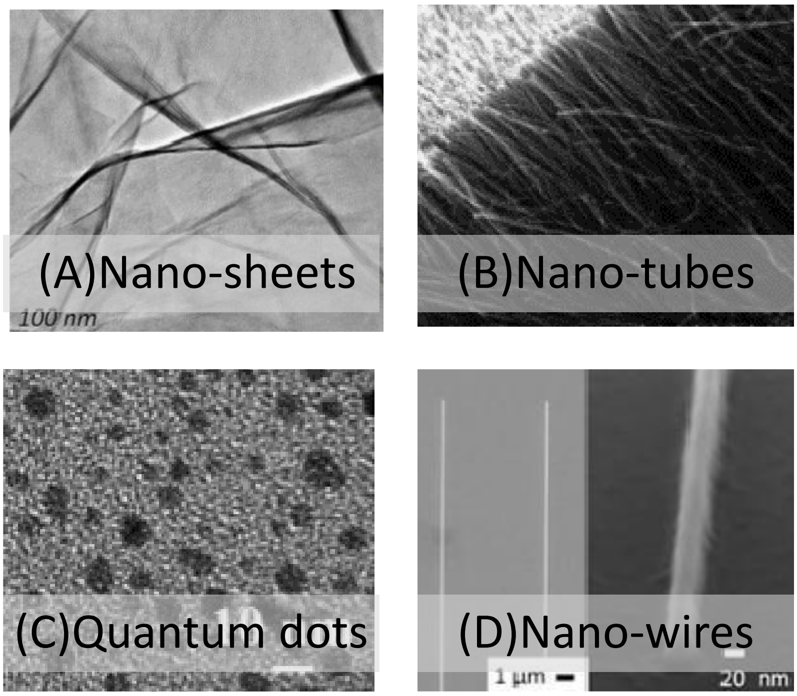

Figure 3: Highly magnified nanostructures (A) nano-sheets, (B) nano-tubes, (C) quantum dots, (D) nano-wires **(Jurczyk, 2013; Zhu *et al.*, 2014; Li, 2015; Roy *et al.*, 2015;)**.

3.3 Classification According to Origin

- **Natural Nanomaterials:**

Materials produced in nature either by biological species or through anthropogenic activities. The production of artificial surfaces with exclusive micro and nanoscale templates and properties for technological applications are readily available from natural sources. Earth is comprised of nanomaterials that are naturally formed and are present in the earth's spheres such as the atmosphere, which includes the whole of troposphere; the hydrosphere, which includes oceans, lakes and rivers; the lithosphere, which is comprised of rocks, soils, or lava; and the biosphere,which covers micro-organisms and humans **(Hochella *et al.*, 2015; Sharma *et al.*, 2015)**.

- **Synthetic (Engineered) Nanomaterials:**

Materials produced by mechanical grinding, engine exhaust and smoke, or are synthesized by physical, chemical, biological or hybrid methods. The major challenge among engineered nanomaterials is whether existing knowledge is enough to forecast their behaviour or if they exhibit a distinct environment related behaviour, different from natural nanomaterials **(Wagner *et al.*, 2006)**.

4. Properties of Nanomaterials

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)**.

Introducing nano-sized particles allows for an interaction on a molecular level, by that increasing the overall efficacy and affinity of atoms that are the building blocks in biological tissue in comparison to biological molecules interacting with micro or macro sized particles, thus offering unique properties **(Li *et al.*, 2008)**.

The high surface to core ratio, is a unique physical characteristic in nanoparticles, meaning that there are more atoms on the surface of the nanoparticle than deep within its core. This is particularly useful since surface atoms have unbound surfaces in comparison to core atoms, with the potential for creating new and strong bonds, and hence, nanoparticles are more reactive and can be easily arranged in a number of packing configurations due to their high surface to core ratio, making them easily manipulated and utilised in various applications in comparison to micro and macro particles which have more core than surface atoms **(Binns, 2010)**.

The greater thermal vibrations expressed by surface atoms in comparison to core atoms contribute to the lower melting temperature in nanomaterials compared to the same material in bulk. This might be of particular importance when using nanomaterials to construct porcelain fused to metal (PFM) crowns, cast post and cores, or denture frameworks **(Al Kahtani, 2018)**.

5. Nanodentistry

Nanodentistry is defined as the science and technology of diagnosing, treating and preventing oral and dental diseases, relieving pain, preserving and improving dental health using nanostructured material. There are varieties of new dental products available, ranging from implants to oral hygiene products that rely on nanoscale properties **(Sharma et al., 2010)**.

The fabrication techniques of these structures can be divided into 2 approaches; "top-down" and "bottom up".

- **The Top-Down Approach**

This approach deals with the enhancement of existing materials, where the existing structures are contracted and miniaturized into the nano-range with their molecules consecutively rearranged to achieve the desired properties **(Silva, 2004; Cyril and Lung, 2014)**.

- **The Bottoms-Up Approach**

A technique that deals with the creation and development of new 'intelligent' materials or devices, wherein various processes are utilized to induce nanostructures to self-assemble at a desired scale and then organize into higher macroscale structures **(Silva, 2004; Cyril and Lung, 2014)**.

5.1 Nanodentistry as Top-Down Approach

- **Nanocomposites:**

Nanoproducts corporation has successfully manufactured non-agglomerated discrete nanoparticles that are homogeneously distributed in resins or coatings to produce nanocomposites **(Jhaver, 2005)**.

The nanofiller used includes an aluminosilicate powder that offer some advantages such as **(Kanaparthy and Kanaparthy, 2011; Nagpal *et al.*, 2011; Chandki *et al.*, 2012)**:

- Superior hardness
- Superior flexural strength, modulus of elasticity, and translucency

- 50% reduction in polymerization shrinkage
- Excellent handling properties

- **Nanosolutions:**

Nanosolutions manufactured using soluble nanoparticles when used in bonding agents lead to a homogenous and well-mixed adhesive consistently **(Patil *et al.*, 2008)**.

They have high bond strength, long shelf-life, good marginal seal, fluoride release, and good stress absorption **(Jhaver, 2005; Jena and Shashirekha, 2015)**.

- **Impression materials:**

Nanofillers integrated into vinylpolysiloxanes resulted in impression materials with better flow, improved hydrophilic properties, and enhanced reproduction of surface details **(Jhaveri and Balaji, 2005)**.

- **Nanoencapsulation:**

The process of encapsulating substances with various coating materials at the nanoscale range. This technique is primarily used within the pharmaceutical, food and cosmetic industries **(Jafari, 2017)**.

The main reason nanoencapsulation is so widely used is its efficiency in protecting the core material and ultimately releasing the active pharmaceutical ingredients (API) when required. Some of the most common applications of nanoencapsulation therefore can be found in **(Jafari, 2017)**:-

- Targeted drug delivery systems that will only release drug upon its arrival at the correct location within the body.
- Timed release drug delivery systems, in which slow degradation of the external phase allows for controlled release in the body. One example of this type of drug delivery system can be found in nasal drug delivery devices.
- Increased shelf life and stability of over the counter pharmaceutical products, such as vitamins.

- **Nanoneedles:**

Suture needles incorporating nano-sized stainless-steel crystals have been developed; furthermore, nanotweezers are also under development which will make cell-surgery possible in the near future **(Kanaparthy and Kanaparthy, 2011; Chandki *et al.,* 2012)**.

- **Bone replacement materials:**

When the area of a bone defect is filled with hydroxyapatite (HA), the cycle of bone resorption by osteoclasts and bone formation by osteoblasts resumes at the bone surface, leading to the formation of new autologous bone. The highly porous and nanometer-sized granules increase the activity of osteoblasts, resulting in more rapid proliferation, adhesion, and differentiation of bone cells **(Karageorgiou and Kaplan, 2005)**.

5.2 Nanodentistry as Bottom-Up Approach

- **Local Anaesthesia:**

Nanorobotic local anaesthetics are composed of a colloidal solution of activated nanosized local anaesthetic molecules. When applied to the gingival or the oral mucosa and signalled, the anaesthetic travels via the epithelial and connective tissues of the gingiva to reach the pulp, thus providing selective anaesthesia, which is under the control of the clinician. These ambulatory nano-active solutions are directed to the target site by chemical and temperature gradients. Upon reaching the pulp and establishing control over the nerve-impulse traffic, these nanorobots may be commanded to shut all neurosensory sensations to a particular tooth or multiple teeth as desired by the dentist. On completion of the procedure, the nanorobots may again be signalled to restore the sensation and, following this, they are aspirated. 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 **(Freitas 2000)**.

- **Hypersensitivity Cure:**

Dentin hypersensitivity may be caused by changes in pressure transmitted hydrodynamically to the pulp. This is based on the fact that hypersensitive teeth have 8 times higher surface density of dentinal tubules and tubules with diameters twice as large than non-sensitive teeth.

Reconstructive dental nanorobots are able to selectively and precisely block dentinal tubules, offering a quick and permanent cure. These nanorobots travel toward the dental pulp via the dentinal tubules. Desensitizing toothpaste containing 15% hydroxyapatite nanoparticles has been found to be effective in reduction of dentin hypersensitivity clinically even after single application for a period of 4 weeks (**Jena and Shashirekha, 2015)**.

- **Nanorobotic Dentifrice (Dentifrobots):**

Dentifrobots are nanorobots incorporated into dentifrices and mouthwashes that help to clean organic residues by moving throughout the gingival tissues at a speed of approximately 10 microns/second, continuously preventing the accumulation of calculus. They can also be deactivated when accidentally swallowed by the patient **(Saravana and Vijayalakshmi, 2006)**. Dentifrobots can selectively identify and destroy pathogenic bacterial species in plaque biofilms and prevent halitosis **(Kong *et al.*, 2006)**.

- **Orthodontic Treatment**

Orthodontic nanorobots could directly manipulate the periodontal tissues, allowing rapid and painless tooth straightening, rotating, and vertical repositioning within minutes to hours **(Shellart and Oesterle, 1999)**.

- **Dental durability and cosmetics**

Tooth durability and appearance may be improved by replacing upper enamel layers with pure sapphire and diamond which can be made more fracture resistant as nanostructured composites, possibly including embedded carbon nanotubes **(Yunshin et al., 2005)**.

- **Diagnosis and Treatment of Oral 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, 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 *et al.*, 2008)**.

Dendritic polymeric nano-devices can detect cancer cells, identify cancer signature, and provide targeted delivery of anti-cancer therapeutics **(Ravindran, 2011)**.

Nanotech based cancer therapeutics and diagnosis 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 and Huilgol, 2006)**.

The possibility of tackling "pain the bitter side of cancer therapy," through nanotechnology would be considered one of the biggest breaks through achievement **(Kam *et al.*, 2005)**.

6. Applications of Nanotechnology in Dentistry

The applications of nanotechnology in dentistry was expanded to include: diagnostic, preventive, restorative, regenerative, reconstructive, and rehabilitative purposes **(Bhavikatti *et al.*, 2014)**.

Nevertheless, there are disadvantages in using this technology in dental field; which are the high costs of synthesizing nanomaterials and the lack of knowledge regarding their toxicity **(Arruda *et al.*, 2017)**.

6.1 Dental Diagnostics

In an attempt to improve upon medical diagnostics, the concept of nano-biosensing was introduced. A biosensor is "an analytical device which incorporates a biologically 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, 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 1) **(Touhami, 2014)**.

Replacing micro-sized particles with nano-sized ones transforms the biosensor into a nanobiosensor, with the advantage of rapidly identifying targeted biological tissues at an ultra-low molecular level. Its high sensitivity is particularly useful in cases of cancer diagnosis as nanobiosensors are able to detect cancer cell molecules at very early stages and in very low concentrations **(Foster, 2005; Touhami, 2014)**.

Table 1 Detection principles in nano-biosensors (Touhami, 2014)

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 (eg: 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.

6.2 Preventive Nanodentistry

A nano-toothbrush was developed by incorporating nanogold or nanosilver colloidal particles between toothbrush bristles. 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 **(Raval *et al.*, 2016).**

Oral hygiene products such as toothpastes and mouthwash solutions were nano-modified. Nano-calcium fluoride, for instance, was added to mouthwash products to reduce caries activity, reduce dentine permeability, and increase labile fluoride concentration in oral fluid **(Sun and Chow, 2008)**.

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-additives **(Danelon *et al.*, 2015)**. Toothpastes containing nano-hydroxyapatite crystals (nHA) significantly increased microhardness values in human enamel following an erosive challenge, in comparison to the same toothpaste without (nHA) **(Ebadifar *et al.*, 2017)**.

- Caries Vaccine

Several attempts 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 **(Su *et al.*, 2014; Wang *et al.*, 2014)**.

Most of the anticaries vaccines work by preventing bacterial accumulation either 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 Streptococcus mutans to tooth surfaces **(Jimson *et al.*, 2013)**.

Furthermore, the surface charge of the delivery vehicle could be potential hydrogen (pH) dependent to enable the release of the vaccine in a pH-dependent manner **(Chen *et al.*, 2013)**.

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)**.

6.3 Therapeutic Nanodentisrty

There are new treatment opportunities including;

- Nano-solutions, which can be used in bonding agents by producing unique nanoparticles. This predominantly ensures a homogenous adhesive mixture **(Chandki *et al.*, 2012)**.

- Hypersensitivity cure; dental hypersensitivity can be produced by altered pressure transmitted hydro-dynamically to the pulp. Dental nano-robots can selectively occlude the dentinal tubules within minutes, by delivering biological materials; thus, giving a rapid and permanent cure **(Jurczyk, 2013)**.
- Complete replacement of the whole tooth, comprising mineral and cellular components by combining nanotechnology with genetic and tissue engineering **(Shetty *et al.*, 2013)**.
- Nano-fillers having very small particle sizes can lower the polymerization shrinkage, thermal expansion, and improve hardness and wear resistance of composite restorations **(Bhavikatti *et al.*, 2014)**.
- Coating titanium dental implant surface with nano-hydroxyapatite will provide a better implant performance, improve osseointegration and physiological implant functions **(Ogle and Byles, 2014)**.

6.4 Prosthodontics

Incorporating 0.4% titanium dioxide (TiO_2) nanoparticles into a three-dimensional printed poly-methylmethacrylate (PMMA) denture base in an attempt to improve its antibacterial characteristics and mechanical properties **(Totu *et al.*, 2017)**. According to measurements using Scanning Electron Microscopy (SEM), 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 **(Ahmed and Ebrahim, 2014)** .

Researchers also investigated the tribological behaviour of a 7% nano-zirconium oxide modified heat cured PMMA. The addition of 7% zirconium oxide nanoparticles to PMMA denture base has 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 **(Gad *et al.*, 2016)**.

Solutions of chlorhexidine mixed with sodium triphosphate (TP), trimetaphosphate (TMP) or hexametaphosphate (HMP) nanoparticles were used to investigate the antifungal properties of a chlorhexidine coating in order to inhibit fungal infestations in dental silicones commonly used as denture soft liners and obturators **(Garner *et al.*, 2015)**. The nano-modified chlorhexidine coatings have released soluble chlorhexidine following immersion artificial saliva, with a slow and sustained release by the chlorhexidine-HMP coating, and a rapid, more concentrated release by the chlorhexidine-TP and chlorhexidine-TMP coatings. The chlorhexidine-HMP coating proved to be the most effective in its antifungal activity by inhibiting the metabolic activity of Candida albicans. These coatings might potentially become clinically essential for insuring longevity of the dental prosthesis and maintenance of oral health at a much lower cost **(Sadat-Shojai *et al.*, 2010)**.

6.5 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 osseo-conductivity **(Utneja *et al.*, 2015)**.

Studies were conducted to improve upon gutta percha (GP), by incorporating nano-diamond particles. Digital radiography and micro-computed tomography imaging revealed that obturation following a conventional technique, using nanodiamond impregnated gutta percha, demonstrated superior chemical properties, biocompatibility, and superior mechanical properties. Additionally, high quality adaptation to the canal walls and minimum void formation was reported, which demonstrates the great potential for the use of nano-GP as an improved endodontic filling **(Lee *et al.*, 2015)**.

6.6 Conservative and Aesthetic Dentistry

The new development of a rechargeable nano-amorphous calcium phosphate (nACP) filled composite resin has been reported. The nanoparticles were able to not only improve composites' remineralising properties, it also maintained the same level of calcium (Ca) and phosphorus (P) release through recharge and release **(Xie *et al.*, 2016)**. 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 **(Wu *et al.*, 2015)**. Researchers has reported a possibility for integrating nACP in other dental materials such as luting cements and bonding agents, showing a significant remineralising ability in a dental bonding agent with nACP through the recharge and release of (Ca) and (P) ions for up to 3 weeks, without altering the bonding strength to dentine **(Zhang *et al.*, 2015)**.

An additional attempt to enable restorative materials to actively prevent the initiation and progression of secondary caries, was through the application of a nanocomposite coating consisting of lactose-modified chitosan (Chitlac) with silver nanoparticles (nAg). Nanoparticles were evenly dispersed and were able to significantly reduce biofilm formation on the restoration surface by 80% after 48 hours of application **(Ionescu *et al.*, 2015)**.

Tooth whitening agents were additionally nano-modified to increase their whitening efficiency and minimise their harmful side effects. Calcium peroxide nanoparticles, for instance, were able to penetrate deeper into the tooth structure through micro and nano cracks, leading to a longer surface contact and therefore an increase in the effectiveness of the whitening agent as its deeper penetration into the tooth structure allows for a longer action time and ultimately a significant improvement in aesthetics when compared to a whitening agent with micro or macro particles **(Velkoborsky, 2010)**.

6.7 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 site **(Sharma *et al.*, 2016)**. 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 100nm in size **(Pradeepkumar *et al.*, 2012)**.

Combining a light curable, methacrylate resin matrix, with nACP as a bone grafting agent giving the ability to strongly adhere to wet bone, and in recrystallizing nACP to hydroxyapatite in a matter of minutes **(Pradeepkumar *et al.*, 2012)**.

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 10nm and 100nm in size **(Tomsia *et al.*, 2011)**. Surface coatings such as hydroxyapatite, gold, silver, and titanium oxide nanoparticles have the ability to improve the adhesion of the fibrin clot which serves as a bridge for osteogenic cells and the overall osseointegration of implants. Additionally, the presence of mechanical nano-features such as nano-grooves or nano pillars have been proved effective as well, with particular emphasis on the distribution and order of such features on the implant surface **(Tomsia *et al.*, 2011; Cheng *et al.*, 2012; Besinis *et al.*, 2017)**.

7. Implications of Nanotechnology

- Ethical Implications

Following the research and development phase of any dental or medical nanoproduct, it undergoes extensive clinical testing to investigate its mechanical, toxicological, and immunological properties. Therefore, test subjects must understand the level of risk associated with the exposure to novel materials and safety monitoring boards must be appointed in every clinical trial, to carefully track and record any adverse side effects early on, and ensure the safety and wellbeing of test subjects **(Resnik and Tinkle, 2007).**

The unpredictability of nanomaterials creates an ethical dilemma for dentists when faced with a wide range of materials to choose from, some having very long track records supporting their clinical use such as hybrid or micro-filled composite resins; while others such as the nano-filled composite resins are supported by short term clinical studies **(Khushf, 2006; Brey, 2012; Hester *et al.*, 2015).**

- Nanotechnology and Society

Since society is the consumer, funding party, and policy and decision maker, the public's attitude towards nanotechnology plays a fundamental role in its success and failure **(Gupta *et al.*, 2015)**. Although nanotechnology is integrated in fields that directly affect the public such as in energy supply, health care and diagnostics, telecommunications, and pollution control, this has created fear as these advancements might cost the public thousands of jobs to accommodate for a more machinery reliant system. This calls for an immediate engagement with the public to address concerns and spread awareness on current and future applications of nanotechnology to gain and maintain public support **(Kurzweil, 2005)**.

- **Health Implications**

The effects of nanomaterials are significantly size dependant, meaning that nontoxic 100 nm sized particles could dramatically transform into toxic elements as their size reduce to 1 nm for example and vice versa. A non-toxic nano material could disintegrate or aggregate forming toxic nanoparticles as well. This unpredictability of how our bodies react to nanomaterials not only relies on size but in how our immune system react to the nanoproduct, as studies have shown that nanoparticles could react differently in a cell culture than in an organism.

Studies have shown that nanoparticles can be inhaled and can cross cell membranes and reach the liver, lymph nodes, spleen, and bone marrow **(Resnik and Tinkle, 2007)**. Although claims of nano-toxic effects following inhalation have been clearly expressed, the literature lacks solid scientific evidence confirming or denying these claims **(Stone *et al.,* 2010)**. Therefore, governmental bodies must investigate the long-term effects of nanomaterials and report any adverse side effects to legislative and regulatory bodies such as the food and drug administration (FDA).

Conclusion

Nanotechnology is a relatively novel field, which involves manipulation of matter at the molecular level, including individual molecules and the interactions among them. It focuses on achieving positional control with a high degree of specificity, thereby achieving the desired physical and chemical properties. There has been an interest in working out the property of matter at this dimension, thus making nanotechnology one of the most promising and influential areas of scientific research.

The applications of nanotechnology in various fields of dentistry have been reviewed in this project. These applications will pave the way for further research in device and drug development, thus commencing an era of unprecedented advances in dental diagnostics and therapeutics.

Though the science of nanotechnology may appear as fiction, the future holds strong promise for utilizing and maximizing this technology for the benefit of mankind. Nanotechnology has changed 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.

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