Nanodentistry

A Handbook on Nanodentistry- The Next Big Thing is Small

Dr. Moupriya Bera, et al.

Medical and Research Publications

Nanodentistry

Contributing Authors

Dr. Suman Kar Ass. Prof.

Dr. Boudhayan Maiti Researcher.

Nanodentistry

Medical and Research Publications

First printing, 2021.

Published by

Medical and Research Publications,

124SpencerRd,Stoke-on-TrentST42BE,

United Kingdom.

www.medicalandresearch.com

Email: info@medicalandresearch.com

CONTENTS

INTRODUCTION

Most of the greatest inventions, have been the product of human curiosity and wonder. For many years, people around the world have been harnessing their eager through knowledge of science. The era of nanotechnology has become the greatest invention in the field of science and technology.

Nano is derived from the Greek word “Nannos” which means dwarf, by defi nition one nanometer (10−9) or “one-billionth of a meter.” It is engineering at the molecular scale. Nanotechnology helps us for better understanding of molecular structure and properties of materials.**[**1**]**

The prefix nano is defined as a unit of measurement in which the characteristics dimension is one billionth of a unit. the concept of nanotechnology was first elaborated by Richard P. Feynman in 1959. He suggested that nanomachines, nanorobots, and nanodevices ultimately could be used to develop a wide range of automatically precise microscopic instrumentation and manufacturing tools. In 1980, K Eric Drexler popularized the word nanotechnology. He conceptualized building machines on the scale of molecules, a few nanometers wide motors, robot arms and computers, far smaller than a cell. Nanomaterials are those maerials with components less than 100nm in atleast one dimension.**[**2**]**

The budding nanotechnology has tremendous applications in health care leading to the evolution of nanomedicine (including nanodentistry).

Dental nanorobotics is the most awaited and challenging application in nanodentistry. Nanotechnology has revolutionized the field of dentistry with tremendous potential to provide a comprehensive oral health care using the nanomaterials, advanced clinical tools and devices. Nanotechnology has increased the hope of better oral health care delivery and continuous maintenance through the ongoing research in diagnosis, cure and prevention of oral diseases. Nanotechnology has increased the hope of better oral health care delivery and continuous maintenance through the ongoing research in diagnosis, cure and prevention of oral diseases.**[**3**]**

Nanotechnology deals with nanostructures, which may assume the form of surface nano roughness, nanopits, nanomountains or nanoparticles. The properties at Nano scale differ significantly from the properties at bigger scale because of the increased surface area and the so called “quantum effect” which is the deviation in properties of particles when they are smaller than a characteristic size scale, of the order of few to few hundred nanometers. Under this size do the particulate nature of fundamental matter (molecules, atoms, ions, electrons) start to emerge, due to confinement effects, especially in light-matter interaction. Quantum effect is used to maximize the desirable properties of materials, and restorative dentistry and endodontics have not remained untouched by this trend.**[**4**]**

Why Nano?

The nanostructures can be used in medical field to diagnose disease in the early phase of development and sometimes it can be used to decipher the encoded information from the genes responsible for causing the disease. As the nanoparticles are so small in size, it can easily interact with biomolecules present on the surface and inside the cells so that it can revolutionize the field of medicine in diagnosis and treatment. The material properties drastically change when manipulation happened at the nanometer level in the atoms and with the invention of high-resolution the microscope, it becomes possible to identify atoms individually which widens the scope of nanotechnology in medicine and dentistry. This technology can be used to identify diseases at the cellular and molecular level.

Advantages and Disadvantages of Nanodentistry

Advantages of Nanodentistry:

1. Superior hardness, flexural strength, modulus of elasticity, translucency, durability of Nano-dental materials and excellent handling properties of all Nano-dental products.

2. Faster and accurate diagnosis of oral diseases with small diagnostic machinery.

3. Reduced span of treatment procedures with faster healing properties.

4. Reduced mortality and morbidity rates thus associated with certain oral diseases.

5. Better aesthetics.

6. Reduced frequency of visits to the dental clinics for patients and less fatigue for the practitioners.

7. Obvious better outcome of the treatment procedures.

8. Economical.

Disadvantages of Nanodentistry:

1. Numerous ethical issues to deal with (social acceptance is necessary).

2. Toxicity thus associated with the nanoparticles is harmful to human beings as well as to the environment.

3. Subsequent irretrievable genetic information loss that was essential for better prospects of Nano-dentistry and nanotechnology in general.**[**5**]**

Significance of ‘Quantum Mechanics’ in Nanotechnology

Phenomena in bulk matter and particles are explained on the basis of classical physics where mass, volume, time and energy are related through exact equations. hence it is called as deterministic physics. the laws applicable to atomic and subatomic particles and less certain and hence termed as probabilistic. These are governed by quantum mechanics.

Nanophase matter is made up of only a few atoms and the properties are dominated by the surface atoms. In turn, the surface of this atoms is made up of outer shell electrons. The behaviour of the electrons is understood in terms of quantum mechanics, as applied to electrons, provide an important basis for interpreting nano scale phenomena.

The following are the principles of quantum mechanics applied to electrons:

- Electrons behave as particles as well as waves and exhibit phenomena like interference.
- The energy of an electron can vary only by certain discrete values. Thus, the energy levels of the electrons are quantized.
- The position and the momentum of an electron cannot be determined precisely. Higher the certainty in position, the higher the uncertainty in momentum; and vice versa
- Wavelength of the wave associated with an electron is inversely proportional to its momentum.
- The probability of existence of an electron at a given point in 3- coordinate space, at a given time, is described by the square of the wave function.

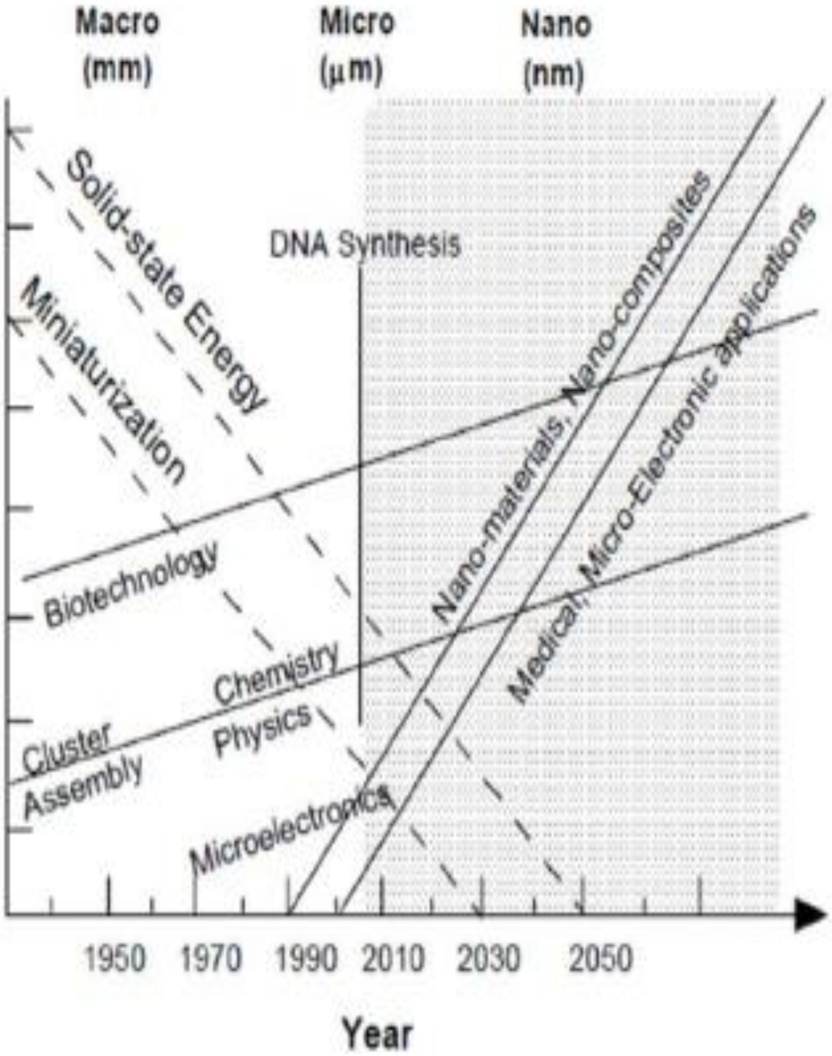
Comprehension of these quantum mechanical concepts will facilitate better understanding of the nano scale phenomenasuch as quantum confinement and quantum tunneling.**[4]**

Nanoscales

- Nuclear scale: 10-15 m or 10-6 nm.
- Atomic scale: 0.1 nm or 1 angstrom (A).
- De Broglie wavelength in metals: ~1 nm.
- DNA molecules: 2 – 12 nm.
- De Broglie wavelength in semiconductors, mean free path in polycrystalline metal fils: 10 nm.
- Viruses: 10 – 100 nm.

- Nanostructures: less than 100 nm.

Nanostructure science and technology is a broad and interdisciplinary area of research and development activity that has been growing explosively worldwide in the past few years. It has the potential for revolutionizing the ways in which materials and products are created and the range and nature of functionalities that can be accessed. It is already having a significant commercial impact, which will assuredly increase in the future.**[**6**]**



Evolution of Science and Technology and the Future

THE ERA

The history of nanotechnology is still debatable. It holds a certain amount of doubt among the accepted opinions by scientists.

There are different views among the scientists regarding the evolution of nanotechnology. Some scientists firmly believe it as, brand new form of science that evolved around the late 1980s or early 1990s.

Although others holdback the history to the year 1959. Still other scientists believe that humans used nanotechnology perhaps even earlier in the ancient times, without any knowledge of the same in the form of steel, paintingsand vulcanizing rubber.**[**7**]**

Richard Feynman

The vision of nanotechnology was again revisited by late Noble Physicist Richard Feynman by a talk given on “There’s Plenty of Room at the Bottom,” at an American Physical Society meeting at Caltech on December 29, 1959.**[**8**]**

Feynman explained how single atom or molecule can be manipulated by the laws of physics that does not limit us for doing so but our lack of vision

and methods are. He predicted that era would arrive soon where in matter can be manipulated at the atomic and molecular level.

The word nanotechnology was coined by Norio Taniguchi, and introduced by Prof. K. Eric Drexler. The term “nanodentistry” was first popularized in 2000 by research Nanodentistry Sasalawad, et al. scientist Robert Freitas.**[**9**]**

History of Nanomaterials

The history of nanomaterials began immediately after the big bang when Nanostructures were formed in the early meteorites. Nature later evolved many other Nanostructures like seashells, skeletons etc. Nanoscaled smoke particles were formed during the use of fire by early humans.

The scientific story of nanomaterials however began much later. One of the first scientific report is the colloidal gold particles synthesized by Michael Faraday as early as 1857. Nanostructured catalysts have also been investigated for over 70 years. By the early 1940's, precipitated and fumed silica nanoparticles were being manufactured and sold in USA and Germany as substitutes for ultrafine carbon black for rubber reinforcements.

Nanosized amorphous silica particles have found large-scale applications in many every-day consumer products, ranging from non-diary coffee creamer to automobile tires, optical fibers and catalyst supports. In the 1960s and 1970's metallic nanopowders for magnetic recording tapes were developed. In 1976, for the first time, nanocrystals produced by the now popular inert- gas evaporation technique was published by Granqvist and Buhrman. Recently it has been found that the Maya blue paint is a nanostructured hybrid material.

The origin of its color and its resistance to acids and biocorrosion are still not understood but studies of authentic samples from Jaina Island show that the material is made of needle-shaped palygorskite (clay) crystals that form a superlattice with a period of 1.4 nm, with intercalates of amorphous silicate substrate containing inclusions of metal (Mg) nanoparticles. The beautiful tone of the blue color is obtained only when both these nanoparticles and the superlattice are present, as has been shown by the fabrication of synthetic samples.

Today nanophase engineering expands in a rapidly growing number of structural and functional materials, both inorganic and organic, allowing to manipulate mechanical, catalytic, electric, magnetic, optical and electronic functions. The production of nanophase or cluster-assembled materials is usually based upon the creation of separated small clusters which then are fused into a bulk-like material or on their embedding into compact liquid or solid matrix materials. e.g. nanophase silicon, which differs from normal silicon in physical and electronic properties, could be applied to macroscopic semiconductor processes to create new devices. For instance, when ordinary glass is doped with quantized semiconductor "colloids," it becomes a high performance optical medium with potential applications in optical computing.**[6]**

Generations of nanotechnology:

First generation: Passive nanostructures

- Dispersed and contact nanostructures-Aerosols, colloids

- Product incorporating nanostructures- coatings, nanoparticle-reinforced composites, polymers, ceramics, nanostructure metals

Second generation : Active nanostructures

- Bioactive, health effects- Targeted drugs, biodevices

- Physicochemical active- Amplifiers, actuators, adaptive structures, 3D transistors

Third generation: systems of nanosystems

- Guided assembling, 3D networking and new hierarchial architectures, robotics, evolutionary

Fourth generation: Molecular nanosystems

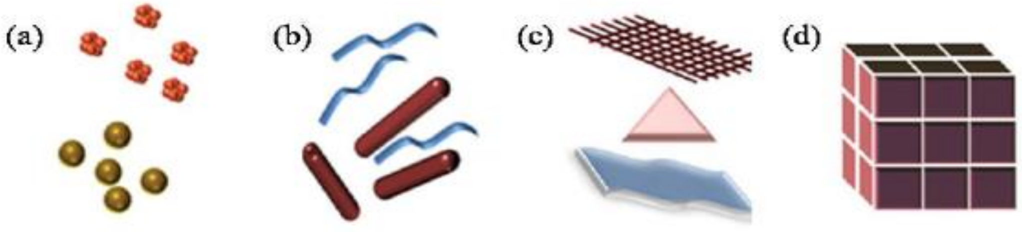
- Molecular devices by design, atomic design, emerging structures

NanoMaterials

Classification of Nanomaterials:

Nanomaterials have extremely small size which having at least one dimension 100 nm or less. Nanomaterials can be nanoscale in one dimension (eg. surface films), two dimensions (eg. strands or fibres), or three dimensions (eg. particles). They can exist in single, fused, aggregated or agglomerated forms with spherical, tubular, and irregular shapes. Common types of nanomaterials include nanotubes, dendrimers, quantum dots and fullerenes. Nanomaterials have applications in the field of nano technology, and displays different physical chemical characteristics from normal chemicals (i.e., silver nano, carbon nanotube, fullerene, photocatalyst, carbon nano, silica).

According to Siegel, Nanostructured materials are classified as Zero dimensional, one dimensional, two dimensional, three dimensional nanostructures.

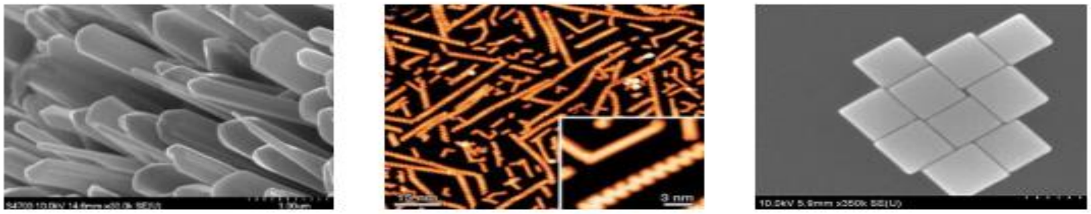


classification of nanomaterials a) OD spheres and clusters; b) ID nanofibres, nanowires and nanorods c) 2D nanofilms, nanoplates and networks , d) 3D nanomaterials

Nanomaterials are materials which are characterized by an ultra fine grain size (< 50 nm) or by a dimensionality limited to 50 nm. Nanomaterials can be created with various modulation dimensionalities as defined by Richard W. Siegel: zero (atomic clusters, filaments and cluster assemblies), one (multilayers), two (ultrafine-grained overlayers or buried layers), and three (nanophase materials consisting of equiaxed nanometer sized grains)

As the properties of nanomaterials are surface-dependent, there are a number of ways one can bring about surface changes leading to concomitant changes in their properties**[**10**]**

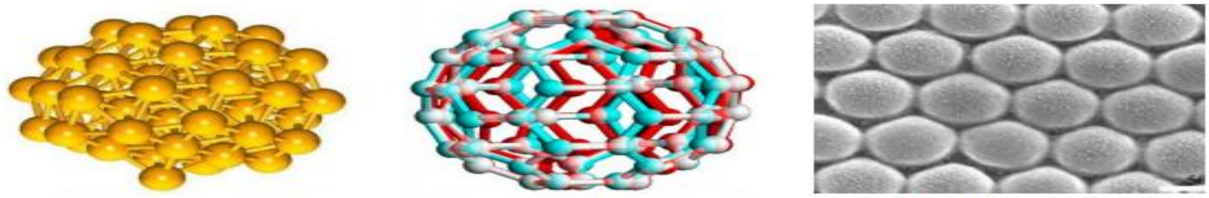
Nano-helics Nano-pyramid Nano-pillers



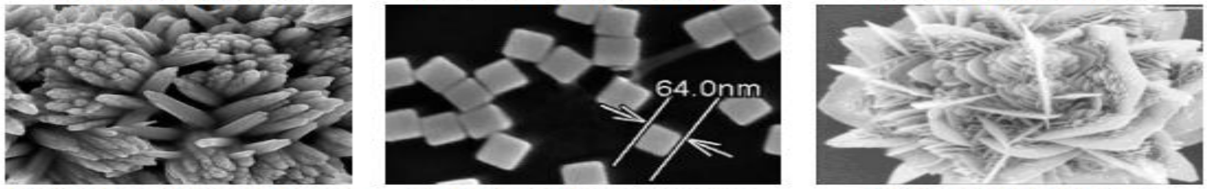
Nano-belts Nano-zigzags Nano-cubes

Different Architectures of Nano-Materials

Examples of Nanomaterials Nanomaterials (gold, carbon, metals, meta-oxides and alloys) with different morphologies (shapes)



(a)Au nanoparticles (b) Buckminsterfullerene (c) FePt nanosphere



(d) Titanium nanoflower (f) Titanium nanoflower (g) SnO_2 nanoflower

Examples of Nanomaterials

Why are nanomaterials important?

These materials have created a high interest in recent years by virtue of their unusual mechanical, electrical, optical and magnetic properties. Some examples are given below:[6]

(i) Nanophase ceramics are of particular interest because they are more ductile at elevated temperatures as compared to the coarse-grained ceramics.

(ii) Nanostructured semiconductors are known to show various non-linear optical properties. Semiconductor Q-particles also show quantum confinement effects which may lead to special properties, like the luminescence in silicon powders and silicon germanium quantum dots as infrared photoelectronic devices. Nanostructured semiconductors are used as window layers in solar cells.

(iii) Nanosized metallic powders have been used for the production of gas tight materials, dense parts and porous coatings. Cold welding properties combined with the ductility make them suitable for metal-metal bonding especially in the electronic industry.

(iv) Single nanosized magnetic particles are mono-domains and one expects that also in magnetic nanophase materials the grains correspond with domains, while boundaries on the contrary to disordered walls. Very small particles have special atomic structures with discrete electronic states, which give rise to special properties in addition to the superparamagnetism behaviour. Magnetic nanocomposites have been used for mechanical force transfer (ferrofluids), for high density information storage and magnetic refrigeration.

(v) Nanostructured metal clusters and colloids of mono- or plurimetallic composition have a special impact in catalytic applications. They may serve as precursors for new type of heterogeneous catalysts (Cortex-catalysts) and have been shown to offer substantial advantages concerning activity, selectivity and lifetime in chemical transformations and electrocatalysis (fuel cells). Enantioselective catalysis was also achieved using chiral modifiers on the surface of nanoscale metal particles.

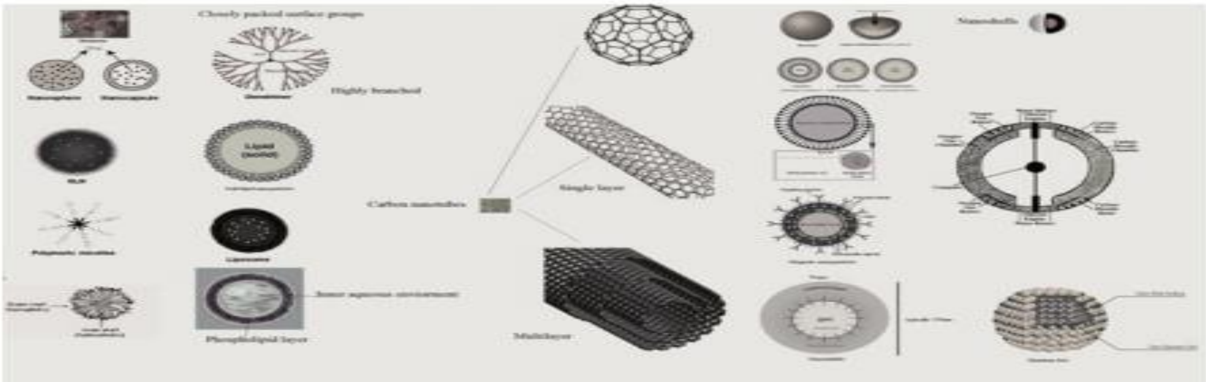
(vi) Nanostructured metal-oxide thin films are receiving a growing attention for the realization of gas sensors (NOx, CO, CO2, CH4 and aromatic hydrocarbons) with enhanced sensitivity and selectivity. Nanostructured metal-oxide (MnO2) finds application for rechargeable batteries for cars or consumer goods. Nanocrystalline silicon films for highly transparent contacts in thin film solar cell and nano-structured titanium oxide porous films for its high transmission and significant surface area enhancement leading to strong absorption in dye sensitized solar cells.

(vii) Polymer based composites with a high content of inorganic particles leading to a high dielectric constant are interesting materials for photonic band gap structure.

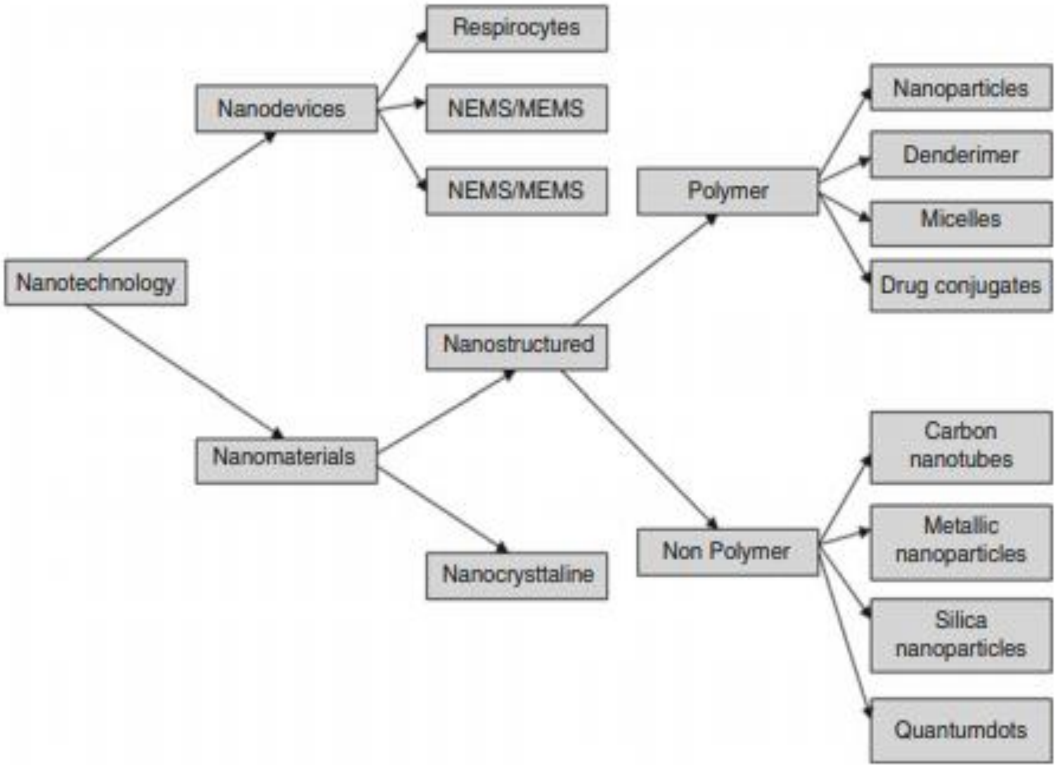
Nanoparticles Types, Classification, Characterization , Fabrication Methods

Nanotechnology is the science of material featuring between 10 −9 and 10 −7 of a meter . Or in another words it’s the science of materials and devices whose structures and constituents demonstrate novel and considerably altered physical, chemical and biological phenomenon due to their nanoscale size. Thus nanotechnology is defined as the manipulation of matter on an atomic, molecular, and supramolecular scale involving the design, production, characterization and application of different nanoscale materials in different potential areas providing novel technological advances mainly in the field of medicine. This forms an independent branch of nanostructures, referred as nanomedicine which is specifically utilized for medicines.

These specified disciplines are overlapping which in many ways. The use of nanotechnology in various sectors of therapeutics has revolutionized the field of medicine where nanoparticles are designed and used for therapeutics, diagnostics, and as biomedical tools for research. With the help of nanotechnology it’s now possible to provide therapy at a molecular level which may further help in treating and pathogenesis of disease.[11]



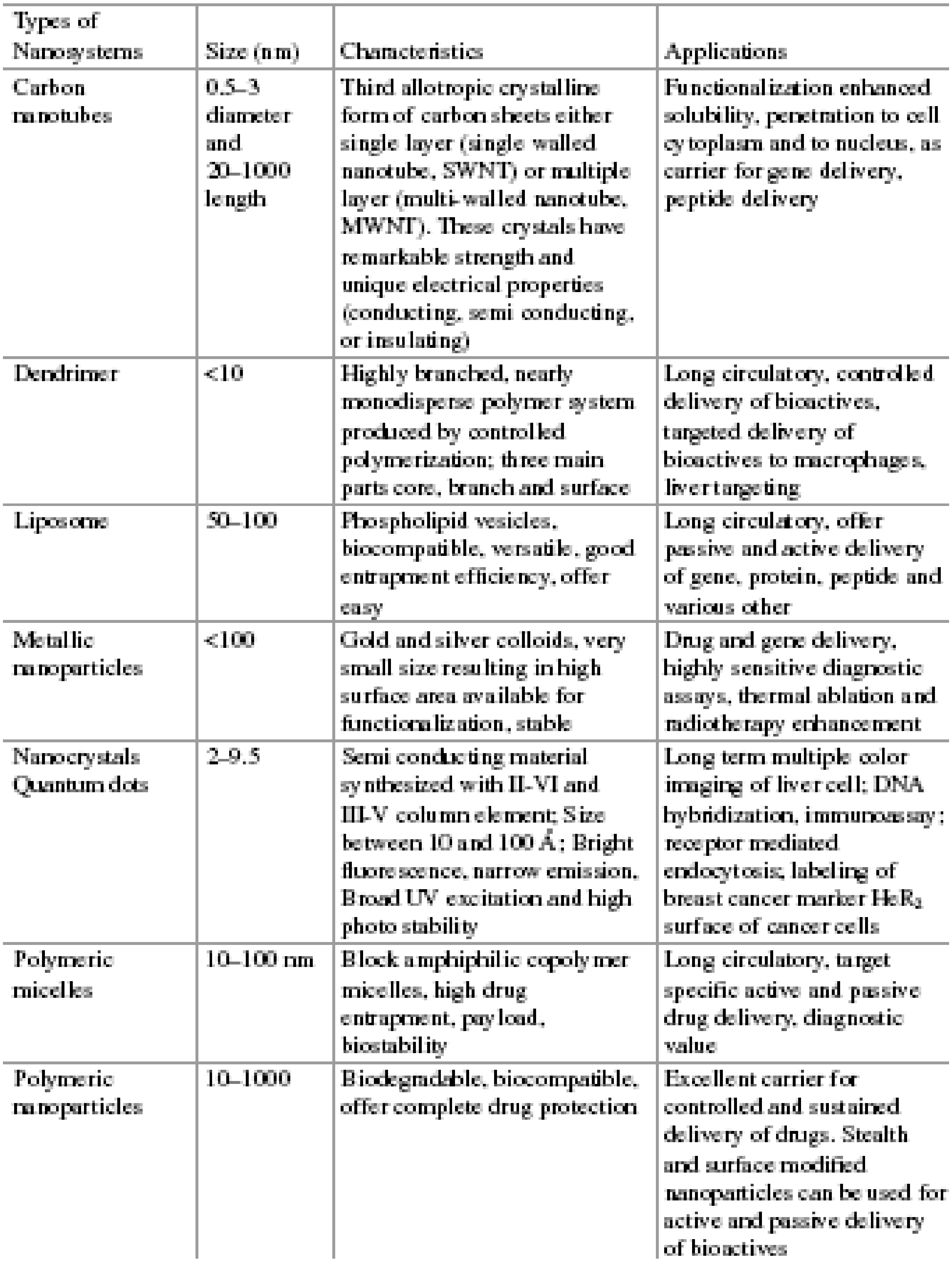
Various nanoforms and their morphological features



Illustrations demonstrating various types of pharmaceutical nanosystems

Nano crystalline materials are readily manufactured and can substitute the less performing bulk materials. Raw nanomaterials can be used in drug encapsulation, bone replacements, prostheses, and implants. Nanostructured materials are processed forms of raw nanomaterials that provide special shapes or functionality, for example quantum dots, dendrimers, fullerenes and carbon nanotubes. Nanodevices are miniature devices in the nanoscale and some of which include nano- and microelectromechanical systems, microfl uidics, and microarrays. Examples include biosensors and detectors to detect trace quantities of bacteria, airborne pathogens, biological hazards, and disease signatures and some intelligent machines like respirocyte

Various characteristics and brief applications of nanosystems[12]



Types of Nanosystems	Size (nm)	Characteristics	Applications
Carbon nanotubes	0.5–3 diameter and 20–1000 length	Third allotropic crystalline form of carbon sheets either single layer (single walled nanotube, SWNT) or multiple layer (multi-walled nanotube, MWNT). These crystals have remarkable strength and unique electrical properties (conducting, semi conducting, or insulating)	Functionalization enhanced solubility, penetration to cell cytoplasm and to nucleus, as carrier for gene delivery, peptide delivery
Dendrimer	<10	Highly branched, nearly monodisperse polymer system produced by controlled polymerization; three main parts core, branch and surface	Long circulatory, controlled delivery of bioactives, targeted delivery of bioactives to macrophages, liver targeting
Liposome	50–100	Phospholipid vesicles, biocompatible, versatile, good entrapment efficiency, offer easy	Long circulatory, offer passive and active delivery of gene, protein, peptide and various other
Metallic nanoparticles	<100	Gold and silver colloids, very small size resulting in high surface area available for functionalization, stable	Drug and gene delivery, highly sensitive diagnostic assays, thermal ablation and radiotherapy enhancement
Nanocrystals Quantum dots	2–9.5	Semi conducting material synthesized with II-VI and III-V column element; Size between 10 and 100 Å; Bright fluorescence, narrow emission, Broad UV excitation and high photo stability	Long term multiple color imaging of liver cell; DNA hybridization, immunoassay; receptor mediated endocytosis; labeling of breast cancer marker HeR_2 surface of cancer cells
Polymeric micelles	10–100 nm	Block amphiphilic copolymer micelles, high drug entrapment, payload, biostability	Long circulatory, target specific active and passive drug delivery, diagnostic value
Polymeric nanoparticles	10–1000	Biodegradable, biocompatible, offer complete drug protection	Excellent carrier for controlled and sustained delivery of drugs. Stealth and surface modified nanoparticles can be used for active and passive delivery of bioactives

Classification of Nanoparticles

Nanoparticles are broadly classified in to three classifications **[** 13 **]**

- **One dimension nanoparticles**

One dimensional system (thin film or manufactured surfaces) has been used for

decades. Thin films (sizes 1–100 nm) or monolayer is now common place in the field of solar cells offering, different technological applications, such as chemical and biological sensors, information storage systems, magneto-optic and optical device, fiber-optic systems.

- **Two dimension nanoparticles**

Carbon nanotubes

- **Three dimension nanoparticles**

Dendrimers, Quantum Dots, Fullerenes (Carbon 60), (QDs)

Characterization of Nanoparticles

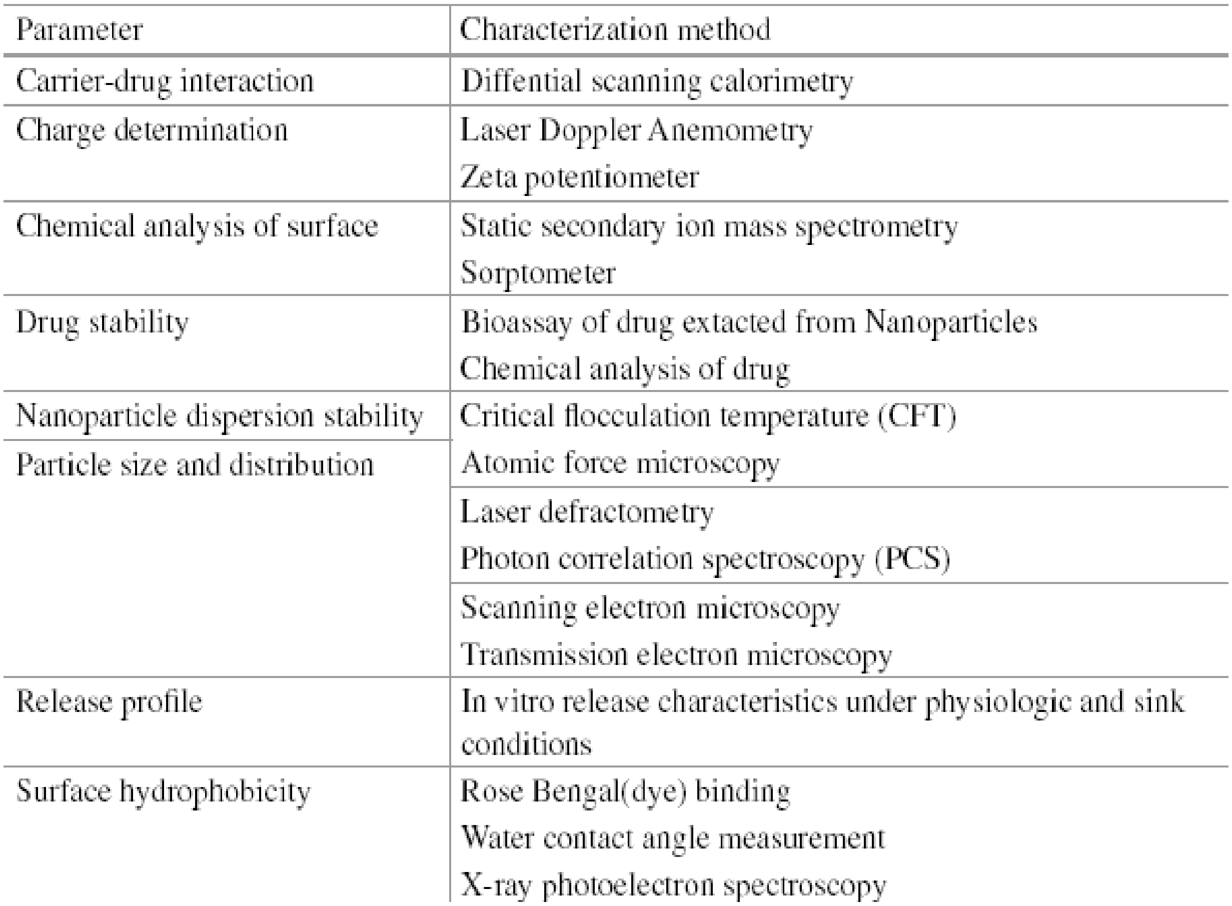
Characterization of nanoparticles is based on the size, morphology and surface charge, using such advanced microscopic techniques as atomic force microscopy (AFM), scanning electron microscopy (SEM) and transmission electron microscopy TEM). Properties such as the size distribution, average particle diameter, charge affect the physical stability and the in vivo distribution of the nanoparticles.

Properties like surface morphology, size and overall shape are determined by electron microscopy techniques. Features like physical stability and redispersibility of the polymer dispersion as well as their in vivo performance are affected by the surface charge of the nanoparticles.

Particle Size

Characterizations of nanoparticles are primarily evaluated by the particle size distribution and morphology. With the aid of electron microscopy it’s now possible to ascertain the morphology as well as the size of nanoparticles.

Various characterization tools and methods for nanoparticles [14]



Parameter	Characterization method
Carrier-drug interaction	Diffential scanning calorimetry
Charge determination	Laser Doppler Anemometry Zeta potentiometer
Chemical analysis of surface	Static secondary ion mass spectrometry Sorptometer
Drug stability	Bioassay of drug extacted from Nanoparticles Chemical analysis of drug
Nanoparticle dispersion stability	Critical flocculation temperature (CFT)
Particle size and distribution	Atomic force microscopy
	Laser defractometry Photon correlation spectroscopy (PCS)
	Scanning electron microscopy Transmission electron microscopy
Release profile	In vitro release characteristics under physiologic and sink conditions
Surface hydrophobicity	Rose Bengal(dye) binding Water contact angle measurement X-ray photoelectron spectroscopy

Smaller the size of nanoparticles larger surface area, which results in to fast drug release. Loaded drug when exposed to the particle surface area causes significant drug release. In contrast, inside the nanoparticles drugs slow diffusion of larger particles occurs. Consequently smaller particles tend to aggregate during storage and transportation of nanoparticle dispersion. Therefore there is a mutual compromise between maximum stability and small size of nanoparticles **[** 15 **]**.

In addition degradation of the polymer can also be affected by the particle size e.g. the extent of poly (lactic-co-glycolic acid) degradation was found to increase with increasing particle size in vitro**[**16**]**

Various techniques are now available for determining nanoparticle size discussed below :

1. Photon-Correlation Spectroscopy (PCS) or Dynamic Light Scattering (DLS)

Current research demands the fastest and most popular method of determining particle size. The fastest and most popular techniques like photon-correlation spectroscopy (PCS) or dynamic light scattering (DLS), widely used to determine the size of Brownian nanoparticles in colloidal suspensions in the nano and submicron ranges.

In this technique solution of spherical particles in Brownian motion causes a Doppler shift when they are exposed against shining monochromatic light (laser). Such monochromatic light exposure hits the moving particle which results in changing the wavelength of the incoming light. Extent of this change in wavelength determines the size of the particle. This parameter assists in evaluation of the size distribution, particle's motion in the medium, which may further assists in measuring the diffusion coefficient of the particle and using the autocorrelation function.

Dynamic light scattering (DLS) offer the most frequently used technique for accurate estimation of the particle size and size distribution.**[**17**]**

2. Scanning Electron Microscopy (SEM)

This electron microscopy based technique determines the size, shape and surface morphology with direct visualization of the nanoparticles. During the process of SEM characterization, solution of nanoparticles should be initially converted into a dry powder. This dry powder is then further mounted on a sample holder followed by coating with a conductive metal (e.g. gold) using a sputter coater. Whole sample is then analyzed by scanning with a focused fine beam of electrons **[**18**]**. Secondary electrons emitted from the sample surface determine the surface characteristics of the sample. This electron beam can often damage the polymer of the nanoparticles which must be able to withstand vacuum.

Average mean size evaluated by SEM is comparable with results obtained by dynamic light scattering.**[**19**]**

3. Transmission Electron Microscope

Experimental difficulties in studying nanostructures stem from their small size, which limits the use of traditional techniques for measuring their physical properties.

Transmission electron microscopy techniques can provide imaging, diffraction and spectroscopic information, either simultaneously or in a serial manner, of the specimen with an atomic or a sub-nanometer spatial resolution. TEM operates on different principle than SEM, yet it often brings same type of data. The sample preparation for TEM is complex and time consuming because of its requirement to be ultra thin for the electron transmittance. High-resolution TEM imaging, when combined with nanodiffraction, atomic resolution electron energy-loss spectroscopy and nanometer resolution X-ray energy dispersive spectroscopy techniques, is critical to the fundamental studies of importance to nanoscience and nanotechnology.

During the TEM characterization nanoparticles dispersion is deposited onto support grids or films. After dispersion they are fixed using either a negative staining material (phosphotungstic acid or derivatives, uranyl acetate, etc., or by plastic embedding). This is done to make nanoparticles withstand against the instrument vacuum and facilitate handling. Alternatively nanonoparticles sample can also be exposing to liquid nitrogen temperatures after embedding in vitreous ice. When a beam of electrons is transmitted through an ultra thin sample it interacts with the sample as it passes through The surface characteristics of the sample are obtained **[**20**]**. TEM imaging mode has certain benefits compared with the broad-beam illumination mode:

- Collection of the information about the specimen using a high angular annular dark field (HAADF) detector (in which the images registered have different levels of contrast related to the chemical composition of the sample)

- It can be utilized for the analysis of biological samples is its contrast for thick stained sections, since high angular annular dark field images (samples with thickness of 100–120 nm) have better contrast than those obtained by other techniques.

- Combining HAADF-TEM imaging leads to imaging the atomistic structure and composition of nanostructures at a sub-angstrom resolution.

- Availability of sub-nanometer or sub-angstrom electron probes in a TEM instrument, due to the use of a field emission gun and aberration correctors, ensures the greatest capabilities for studies of sizes, shapes, defects, crystal and surface structures, and compositions and electronic states of nanometer-size regions of thin films, nanoparticles and nanoparticle systems.

4. Atomic Force Microscopy

This technique is also known as scanning force microscopy (technique that forms images of surfaces using a prob that scans the specimen), very high resolution type of scanning probe microscopy, with reported resolution on the order of fractions of a nanomerter, more than 100 times better than the optical diffraction limit. The atomic force microscopy is based on a physical scanning of samples at sub-micron level using a probe tip of atomic scale and offers ultra-high resolution in particle size measurement **[**21**]**. Depending upon properties, samples are usually scanned in contact or noncontact mode. During contact mode, the topographical map is generated by tapping the probe on to the surface across the sample and probe hovers over the conducting surface in non-contact mode. One of the prime advantage of AFM is its ability to image non-conducting samples without any specific treatment. This feature allows the imaging of delicate biological and polymeric nano and microstructures**[**22**]**. Moreover AFM (without any mathematical calculation) providesthe most accurate description of size, size distribution and real picture which helps in understanding the effect of various biological conditions **[**23**]**.

5. Surface Charge

Surface charge and intensity determines the interaction of nanoparticles with the biological environment as well as their electrostatic interaction with bioactive compounds. Stability of colloidal material is usually analyzed through zeta potential of nanoparticles. Zeta potential is an indirect measure of the surface charge. It can be obtained by evaluating the potential difference between the outer Helmholtz plane and the surface of shear. Thus zeta potential of colloidal based dispersion assists in directly evaluating its storage stability. Zeta potential values (high zeta potential values, either positive or negative) are achieved in order to ensure stability and avoid aggregation of the particles. Zeta potential values can be utilized in evaluating surface hydrophobicity and the nature of material encapsulated within the nanocapsules or coated onto the surface **[**24**]**.

6. Surface Hydrophobicity

Techniques such as hydrophobic interaction chromatography, biphasic partitioning, adsorption of probes, contact angle measurements etc. can be utilized for the determination of surface hydrophobicity. Recent advancement in research offers several sophisticated analytical tools for surface property analysis of nanoparticles.Modern technique such as X-ray photon correlation spectroscopy not only determine surface hydrophobicity but also permits the identification of specific chemical groups on the surface of nanoparticles **[**25**]**.

7. Drug Release

It’s very essential to determine extent of the drug release and in order to obtain such information most release methods require that the drug and its delivery vehicle be separated. drug loading capacity of the nanoparticles is defined as the amount of drug bound per mass of polymer or in another term it is the moles of drug per mg polymer or mg drug per mg polymer or it could also be given as percentage relative to the polymer.

Various techniques such as UV spectroscopy or high performance liquid chromatography (HPLC) after ultracentrifugation, ultra filtration, gel filtration, or centrifugal ultrafiltration are used to determine this parameter. Methods that are employed for drug release analysis are also similar to drug loading assay which is more often assessed for a period of time to evaluate the drug release mechanism **[**26**]**.

Preparation of Nanoparticles

The selection of appropriate method for the preparation of nanoparticles depends on the physicochemical character of the polymer and the drug to be loaded. Nanoparticles can be prepared from a variety of materials such as proteins, polysaccharides and synthetic polymers. The selection of matrix materials is dependent on many factors including **[**27**]**:

- Antigenicity of the final product.
- Biocompatibility and toxicity
- Degree of biodegradability

- Drug release profile desired

- Inherent properties of the drug (aqueous solubility and stability)

- Size of nanoparticles required

- Surface characteristics (charge and permeability)

Nanoparticles have been usually prepared by three methods:

- Dispersion of preformed polymers

- Ionic gelation or coacervation of hydrophilic polymers

- Polymerization of monomers

However, other methods such as supercritical fluid technology **[**28**]** and particle replication in non-wetting templates **[**29**]** have also been described in the literature for production of nanoparticles. The latter was claimed to have absolute control of particle size, shape and composition, which could set an example for the future mass production of nanoparticles in industry.

Dispersion of preformed polymers: This technique is based on the preparation of biodregerable nanoparticles via dispersion of biodegradable polymers such as poly (D , L -glycolide), poly (lactic acid) (PLA); poly (cyanoacrylate) (PCA), and PLG; poly (D , L -lactide-co-glycolide) (PLGA) **[**30**]**.

Dispersion of preformed polymers to prepare the nanoparticles can be used in various ways:

1. Solvent Evaporation Method

Solvent evaporation method is one of the most frequently used methods for the preparation of nanoparticles. This method involves two steps (first is emulsification of the polymer solution into an aqueous phase and second is evaporation of polymer solvent, inducing polymer precipitation as nanospheres). This method is based on the solubility of polymer and hydrophobic drug since both polymer and hydrophobic drug are dissolved in an organic solvent (dichloromethane, chloroform or ethyl acetate) which is also used as the solvent for dissolving the. Mixture obtained from polymer and drug solution is then emulsified in an aqueous solution. This aqueous solution contains surfactant or emulsifying agent to form oil in water (o/w) emulsion.

Once the stable emulsion forms, the organic solvent is evaporated either by continuous stirring or by reducing the pressure. Size range of nanoparticles was found to be influenced by the concentrations and type of stabilizer, polymer concentration and homogenizer speed **[**31**]**. Ultrasonication or high-speed homogenization may be often employed in order to produce small particle size **[**32**]**. The nano particles are collected by ultracentrifugation and washed with distilled water to remove stabilizer residue or any free drug and lyophilized for storage **[**33**]** . Modification of this method is known as solvent evaporation method and high pressure emulsification **[**34**]**. This method involves preparation of a emulsion which is then subjected to homogenization under high pressure followed by overall stirring to remove organic solvent **[**35**]**. The size can be controlled by adjusting the stirring rate, type and amount of dispersing agent, viscosity of organic and aqueous phases and temperature **[**36**]**. However this method can be applied to liposoluble drugs and limitation are imposed by the scale up issue. Polymers used in this method are PLGA **[**37**]** , PLA **[**38**]**, cellulose acetate phthalate **[**39 **]**, EC **[**40**]**, Poly (β -hydroxybutyrate) (PHB) **[**41**]**, Poly (β-caprolactone)\ (PCL) **[**42**]**.

2. Spontaneous Emulsification or Solvent Diffusion Method

This method is developed from solvent evaporation method **[**43**]**, in which the water miscible solvent along with a small amount of the organic solvent (water immiscible) is used as an oil phase. During the spontaneous diffusion of solvents between the two phases an interfacial turbulence is generated which may ultimately leads to the formation of small particles. Smaller particle size can be achieved by increasing the concentration of water miscible solvent increases. This method can be used for hydrophobic or hydrophilic drugs. In the case of hydrophilic drug, a multiple w/o/w emulsion needs to be formed with the drug dissolved in the internal aqueous phase.

3. Double Emulsion and Evaporation Method

Most of the emulsion and evaporation based methods suffer from the limitation of poor entrapment of hydrophilic drugs. Therefore to encapsulate hydrophilic drug the double emulsion technique is employed, which involves the addition of aqueous drug solutions to organic polymer solution under vigorous stirring to form w/o emulsions. This w/o emulsion is added into second aqueous phase with continuous stirring to form the w/o/w emulsion. The emulsion then subjected to solvent removal by evaporation and nano particles can be isolated by centrifugation at high speed. The formed nanoparticles must be thoroughly washed before lyophilisation **[**44**]**. In this method the amount of hydrophilic drug to be incorporated, the concentration of stabilizer used, the polymer concentration, the volume of aqueous phase are the variables that affect the characterization of nanoparticles **[**45**]**.

4. Salting Out Method

Method involves the separation of a water-miscible solvent from aqueous solution via a salting-out effect **[**46**]** . It's based on the on the separation of a water miscible solvent from aqueous solution via a salting-out effect. During the initial process polymer and drug are dissolved in a solvent which is subsequently emulsified into an aqueous gel containing the salting out agent and a colloidal stabilizer. Various types of salting out agents (electrolytes, such as magnesium chloride and calcium chloride, or non- electrolytes such as sucrose) and colloidal stabilizer (such as polyvinylpyrrolidone or hydroxyethylcellulose) have been used. This lead to formation of oil/water emulsion which is further diluted with a sufficient volume of water or aqueous solution to enhance the diffusion of solvent into the aqueous phase, ultimately induce the formation of nanospheres. Parameters such as stirring rate, internal/external phase ratio, concentration of polymers in the organic phase, type of electrolyte concentration and type of stabilizer in the aqueous phase can be varied in this process **[**47**]**. Salting out method is reported for preparation of ethyl cellulose and PLA, Poly(methacrylic) acids nanospheres. leads to high efficiency and is easily scaled up **[**48**]**.

Advantages

- Does not require an increase of temperature and therefore may be useful when

heat sensitive substances have to be processed **[**49**]**.

Disadvantages

- Limited application to lipophilic drug and the extensive nanoparticles washing steps

5 Emulsions-Diffusion Method

This is another widely used method to prepare nanoparticles. The encapsulating polymer is dissolved in a partially water-miscible solvent (such as propylene carbonate, benzyl alcohol), and saturated with water to ensure the initial thermodynamic equilibrium of both liquids. Subsequently, the polymer-water saturated solvent phase is emulsified in an aqueous solution containing stabilizer, leading to solvent diffusion to the external phase and the formation of nanospheres or nanocapsules, according to the oil-to-polymer ratio. Finally, the solvent is eliminated by evaporation or filtration, according to its boiling point. This technique presents several advantages, such as high encapsulation efficiencies (generally 70 %), no need for homogenization, high batch-to-batch reproducibility, ease of scaleup, simplicity, and narrow size distribution.

Disadvantages

Disadvantages are the high volumes of water to be eliminated from the suspension and the leakage of water-soluble drug into the saturated-aqueous external phase during emulsification, reducing encapsulation efficiency **[**50**]**. Several drugloaded nanoparticles were produced by the technique, including mesotetra (hydroxyphenyl) porphyrin-loaded PLGA (p-THPP) nanoparticles**[**51**]** , doxorubicin- loaded PLGA nano particles, and cyclosporine (cy-A-); loaded sodium glycolate nanoparticles **[**52**]**.

6 Solvent Displacement/Precipitation Method

In this method preformed polymer is precipitated in an organic solution and organic solvent is diffused in the aqueous medium. Diffusion of organic solvent can be achieved in the presence or absence of surfactant. Semi polar water miscible solvent such as acetone or ethanol can be used to dissolve the polymers, drug, and or lipophilic surfactant. After their complete dissolution, solution is then poured or injected into an aqueous solution containing stabilizer under magnetic stirring. Nano particles are formed immediately by the rapid solvent diffusion.

This step is followed by the removal of solvent from the suspensions under reduced pressure. Particles size is dependent on the extent of addition of the organic phase into the aqueous phase. It was also found that decrease in both particles size and drug entrapment occurs as the mixing rate of the two phase increases **[**53**]** . This method is more suitable for poorly soluble drugs. Optimization of various parameters (preparation parameters) can effectively control size, drug release and yield of nanosphere. Nanosphere size, drug release and yield were shown to be effectively controlled by adjusting preparation parameters. Regulation the concentration of polymer in the organic phase was reported to be useful in the production of smaller sized nanospheres. However size range is restricted to minimum range of the polymer to drug ratio.

7. Coacervation or Ionic Gelation Method

Recent exploration of biodegradable polymers such as gelatin and sodium alginate has been focused now to yield biodegradable nanoparticles having features like biocompatibility and low toxicity. Methods such as ionic gelation can be used for preparing hydrophilic polymer based nanoparticles. Calvo and co-workers developed method for preparing chitosan based nanoparticles by ionic gelation method **[**54,55**]**. In this method two different aqueous phases are prepared for polymer **[**chitosan, a di-block co-polymer ethylene oxide or propylene oxide (PEO-PPO)**]** and the other is for polyanion sodium tripolyphosphate. This method is based on the strong electrostatic interaction between positively charged amino group of chitosan and negative charged tripolyphosphate to form coacervates with a size in the range of nanometer. Existence of strong electrostatic interaction between two aqueous phases leads to the formation of coacervates. In contrast ionic gelation involves the material undergoing transition from liquid to gel due to ionic interaction conditions at room temperature.

8. Polymerization Method

This method involves polymerization of monomers to form nanoparticles in an aqueous solution. In polymerization drug is incorporated at two different stages (either by being dissolved in the polymerization medium or by adsorption onto the nanoparticles after polymerization completed) **[**56,57**]**. Ultracentrifugation can be used to purify nanoparticle suspension by removing various stabilizers and surfactants employed for polymerization, followed by the re-suspension of particles in an isotonic surfactant-free medium. This technique is reported for making poly (alkylcyanoacrylate) or polybutylcyanoacrylate nanoparticles. Desirable size of nanocapsule can be achieved by optimization of concentration of the surfactants and stabilizers **[**58**]**.

9 . Production of Nanoparticles Using Supercritical Fluid Technology

Above mentioned conventional methods (such as solvent extraction-evaporation, solvent diffusion and organic phase separation methods) obligatory use organic solvents which are hazardous to the environment as well as to physiological systems.

Therefore, there is an urgent requirement of suitable technology which avoid the usage of organic solvents or any other ingredient hazardous to health. Since supercritical fluids are environmentally safe, therefore, the supercritical fluid technology has been investigated as an alternative to prepare biodegradable micro- and nanoparticles **[**59**]** . Supercritical fluid technology technique, although environmentally friendly and suitable for mass production, requires specially designed equipment and is more expensive. Supercritical fluids are those fluids which are at a temperature above its critical temperature remains in a single phase regardless of pressure **[**60**]**. CO_2 (SC CO_2) is the most widely used supercritical fluid because of its mild critical conditions, non-flammability, low price and nontoxicity.

Among the various processing techniques involving supercritical fluids, supercritical anti-solvent (SAS) and rapid expansion of critical solution (RESS) are the most common one. In former process a liquid solvent (methanol) is selected on the basis of it's completely miscibility with the supercritical fluid (SC CO_2). This is done to dissolve the solute to be micronized at the process conditions. Since the solute is insoluble in the supercritical fluid, the extract of the liquid solvent by supercritical fluid leads to the instantaneous precipitation of the solute, results in the formation of nanoparticles.

This process is reported for formation of hydrophilic drug dexamethasone phosphate drug nanoparticles for microencapsulation purpose. In later process called as RESS, solute is dissolved in a supercritical fluid such as supercritical methanol and then the solution is rapidly expanded through a small nozzle into a region lower pressure **[**61**]**. This dramatically affects the solvent power of supercritical fluids which is ultimately decreases and the solute eventually precipitates. RESS and its modified process have been used for the product of polymeric nanoparticles **[**62**]**.

Properties of Nanomaterials

Mechanical properties of nanoparticles[20]

Nanoparticles, microscopic objects with at least one dimension less than 100 nm , have attracted intensive scientific attention. Distinctive size-dependent properties of nanoparticles often exist, which are mainly due to their relatively large surface area . Moreover, when the size of a particle approaches nanoscale with the characteristic length scale close to or smaller than the de Broglie wavelength of the charge carrier (electrons and holes) or the wavelength of light, the periodic boundary conditions of the crystalline particle are destroyed, or the atomic density on the amorphous particle surface is changed . Due to these, a lot of the physical properties of nanoparticles are quite different from bulk materials, yielding a wide variety of new applications. For example, nanoparticles encapsulated or adsorbed in matrix materials have been used as carriers for delivering drug molecules . Stability, self-assembly behaviour and mutual interactions of nanoparticles at fluid interfaces are very relevant to many colloid applications . Special optical properties due to the excitation of surface plasmons in metallic nanoparticles can be used in biomedicine, energy and environment protection technologies. Magnetic nanoparticles could become superparamagnetic and respond to external magnetic fields very fast with almost zero remanence ; these properties lay bases for applications such as biomedical imaging and information storage technology . Some of the basic functions of nanoparticles, e.g., a catalysis of electrochemical reactions and the enhancement of electron transfer, make them very useful in designing novel electrochemical sensing systems .

Nanoparticles show different mechanical properties relative to microparticles and bulk materials, providing more effective options for the surface modification of many devices in the mechanical strength, or to improve the quality of nanomanufacturing/nanofabrication, etc. To be more specific, on the one hand, the mechanical effects of nanoparticles can affect the tribological properties of lubricants with nanoparticles as well as reinforce composite coatings . In a lubricated contact, the comparison in the hardness between nanoparticles and the contacting surface determines whether particles are deformed or indented into the surface when the contact pressure is sufficiently large nanoparticles are usually used as abrasives in the nanopolish of ultra-smooth surfaces by chemical mechanical polishing (CMP), which is the most effective planarization tool in the manufacture of an integrated circuit (IC), till now. Good controls over the mechanical properties of particles and their interactions with the polished surface etc are important for improving the surface quality and enhancing material removal . Successful applications in these fields usually need a deep understanding of the basics of the nanoparticles' mechanical properties, such as hardness and elastic modulus, interfacial adhesion and friction, movement law, as well as their size-dependent effects. In order to acquire more of this information, different testing methods have been developed, e.g., nanoindentation with atomic force microscopy (AFM) , in situ compression by a force probing holder based on the observation with transmission electron microscopy (TEM) . However, the obtained results are still inadequate and some are controversial. For instance, there is still no definite conclusion as to whether the elastic modulus of nanoparticles measured with AFM is affected by the particle size and the indentation depth . Furthermore, the contact mechanics, especially the frictional and mechanical behaviours related to nanoparticles, have not been fully understood.

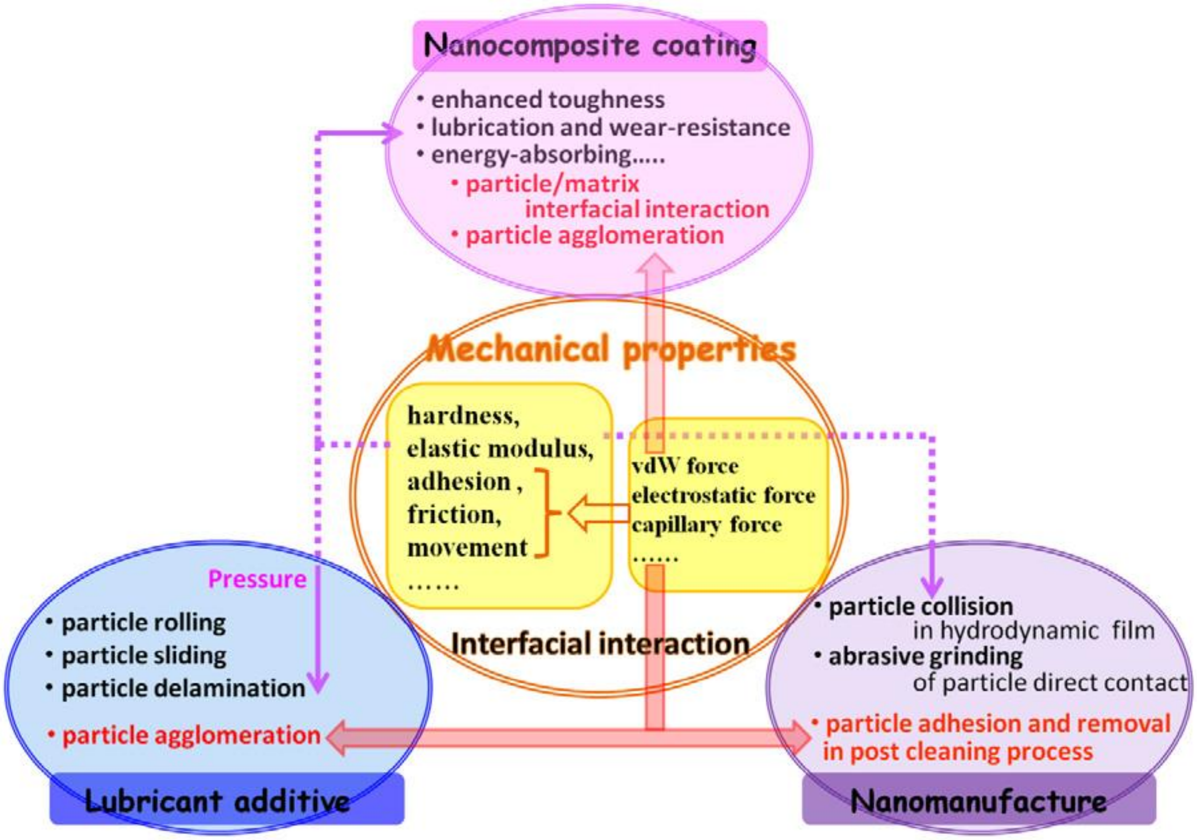
Interaction Forces and Basic Theories Relevant to the Mechanical Properties of Nanoparticles

‘As we go down in size, there are a number of interesting problems that arise.’—Feynman . The first problem is the diverse interaction forces between the nanoparticles themselves, or between them and the surface.

1. Van der Waals (vdW) forces

VdW forces are the weak interaction between all molecules and particles, which play important roles in the particles’ mechanical properties. This kind of force includes three parts: one is the orientation force (the Keesom force) , resulting from the interaction between the permanent dipole moment of polar molecules. The second is the induction force (the Debye force) , which comes from the interaction between the permanent dipole moment of the polar molecule and the induced dipole moment. The third is the dispersion force (the London force) , which exists in a wide variety of polar and nonpolar molecules, coming from the induced instantaneous dipole polarization. VdW energies are usually from several to dozens of thousands of Joules per mole, one or two orders of magnitude smaller than the chemical bond energy. The vdW forces are long-range forces and can be effective in a large range of distances, varying from long distances greater than 10 nm down to atomic scale distance (about 0.2 nm) . The methods for calculating the vdW interaction forces or energies between small molecules or large macroscopic bodies have been well established .

The vdW forces of objects with any shape can be transformed with the Derjaguin approximation to those between two planes per unit area . Based on the quantum electrodynamics theory, Lifshitz deduced the expression for calculating Hamaker constants, which can be used to solve problems with media involved . Typically, the Hamaker constants for interactions in a medium are an order of magnitude lower than those in a vacuum . The vdW force is always attractive between identical materials, but it may be repulsive between dissimilar materials in a third medium (usually liquid) .



Schematic diagram of the framework

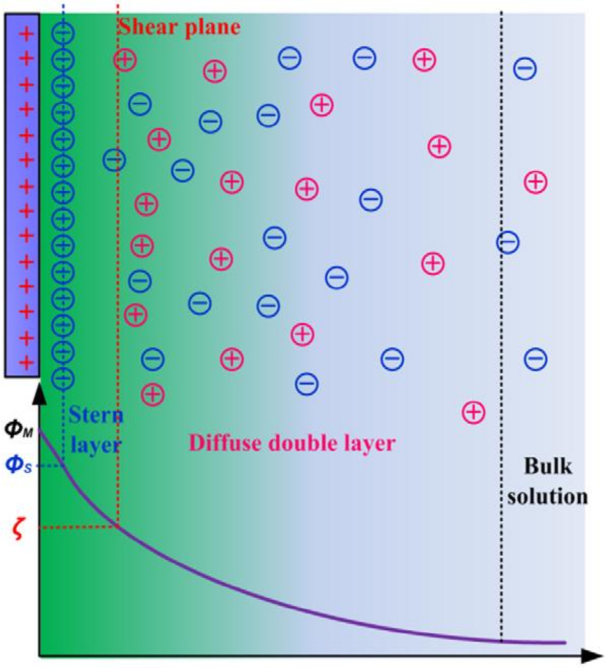
2. Electrostatic force and electrical double layer (EDL) force

For particles suspended in water or any liquid with a high dielectric constant, they are usually charged and can be prevented from coalescing due to the repulsive electrostatic force. The charging of a surface in a liquid has three main sources : (1) the ionization or dissociation of surface groups; (2) the adsorption or binding of ions from the solution onto a previously uncharged surface; (3) when two dissimilar surfaces are very close, charges can hop across from one surface to the other. The surface charges are balanced by an oppositely charged ion layer in the solution at some distance away from the surface, forming the EDL. The idea of the EDL was first formally proposed by Helmholtz, who derived the charge distribution in the solution based on the simple molecular capacitor model .

In reality, the thermal motion of ions in the solution introduces a certain degree of chaos causing the ions to be spread out in the region of the charged surface, forming a ‘diffuse’ double layer. In that case, the analysis of the electronic environment near the surface is more complex and requires more detailed analyses . Gouy , Chapman and Stern put forward more accurate models for analysing the surface and electrolyte interfaces, making great contributions to the development of EDL theories. Gouy and Chapman independently developed theories of a so called ‘diffuse double layer’, in which the change in the concentration of the counter ions near a charged surface follows the Boltzmann distribution. The Gouy–Chapman theory provides a better approximation of the real system than the Helmholtz theory, but it still has limited quantitative applications. It assumes that ions behave as point charges and that there is no physical limit for the ions in their approach to the surface.

Then, the Gouy–Chapman diffuse double layer was modified by Stern so that ions have a finite size and cannot approach the surface closer than a few nanometres: the first layer of ions in the Gouy–Chapman diffuse double layer are not at the surface, but at some distance away from the surface. As a result, the potential and concentration of the diffuse part of the layer is low enough to justify treating the ions as point charges. Stern also assumed that some ions are probably adsorbed by the surface in a plane; this layer is known as the ‘Stern layer’ . Within this layer, thermal diffusion is not strong enough to overcome the electrostatic forces. In the diffusive outer layer, the ions are far enough from the solid surface and are subjected to weak electrostatic forces from the surface only, hence they remain mobile.

Adouble layer is formed to neutralize the charged surface, which in turn causes an electrokinetic potential between the surface and any point in the mass of the suspending liquid. This voltage difference is of the order of millivolts and is referred to as the surface potential. The magnitude of the surface potential is influenced by the surface charge and the thickness of the double layer. Starting from the surface, the potential drops off roughly linearly in the Stern layer and then exponentially through the diffuse layer, approaching zero at the imaginary boundary of the double layer. The potential curve is useful because it can suggest the electrical force strength between particles and the critical distance within which this force comes into play. A charged particle’s mobility is related to the dielectric constant and the viscosity of the suspending liquid, as well as the zeta potential, which is a potential at the boundary between the moving particle and the liquid. The boundary is called the slip plane and usually defined as the point where the Stern layer and the diffuse layer meet .



Schematic model of EDL

3. Capillary force

Capillary force is mainly due to the formation of liquid menisci (also termed the meniscus force), the ignificance of which was realized by Haines and Fisher . Capillary force can be classified into two types: normal capillary force and lateral capillary force . A comprehensive review of the normal capillary force was given by Butt and Kappl . Denkov et al and Kralchevsky and Nagayama contributed a lot to the study of the structure of colloid nanoparticles due to the lateral capillary force. Capillary forces should be considered in the studies on powders, soils and granular materials , the adhesion between particles or particles to surfaces and the stiction in micro/nano-electromechanical systems .It is also relevant to nanoparticle assembling or living cells selfassemble technologies .

The normal capillary force arises from the Laplace pressure within the curved meniscus formed by liquid condensation or vapour bridges around two adhering solid surfaces . It can be attractive or repulsive depending on whether the capillary bridge is concave or convex. Two equations are important to understand the capillary forces, i.e. the Young–Laplace equation and the Kelvin equation.

The Young–Laplace equation relates the curvature of a liquid interface to the pressure difference, while the Kelvin equation describes capillary condensation, which is the physical basis for many adhesion phenomena . Capillary condensation is the condensation of vapour into capillaries or fine pores even for vapour pressures belowthe saturation vapour pressure. The Kelvin equation relates the actual vapour pressure to the surface curvature of the condensed liquid. The normal capillary force is owing to two actions: one is the pressure difference across the curved interface and the other is the action of the surface tension force exerted around the annulus of the meniscus. Butt and Kappl gave the usual derivations and expressions for capillary forces between different geometries.

The origin of the lateral capillary forces is the overlap of the perturbations in the shape of a liquid surface due to the presence of attached particles . The larger the interfacial deformation created by the particles, the stronger the capillary interaction between them. The theories and expressions of lateral capillary forces for particles bound to interfaces, liquid films and biomembranes were included in a good review by Kralchevsky and Nagayama . The lateral capillary forces are effective in controlling small colloidal particles and protein macromolecules confined in liquid films to form fine microstructures.

4. Other forces—solvation, structural and hydration forces

Apart from vdW forces and EDL forces, some other forces, i.e. solvation, structural or hydration forces, come into play when two surfaces or particles approach very close (separation less than a few nanometres) in the liquid. These forces can be monotonically repulsive, monotonically attractive or oscillatory and they can be much stronger than either the vdW forces or EDL forces at small separations. Solvation, structural or hydration forces (in water) arise between two particles or surfaces if the solvent or water molecules become ordered by the surfaces .

When the ordering occurs, an exponentially decaying oscillatory force with a periodicity equal to the size of the confined liquid molecules, micelles or nanoparticles appears . Solvation forces depend not only on the properties of the liquid medium but also on the surface physicochemical properties, such as hydrophilicity, roughness, crystalline state, homogeneity, rigidity and surface micro-texture. These factors affect the structure of the confined liquids between two surfaces, which in turn affects the solvation force .

The hydration force is a strong short-range repulsive force between the polar surfaces separated by a thin polar liquid layer (thickness <3 nm); the force magnitude decays exponentially with the liquid layer thickness A well knowninterpretation of hydration force is that the solvent molecules are bound strongly and are restructured by polar surfaces. An ordered-solvent layer was formed at the surface-solution interface, which exponentially decays away from the surface; the overlap of the ordered-solvent layers near the two mutually approaching surfaces creates a force . The hydration force could determine the behaviours of many diverse systems, e.g., the colloidal dispersion stability, the swelling of clays and the interactions of biological membranes.

5. DLVO theory

The DLVO (Derjaguin–Landau–Verwey–Overbeek) theory as introduced by Derjaguin and Landau in 1941 andVerwey and Overbeek in 1948 for describing the stability of colloidal dispersions. The theory combines the effects of the vdW attraction and the electrostatic repulsion. It can explain many phenomena quantitatively in colloidal science, e.g., the adsorption and the aggregation of nanoparticles in aqueous systems, and describe the force between charged surfaces interacting through a liquid medium .

It can be seen that a strong long-range repulsion with a high energy barrier is present for highly charged surfaces in dilute electrolyte (i.e. long Debye length). When the surface charges are reduced or the concentration of the electrolyte solutions are increased, a small secondary minimum in the potential energy curve appears. Colloid particles may undergo a reversible flocculation due to the secondary minimum because of its weak energy barrier , resulting in slow particle aggregation for the surface with a low charge density. Below a certain surface charge or above a certain electrolyte concentration (known as the critical coagulation concentration), the energy barrier falls below the zero axis and particles then coagulate rapidly.

Consequently, the colloid system becomes unstable. Although the DLVO theory is the basis for understanding colloid stability and has a considerable amount of experimental support, it is inadequate for the colloid properties in the aggregated state. This is because short-range interactions are dominant in this state and the specific properties of ions should be taken into account rather than regarded as point particles.

Most deviations of experimentally measured forces from those expected from the DLVO theory are due to the existence of a Stern-layer or non-DLVO forces, e.g., ion-correlation, solvation, hydrophobic and steric forces .

6. Contact, adhesion and deformation theories of nanoparticles

In traditional contact theories for two objects in contact with each other under external forces, for instance, the simplest case of two interacting elastic spheres deduced by Hertz in 1882 , surface forces were not included. In these models, the displacement and the contact area are equal to zero when no external force is applied. However, as the size of the object is decreased to the nanoscale, the surface forces play a major role in their adhesion, contact and deformation behaviours.

Modern theories of the adhesion mechanics of two contacting solid surfaces are based on the Johnson–Kendall–Roberts (JKR) theory or the Derjaguin–Muller–Toporov (DMT) theory . The JKR theory is applicable to easily deformable, large bodies with high surface energies. Strong, short-range adhesion forces dominate the surface interaction; the effect of adhesion is included within the contact zone. In contrast, the DMT theory better describes very small and hard bodies with low surface energies . In this case, the adhesion is caused by the presence of weak, long-range attractive forces outside the contact zone.

Tabor introduced a nondimensional physical parameter, often referred to as Tabor’s parameter,o quantify the limits of JKR, DMT and the cases between them. The intermediate regime between the JKR and the DMT theories has also been described by Maugis using the Dugdale model ; a ‘transition parameter’ roughly equivalent to Tabor’s parameter was defined . A summary of the different conventions used for defining the ‘transition parameter’ was given by Greenwood . Carpick et al provided a simple analytic equation to determine the value of the ‘transition parameter’; it could closely approximate Maugis’ solution. The expansion of the JKR theory by Maugis and Pollock leads to the additional description of plastic deformation.

Although the Hertz, JKR and DMT theories have been widely used to study the mechanical properties of nanoparticles whether or not the continuum mechanics can be used to describe a particle at the nanometre scale is still in discussion. The molecular dynamics (MD) simulation method provides an opportunity to understand the atomistic processes in the contact region. Luan and Robbins researched the contact between two nanocylinders by MD simulations and found that the atomic-scale surface roughness produced by discrete atoms led to dramatic deviations from the continuum theory. Contact areas and stresses may be changed by a factor of two, whereas friction and lateral contact stiffness by an order of magnitude.

Also Miesbauer et al analysed the contact between two NaCl nanocrystals with MD simulations.

It was found that the Hertzian theory was a suitable description of the studied system when the system size was larger than 50Å; the discrepancy became more obvious as the particle was even smaller. Cheng and Robbin investigated the nanoscale contact with MD simulations to test the adaptability of continuum contact mechanics at the nanoscale; the results suggested that the continuum contact models could be applied to the case where the forces averaged over the areas containing many atoms. Nonetheless, the continuum theory, because of its concise expression, is still widely applied in the mechanical analysis at the nanoscale, such as designing micro/nanodevices , creating nanostructured materials with optimized mechanical properties and understanding the molecular origins of friction and adhesion .

Main Techniques for Studying Nanoparticles

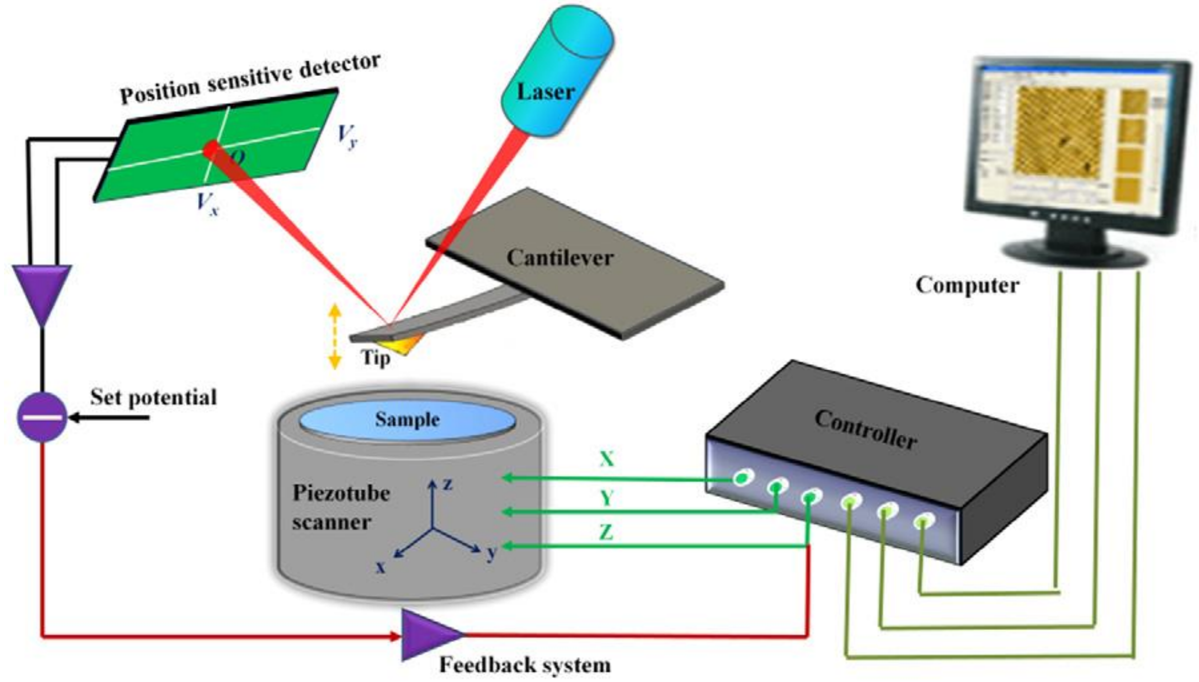
The research methods frequently used in studying the mechanical properties of nanoparticles will be briefly introduced as follows:

1. AFM techniques

AFM is a powerful technique that can be used to obtain both high-resolution images on many kinds of solid surfaces and the vertical force as well as lateral force between a sharp tip and the surface . Briefly, the sharp tip scans over the sample and the deflection of the cantilever is quantified through a laser beam reflected off the backside of the cantilever and received by the photoelectric detector.

If a constant force is kept between the tip and sample during scanning, the topographic image of the sample surface can be obtained by plotting the height of a sample stage on the piezoscanner, which is controlled by a feedback system.

Alternatively, the interaction force between the tip and sample can be obtained with the cantilever's vertical deflection using the force-versus-distance curves, briefly called force curves, together with Hooke's law . These curves can provide valuable information on some of the important properties of nanoparticles, such as hardness, elastic modulus and the adhesion between nanoparticle and substrate. The lateral force is closely related to the torsional deflection of the cantilever; an accurate value can be obtained after careful calibration of the cantilever's torsional coefficient . More details about the basics of AFM can be seen in.



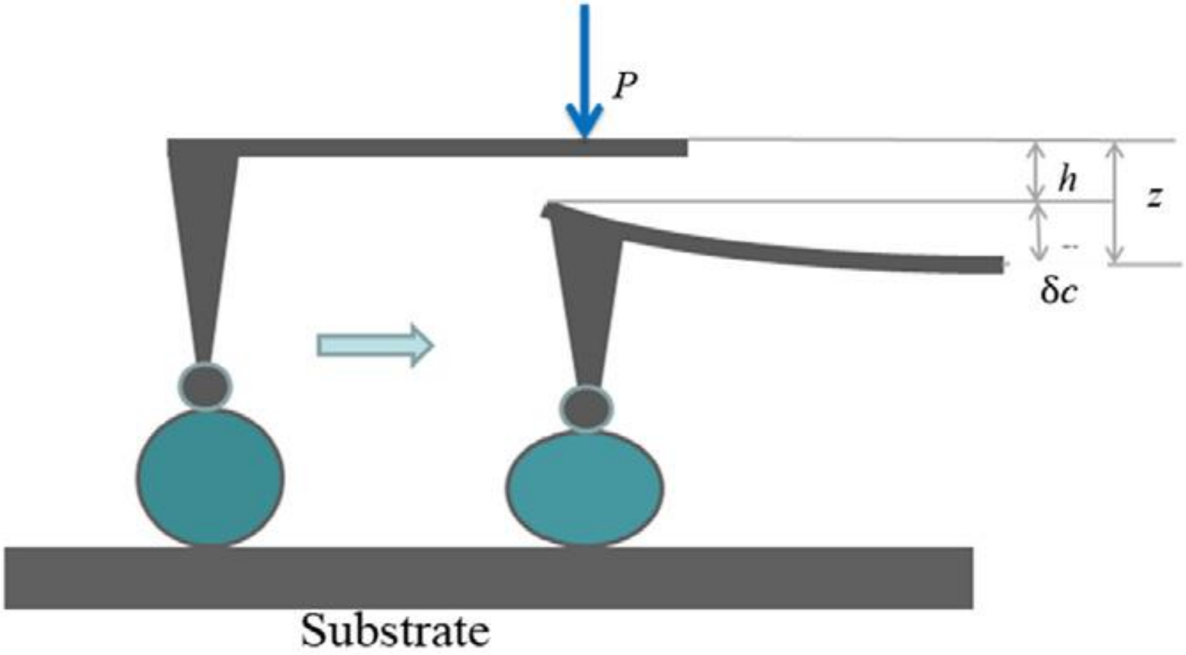
Schematic diagram of the basic working principle of AFM

2. Particle tracking velocimetry (PTV)

PTV is an image-based velocimetry method of measuring the velocity field and tracking individual particles in fluidic systems . Fluorescent particles are usually used as tracers within a defined area where those particles are illuminated; then pictures of these particles are taken. The motion trajectories of the particles can be reconstructed by locating them in those pictures and the velocities of the particles can be calculated correspondingly. Based on these, deep insight into some of the complex and low-velocity flows in a region can be acquired. It is a technique that is slightly different from particle image velocimetry (PIV) where the particles' displacements within a segment of an image are averaged . Currently, there are mainly two different PTV methods, i.e. two-dimensional particle tracking velocimetry (2D-PTV) and three-dimensional particle tracking velocimetry (3D-PTV) . The defined area is a thin light sheet for 2D-PTV while it is an illuminated volume for 3D-PTV, which is usually based on a multiple-camerasystem.

3. In situ TEM

TEM could provide images with a significantly higher resolution than a light microscope by using electrons as ‘light source’ which have a much lower wavelength . The basic principle is that a beam of electrons passes through a very thin sample and, after interacting with the atoms in the sample, some unscattered electrons reach a fluorescent screen to form an image. The image is shown in varied darkness indicating the material density in different parts of the specimen. The image is magnified and can be studied directly from the screen or recorded with a camera for post-analysis. In situTEMoffenrs the capability of real-time observation of the responses of the microstructural evolution of nanostructures to external active stimuli and their relationship with properties . Active stimuli applied to the sample examined in the microscope during simultaneous imaging include mechanical , thermal and electrical ones, etc.



Relative displacements and deformations of the particle-AFM tip system during the indentation process. Left: the AFM tip just touches the particle without deformation of the particle. Right: the particles’ deformation occurs due to the applied force by the AFM tip.

4. MD simulation

Computational simulations are usually considered as very useful complementary tools to experimental studies on the mechanical properties of nanoparticles . Among many different kinds of computation methods, MD simulation is an important aspect which could model the time evolution of the physical motions of interacting atoms or molecules. It is a computation method that is based on statistical mechanics; statistical ensemble averages are normally hypothesized to be equal to the time averages of the system. Mostly, in MD simulation, Newton's equations of motion for the atoms or molecules in a system are numerically solved to get their positions and velocities and finally to describe the thermodynamic behaviours of the system. The interactions and potential energy between atoms or molecules are defined by a molecular mechanics force field.

Basic Mechanical Properties of Nanoparticles

1. Hardness and elastic modulus of nanoparticles

Understanding some basic mechanical properties of nanoparticles, such as the hardness and the elastic modulus, will aid a lot in the proper design of particles in specific applications, as well as evaluating their roles and action mechanisms. To the authors' knowledge, the measurement of the mechanical properties of microparticles has been developed for decades.

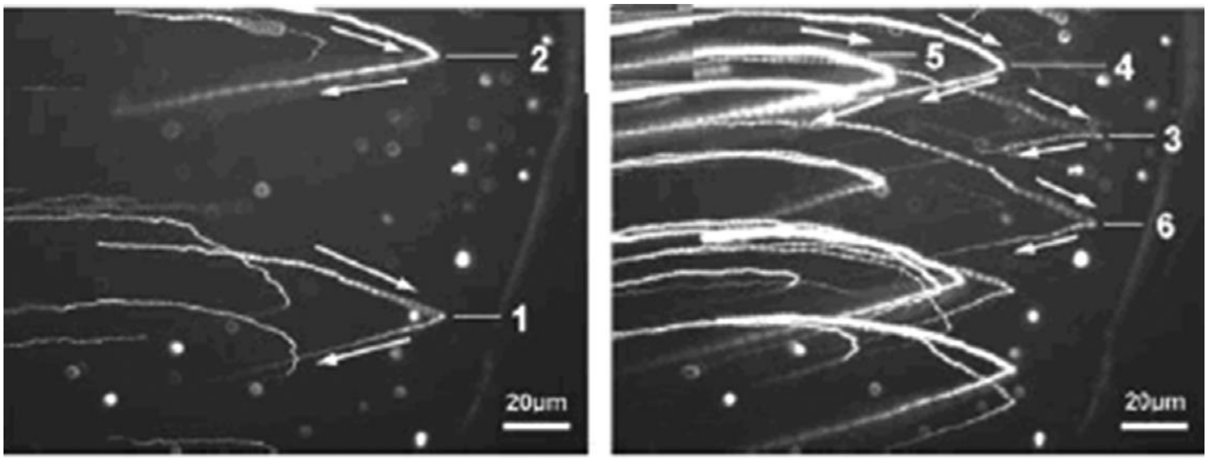
The microindentation technique was used by Steinitz in 1943 to test the hardness of microparticles with indented areas of larger than 100μm2 and a minimum indenter size of 20μm2

2. Adhesion and friction of nanoparticles

The adhesion and the friction of nanoparticles play important roles in nanofabrication, lubrication, the design of micro/nano devices, colloidal stabilization and drug delivery. In this case, characterizing the adhesion and friction behaviours of nanoparticles has attracted significant research interest over the past decade.

3. Movement of nanoparticles

Various forces such as gravitational (buoyancy) forces, surface forces, viscous flow forces and the forces due to Brownian motion result in the movement of nanoparticles in the media in different way. However, the experiments for the direct observation of nanoparticles' movement are limited primarily due to the small particle size preventing the application of the most commonly used imaging techniques. Fortunately, the rapid development of measurement technology provides opportunities for tracking individual nanoparticles or even single molecules. Up to now, several methods have been used for making high-resolution measurements of the motion of single nanoparticles. Among these methods, two groups can be classified: one is to passively track the particle motion without applying significant external stimuli and the other is to measure the particles'



The particle trajectories in a water droplet during the evaporation process motions under external mechanical forces . To be more specific, studies based on two typical methods will be emphasized in the following parts. The first method is particle tracking with the fluorescence technique. The second method is the TEM observations, which could give more delicate details of the particle movement and provide deeper understanding of the roles of particles in specific applications.

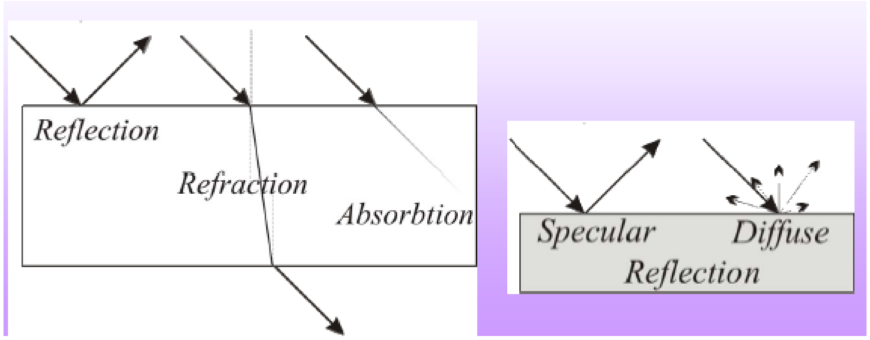
Optical Properties of Nanomaterials

Optical Properties

Many of the optical properties are closely related to the electrical and electronic properties of the material. But as we shall see other factors also come into the picture when dealing with optical properties.

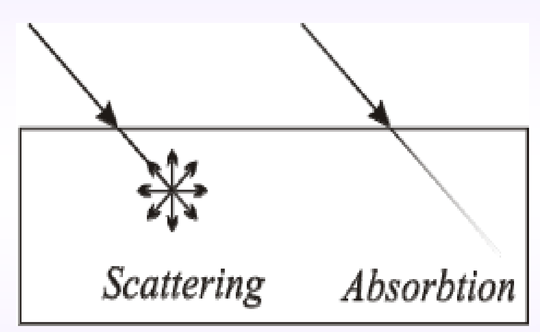
*When one is talking about optical properties, one is usually referring to the interaction of electromagnetic radiation with matter. The simple picture one can start with is by considering a 'ray' of an electromagnetic wave of a single frequency entering a medium from vacuum. This ray could be reflected, transmitted (refracted) or absorbed.

*The reflection could be specular or diffuse.



*From a more fundamental perspective, there are only two possibilities (of interaction of a medium with electromagnetic radiation): (i) scattering & (ii) absorption

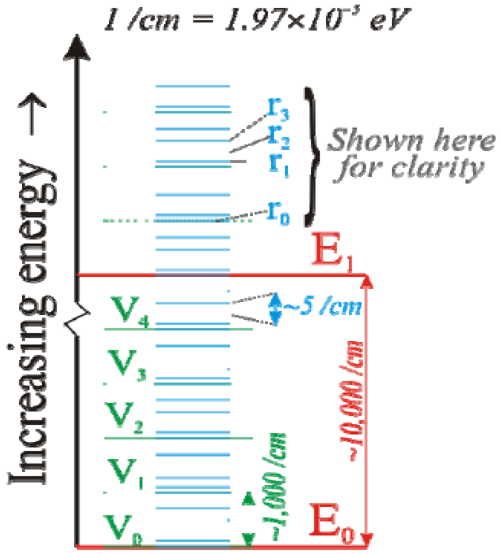
*If one considers a wider spectrum of frequencies, then some part of the spectrum could be absorbed while the other frequencies could be scattered.



*Absorption essentially involves activating some process in the material to take it to an excited state (from the ground state). These processes are: (i) electronic, (ii) vibrational and (iii) rotational excitations

*Further part of the absorbed energy could be re-emitted.

*If the absorbed energy is dissipated as heat, this is called dissipative absorption.



*When an electromagnetic wave impinges on an atom (or a material containing an atomic species), the electron cloud is set into oscillation. This situation is like a dipole oscillator, which emits radiation of the same frequency in all directions. This is the process of scattering. Similar to absorption, scattering is also frequency dependent.

*There are two possible ways in which transmission can take place: (i) if the medium is sparse, the ray (wave) could just pass through the particles of the medium (like in vacuum), which essentially means there is no interaction; (ii) but the more common mechanism for 'denser media' is 'forward scattering' (i.e. what we call as transmission in common usage is actually forward scattering).

*When a wave is being transmitted form one medium (say vacuum) to another, its frequency remains constant, but its velocity decreases (the wave being slower in the medium). The ratio of the velocities c/vmedium is called the refractive index (n):

$$n = \frac{c}{v} = \sqrt{\frac{\varepsilon\mu}{\varepsilon_0\mu_0}} = \sqrt{K_E K_M}$$

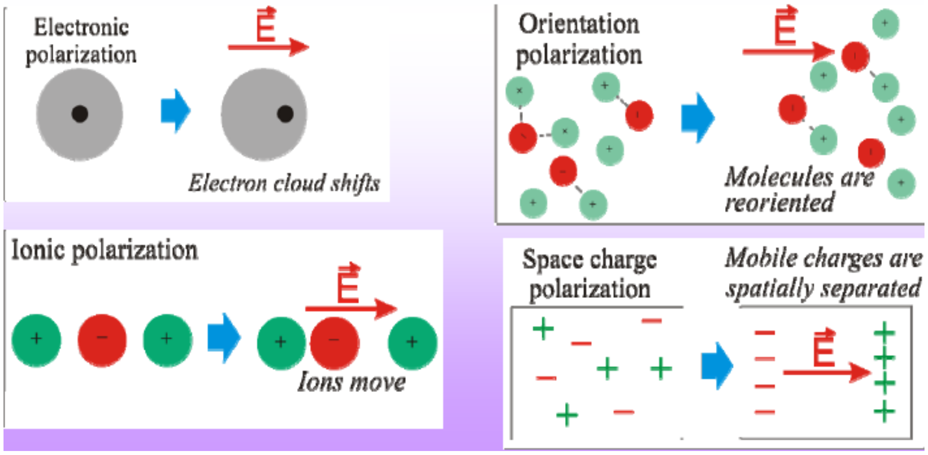
$$K_E = \frac{\varepsilon}{\varepsilon_0}$$

$$K_M = \frac{\mu}{\mu_0}$$

Where, Ɛ is permittivity of the medium and µ is the permeability of the medium. The subscript '0' refer to these values in vacuum. KE is the relative permittivity (dielectric constant) and KM is the relative permeability of the medium.

Usually KM is close to unity. KE is a function of the frequency of the electromagnetic wave and leads to the phenomenon of dispersion (e.g. dispersion of white light by a prism into 'VIBGYOR' colours).

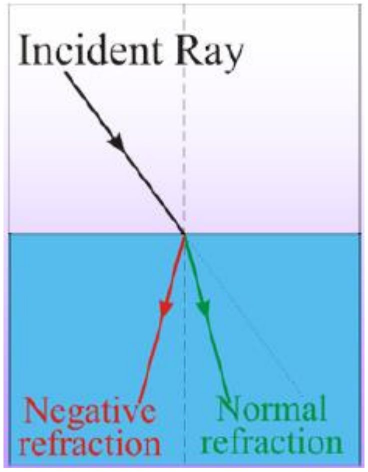
*Physically, the origin of the dependence of 'n' on frequency is due to three factors: (i) orientational polarization (ii) electronic polarization (iii) ionic polarization (iv) space charge.



*Usually the refractive index (n) is greater than one (n>1), but under certain circumstances it can be less than one (n < 1) or even be negative (n < 0).

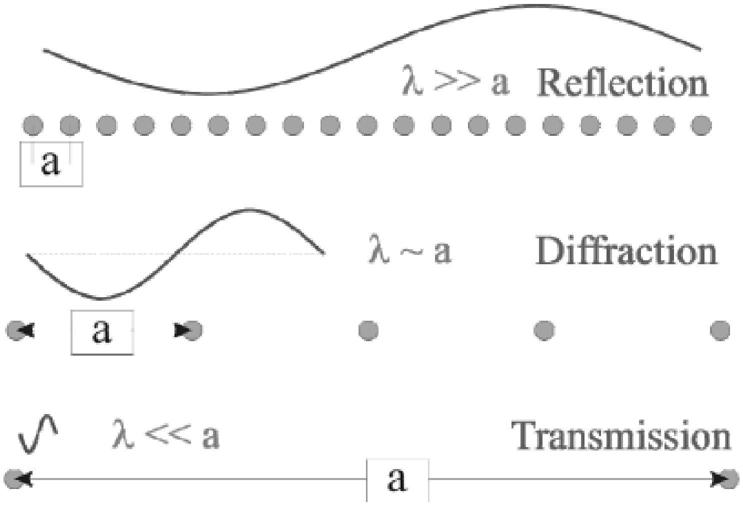
*n <1 implies that light is traveling faster than speed of light which is in 'apparent' contradiction to the theory of Relativity. In cases where n < 1, the velocity which one needs to consider (instead of the 'phase velocity') is the 'group velocity (vg)' (or in still other cases the 'signal velocity' (vs)), which will be less than 'c'. **[**i.e. causality will not be violated!**]**.

*In negative refractive index materials (or typically structures) the refracted beam (in the medium) will be on the other side of the normal.



*A special kind of scattering of importance to materials science is diffraction. Diffraction is nothing but 'coherent reinforced scattering' and comes into play in periodic and quasiperiodic structures. The incoming 'coherent beam' (assumed monochromatic for now) energy is redistributed in space as 'transmitted' and diffracted beams. The transmitted beam in this case is a forward diffracted beam. If there are an array of scatters (1D) with spacing 'a', a schematic of dominant regimes of the three possible outcomes which can take place.

*Though in our discussions here we have considered EM waves, phenomena such as scattering and diffraction are true for all kinds of waves. Young's double slit experiment performed in a ripple tank (with water as the medium) is a good example of scattering and interference, which does not involve EM radiation.



Interaction of electromagnetic radiation with metals: Absorption in metals

*Plasmons (akin to phonons for lattice vibrations) are collective oscillations of free electrons.

*Bulk plasmons are longitudinal oscillations of electrons gas w.r.t. the ion cores.

*Incoming visible electromagnetic radiation sets up plasmon oscillations and hence is absorbed (bulk metals are opaque in the visible region).

Optical properties of semiconductors

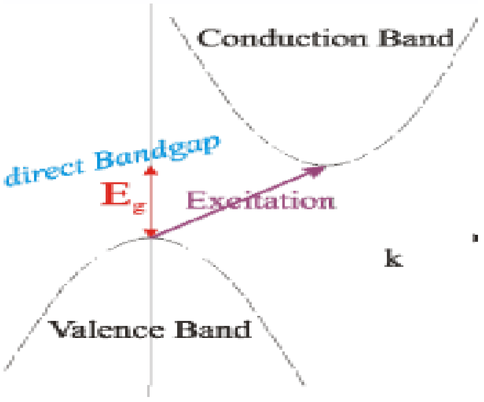
*Ionic crystals show strong absorption and reflection in the IR region (due to interaction of light with optical phonons). Compound semiconductors (GaAs, GaP etc.) have a partial ionic character to their bond and exhibit absorption and reflection in the IR.

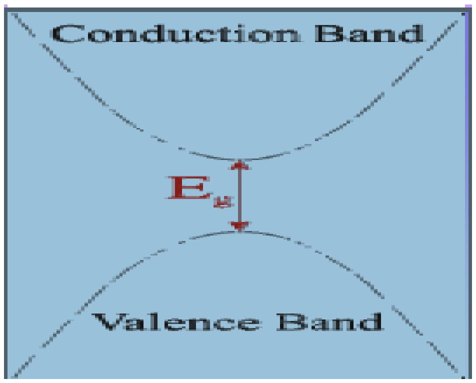
*If energy of the incoming photon is greater than the band gap then the photon can be absorbed. □□h□ > Eg □□□0 = Eg /h is known as the absorption edge.

*As the wave vector of a photon in the optical region is very small (only constant momentum transfers are allowed across the bandgap) →vertical transitions in k-space are allowed (valence to conduction band).

*As the bandgap in semiconductors is ~ 1eV the fundamental edge occurs in the IR.

*In indirect bandgap semiconductors both photon and phonon needs to be absorbed (the phonon energy ~ 0.05eV and can be ignored and hence it can be thought of as contributing only momentum to the electron).



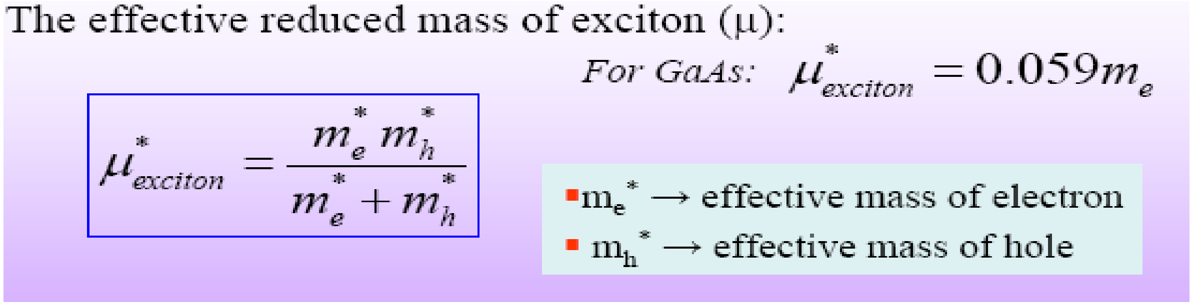


Exciton

*Exciton is a bound state of an electron and hole. The binding is due to electrostatic (Coulomb) attraction →the exciton has lower energy than the unbound electron + hole. □□This brings the energy levels closer to the conduction band (and the Bohr radius increases)

*It is an electrically neutral quasiparticle that exists in insulators and semiconductors.

*The exciton can be considered as an elementary excitation in materials which can transport energy without transporting electric charge (excited state can travel through lattice without transfer of charge). **[**The free exciton (Mott-Wannier) can move in the crystal. Exciton trapped by an impurity is a bound exciton (has a higher binding energy than free exciton)**]**.



The effective reduced mass of exciton (μ):

For GaAs: $\mu^*_{exciton} = 0.059 m_e$

$$\boxed{\mu^*_{exciton} = \frac{m^*_e m^*_h}{m^*_e + m^*_h}}$$

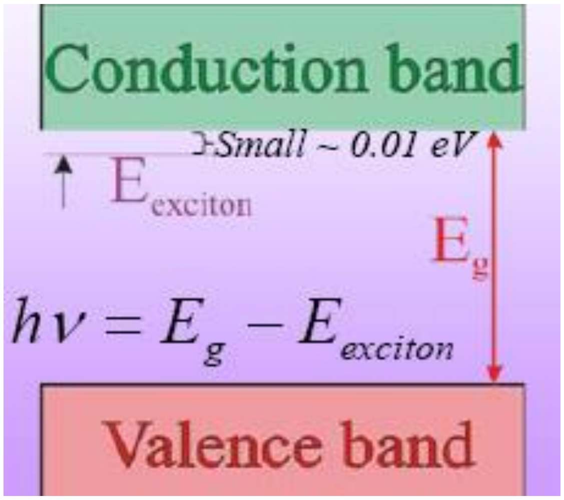
- m_e^* ⟶ effective mass of electron
- m_h^* ⟶ effective mass of hole

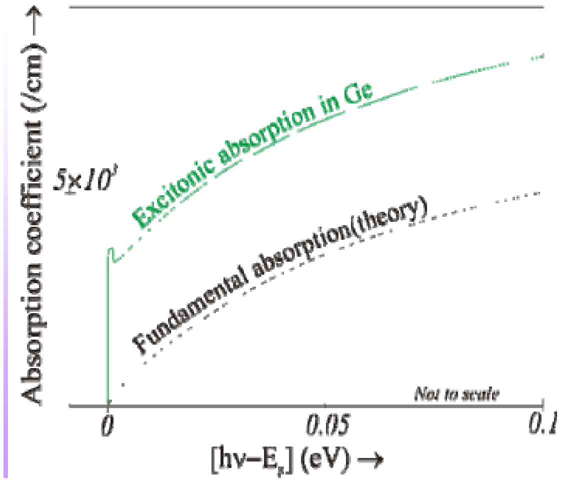
*Photon absorption by a semiconductor can lead to the formation of an exciton.

*The exciton binding energy for most semiconductors is in the range of few to few 10s of meV (milli-electron volts) **[**Eexciton (GaAs)= 4.6 meV, Eexciton (CdS)= 28 meV**]** . For comparison:the binding energy of H2 atom is 13.6 eV and □□kT at room temperature is 40 meV.

*Given the small value of Eex →an exciton can be dissociated by thermal energy at RT.

*The exciton spectrum has a sharp line, just below the fundamental edge →usually observed at low temperature where thermal energy is lower than the binding energy.



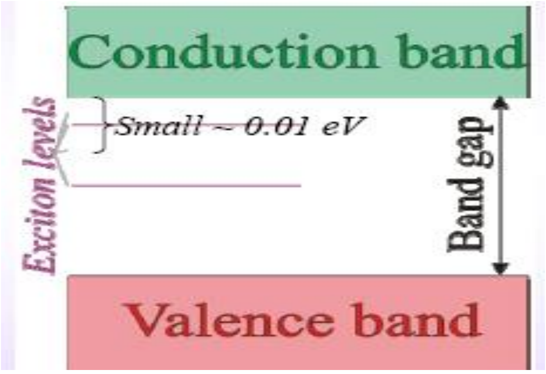


❑The exciton diameter can be calculated as:

$$r_{Bohr}^{Exciton} = \frac{\varepsilon r_B m_e[1+(m_e^*/m_h^*)]}{\varepsilon_0 m_e^*}$$

$$r_{Bohr}^{Exciton} = \frac{\varepsilon_0 \varepsilon h^2}{\pi \mu e^2}$$

- r_B → Bohr radius in the absence of exciton
- ε → dielectric constant of the medium
- ε_0 → dielectric constant of free space
- m_e → mass of free electron
- m_e^* → effective mass of electron
- m_h^* → effective mass of hole



EXCITON RADIUS HAS NANOSCALE

	Exciton energy (meV)	Exciton radius (nm)	Band –gap energy (eV)
GaAs	4.6	~11.8	1.43
CdSe		5	1.74
Cds	28	~3(2.4)	2.58

Hydrogen atom ground state :13.6 eV

If the dimension of the crystal ˜of the exciton diameter (or less)—› confinement effects become prominent .

Optical Properties of Nanomaterials:

Size effect on optical properties-

*Bulk metal samples absorb electromagnetic radiation (say visible region). Thin films of metals may partially transmit, just because there is insufficient material to absorb the radiation. Au films few 10s of nm thick become partially transparent.

*Apart from ‘insufficient material’ effects, there are important phenomena which come into play in nanomaterials.

*These include: dominance of surface plasmons, quantum confinement effects, etc.

*E.g. in semiconductor quantum dots optical absorption and emission shift to the blue (higher energies) as the size of the dots decreases.

*The size reduction is more prominent in the case of semiconductors as compared to metals (i.e. quantum size confinement effects become more important in metals at smaller sizes than semiconductor crystals).

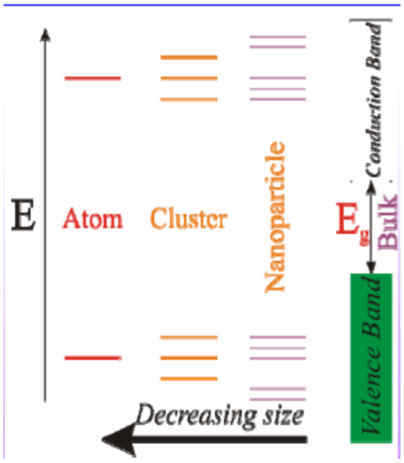
*We have already seen that at very small sizes metal nanoparticles can develop a bandgap (can become a semiconductor or insulator).

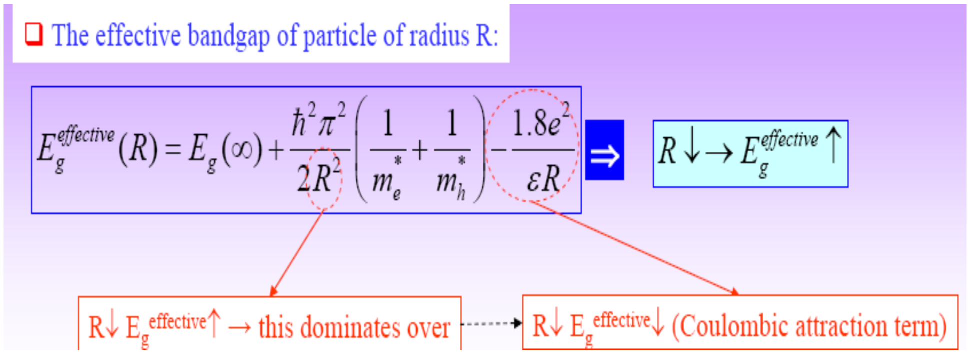
Semiconductor nanoparticles & films-

*On decreasing the size the electron gets confined to the particle (confinement effects) leading to: (i) increase in bandgap energy and (ii) band levels get quantized (discrete).

*Surface states (trap states), which lie in the bandgap become important →alter the optical properties of nanocrystals.

*The energy level spacing increases with decreasing dimension →Qunatum Size Confinement Effect



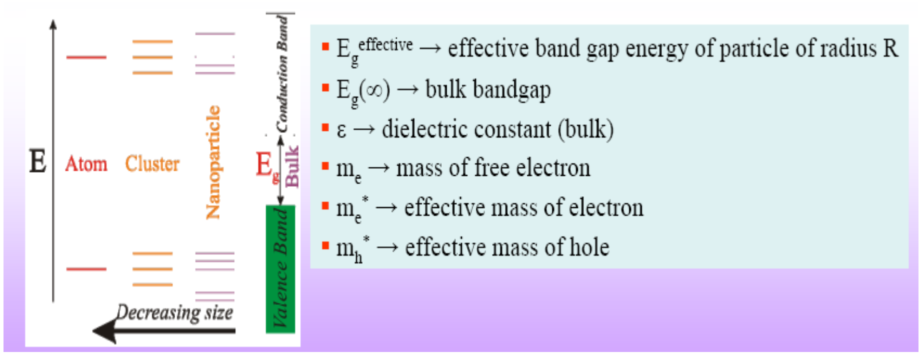


❑ The effective bandgap of particle of radius R:

$$E_g^{effective}(R) = E_g(\infty) + \frac{\hbar^2\pi^2}{2R^2}\left(\frac{1}{m_e^*}+\frac{1}{m_h^*}\right) - \frac{1.8e^2}{\varepsilon R} \Rightarrow R\downarrow \rightarrow E_g^{effective}\uparrow$$

$R\downarrow E_g^{effective}\uparrow$ → this dominates over

$R\downarrow E_g^{effective}\downarrow$ (Coulombic attraction term)

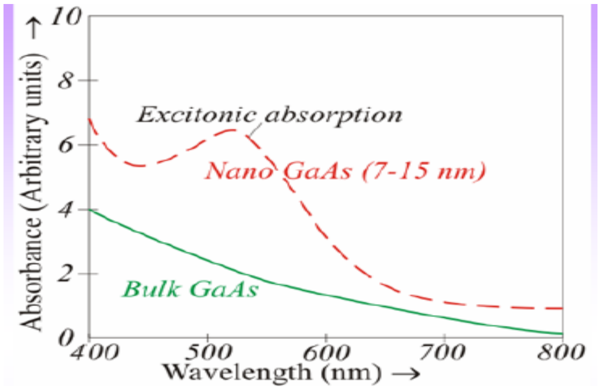


- $E_g^{effective}$ → effective band gap energy of particle of radius R
- $E_g(\infty)$ → bulk bandgap
- ε → dielectric constant (bulk)
- m_e → mass of free electron
- m_e^* → effective mass of electron
- m_h^* → effective mass of hole

In nano-GaAs (with size range 7-15 nm) a broad excitonic peak at 526.0 nm (2.36 eV) is seen →energy gap of the nano-GaAs has been blue shifted by 0.93 eV **[**bulk band gap (1.43 eV)**]** due to the QSE.

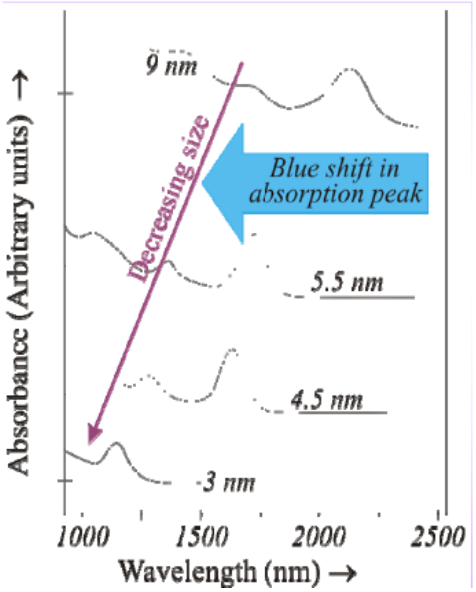
*Enhancement of absorbance over the range of wavelengths seen →enhanced oscillator strength (dimensionless quantity to express the strength of the transition).

*The excitonic peak is broad due to the size distribution of crystallites.**[**63**]**



GaAs nanocrystalline thin film (nano-GaAs) deposited on ITO substrate

*With reducing size of the particle the density of states becomes more quantized and the band gap shifts to higher energies (shorter wavelengths) →the absorption spectrum shows a blue shift



Absorption spectra of PbSe nanocrystals

Photoluminescence-

*In photoluminescence material is excited by EM radiation, followed by relaxation to ground state by emission of photons.

*When the semiconductor relaxes to the ground state by recombination of electron and hole, a photon is emitted.

*If the photon energy lies in the range 1.8 - 3.1 eV the radiation will be in the visible range →luminescence.

*By changing the size of the nanoparticles the frequency of emission can be tailored.

*As the size of the nanoparticles decrease →'blue shift' in frequencies.

Properties of core-shell nanostructures: semiconductor on semiconductor-

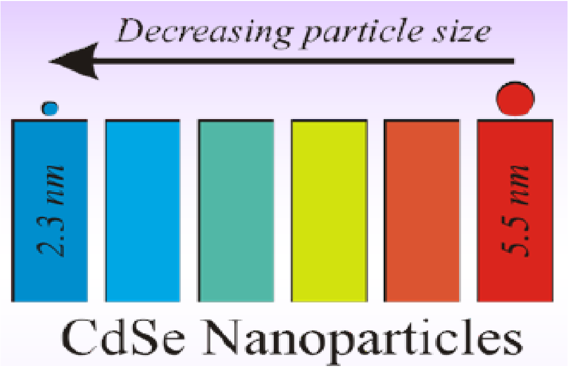
*The luminescent properties are a characteristic of the core.

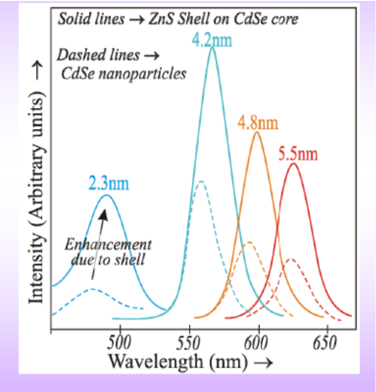
*The shell leads to an enhancement of the luminescent properties of the core (the luminescence of nanoparticles are well defined with narrow spectral ranges, which depend on particle size).

*Deposition of a semiconductor with a larger bandgap than that of the core typically results in ‘luminescence enhancement’ due to the suppression of radiationless recombination mediated by surface states.

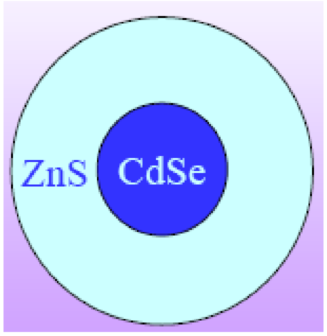
*E.g. CdS coated with MoS4 , ZnSe coated with CdSe, CdSe coated with CdS. Bandgaps tunable in the near-IR, which can be useful as IR biological luminescent markers.

Fluorescence from core-shell quantum dots-[64]





Fluorescence emission of (CdSe)ZnS core-



Colour of metallic nanoparticles-

*Gold nanoparticles were used as a pigment of ruby-colored stained glass dating back to the 17th century. 1-10 nm sized particles give rise to this colour.

*Thin film of Au (~100nm or less) will transmit blue-violet light.

*The colour of metallic nanoparticles depends on size in the nanoscale regime.

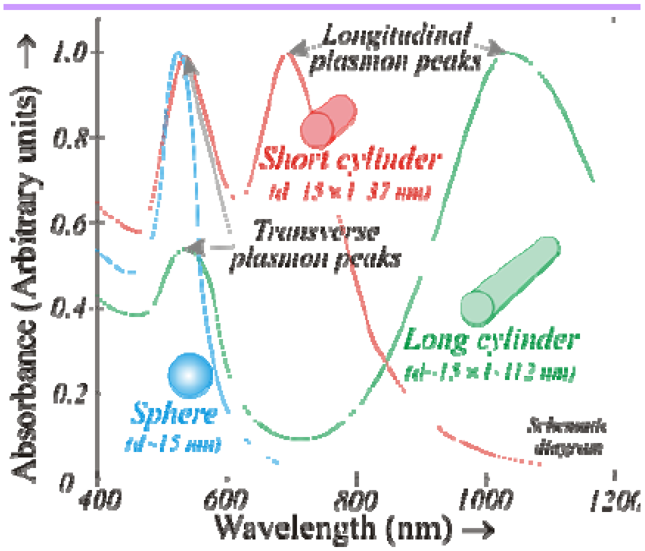
*Bulk Au is ‘golden’ yellow colour. Nanoparticles of gold (colloidal) can have red, purple or blue colour. The colour depends on the size (& shape) of the particle and the dielectric properties of the medium.

*Surface plasmons are excited by incident electromagnetic radiation.

*Surface plasmons have lower energy than bulk plasmons which quantize the (or plasma).

*MFP of Au, Ag ~50 nm □for particles smaller than this there will be no scattering within the particle and all the interactions will be with the surface.

*In particles with shape anisotropy (e.g. cylinders) more than one type of plasmon absorption peak may be observed.



For the sphere (d~15nm) only the Transverse plasmon peak is observed (□~ 520nm).

If the radius of the sphere is doubled (d~30nm), the transverse plasmon absorption peak will only shift slightly →this is unlike semiconductor nanoparticles where the absorbance is strongly affected by size in the nanoscale.

For the cylinder both the surface and longitudinal plasmon peaks are observed.

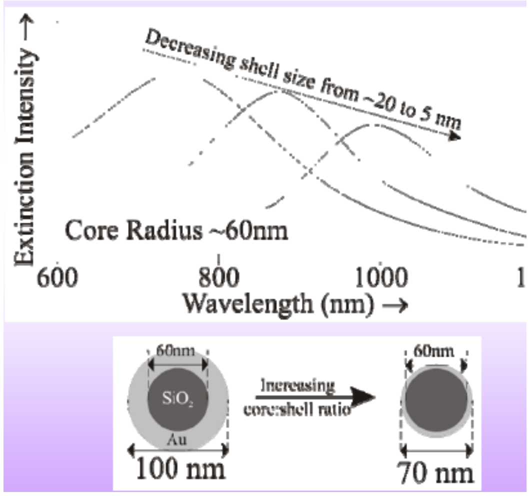
For the longer cylinder the longitudinal plasmon peak shifts to longer wavelengths.

Many applications has been envisaged due to large enhancement of surface electric field.

Properties of core-shell nanostructures: metal on dielectric-

*In Au shells coated on SiO2 cores the plasmon band depends on the core radius and on the core to shell ratio.

*Increasing core to shell ratio red-shifts the plasmon resonance band.**[65]**



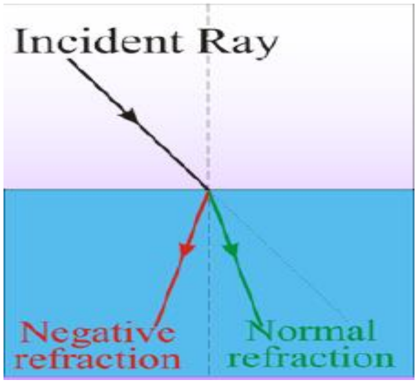
Metamaterials (with negative refractive index)-

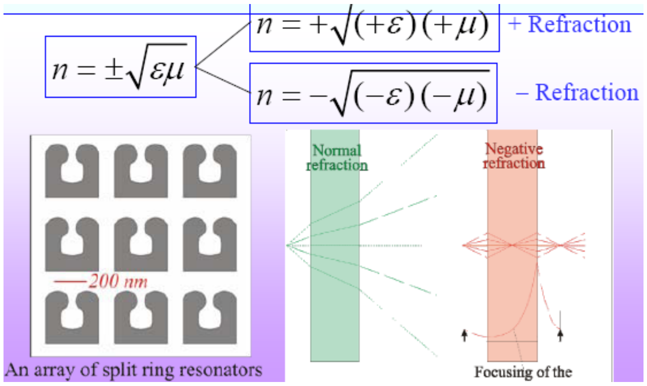
*Negative index metamaterials (negative index materials) are man made structures where the refractive index has a negative value (typically over some frequency range). □□So far this has not been discovered in natural materials.

*Metamaterials have been made with negative effective permittivity and permeability.

*A crystal with Magnetic Split Ring Resonator (SRR) as the motif can be used for the construction of a negative refractive index material.

*When the SRR scale is of the order of ~200nm →negative refractive index can be obtained in the mid-infrared range (100 THz)**[65]**

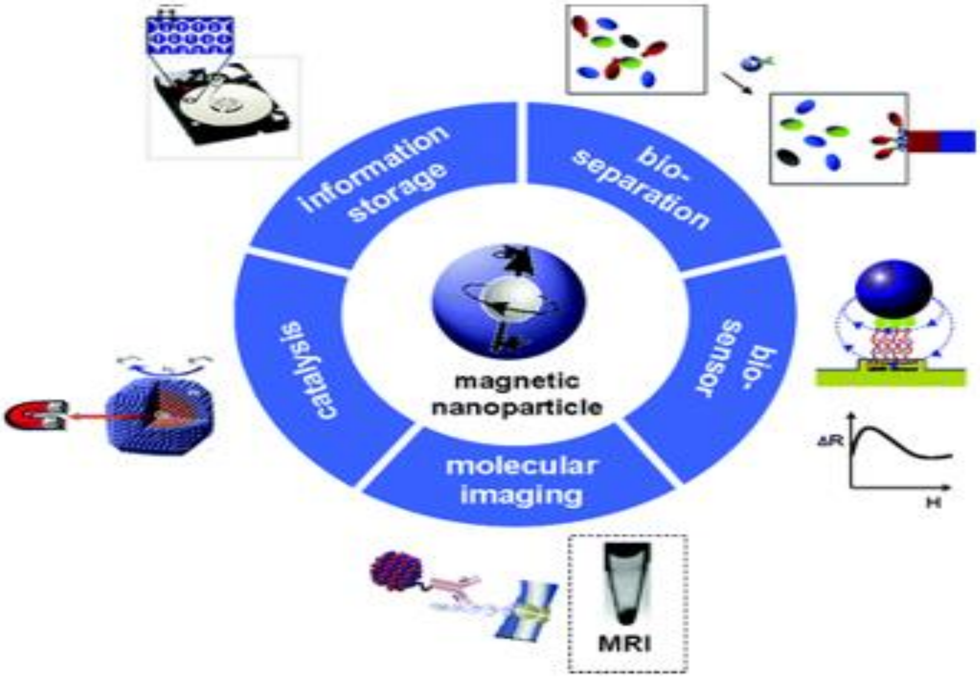




Magnetic Properties of Nanomaterials

Magnetic nanoparticles are nanomaterials consist of magnetic elements, such as iron, nickel, cobalt, chromium, manganese, gadolinium, and their chemical compounds. Magnetic nanoparticles are superparamagnetic because of their nanoscale size, offering great potentials in a variety of applications in their bare form or coated with a surface coating and functional groups chosen for specific uses. Especially, ferrite nanoparticles are the most explored magnetic nanoparticles, which can be greatly increased by clustering of a number of individual superparamagnetic nanoparticles into clusters to form magnetic beads.

Magnetic nanoparticles can be selective attached to a functional molecules and allow transportation to a targeted location under an external magnetic field from an electromagnet or permanent magnet. In order to prevent aggregation and minimize the interaction of the particles with the system environment, surface coating may be required. The surface of ferrite nanoparticles is often modified by surfactants, silica, silicones, or phosphoric acid derivatives to increase their stability in solution. In general, coated magnetic nanoparticles have been widely used in several medical applications, such as cell isolation, immunoassay, diagnostic testing and drug delivery.**[**66**]**



Advantages of Magnetic Nanoparticles:

There had been a growing interest on the properties and broad range of applications of colloids in recent years.magnetic biomaterials provide te ability to be directed and concentrated within the target tissue by means of eternal magnetic field and to be removed once therapy was completed.

Magnetic nanoparticles display the phenomenon of supermagnetism, not keeping magnetized after the action of magnetic field, offering advantage of reducing risk of particle aggregation (RuizHernandez et al,2008).fiest they have sizes that place them at dimensions comparable to those of a virus, a protein or a gene(Tartaj et al,(Tartaj et al,2004). The magnetic nanoparticles, whichused in bioapplications are usually made from biocompatible materials such as magnetic for which susceptibility is large(Sachn Shaw et al, 2009)

Properties

1. Magnetic Property

The properties of magnetic nanoparticles depend on the synthesis method and chemical structure. In most cases, the magnetic nanoparticles range from 1 to 100 nm in size and can display superparamagnetism. Superparamagnetism is caused by thermal effects that the thermal fluctuations are strong enough to spontaneously demagnetize a previously saturated assembly; therefore, these particles have zero coercivity and have no hysteresis. In this state, an external magnetic field is able to magnetize the nanoparticles with much larger magnetic susceptibility. When the field is removed, magnetic nanoparticles exhibit no magnetization. This property can be useful for controlled therapy and targeted drug delivery.

The behavior of substances under an influence of an external magnetic field is determined by two factors: susceptibility and permeability.

Susceptibility (χ) describes the magnetization level (M) of a material in the presence of an external magnetic field (H):

$$M = \chi H$$

These materials in the presence of external magnetic field induce weak magnetic moment antiparallel to external field. Therefore they have small and negative susceptibility .When the external field is removed, the spins come back to initial position and they do not show magnetic features. Water, wood, quartz (SiO2), copper, silver, and most of organic compounds are examples of diamagnetic materials. The common property of this material is that all of them have filled electronic subshells .

Paramagnetic

Paramagnetic substances show weak magnetic field in parallel to applied external field. The susceptibility of these is positive .After elimination of external field, their magnetic moment does not persist. Aluminum, oxygen, magnesium and lithium have paramagnetic properties.

Ferromagnetic

Ferromagnetic materials are also known as magnets have a large and positive susceptibility. The susceptibilities of ferromagnetic substance are determined by external field, temperature and their atomic structures. Unlike two other categories, their magnetic properties are persistent even after elimination of magnetic field. Indeed, after employing of strong magnetic field, the spins of substance are aligned with field. In this time, the maximum magnetization that is named saturation magnetization is obtained. When the magnitude of the field is decreased, the reduction of total magnetization is occurred due to returning of spins to their first directions. However, the magnetic moment of these materials is stable even in the zero field .

In addition, small ferromagnetic materials with the size in the range of tens of nanometers have one large magnetic moment. In the blocking temperature, particles can rotate freely. Therefore after elimination of external field, net magnetization is lost and it becomes zero. Indeed, in this condition, they show superparamagnetic properties. They have higher magnetic susceptibilities in comparison to paramagnetic materials.

By this features, they can preserve their colloidal stability and be useful for biomedical applications. As mentioned earlier, the superparamagnetic properties are observed in small particles but decreasing of size is associated by several important issues. After reduction of size, the surface effects are revealed because of increasing the surface-to-volume ratios .

2. Magnetocaloric Effect

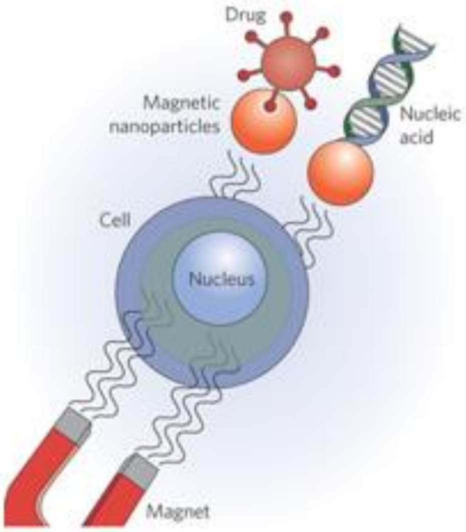
Some magnetic materials heat up when they are placed in a magnetic field and cool down when they are removed from a magnetic field, which is defined as the magnetocaloric effect (MCE). Magnetic nanoparticles provide a promising alternative to conventional bulk materials because of their particle size-dependent superparamagnetic features. In addition, the large surface area in magnetic nanoparticles has the potential to provide better heat exchange with the surrounding environment. By careful design of core-shell structures, it would be possible to control the heat exchange between the magnetic nanoparticles and the surrounding matrix, which provide a possible way for improving therapy technologies, such as hyperthermia.**[**67**]**

Applications

1. Magnetic separation

Properties and Applications of Magnetic Nanoparticles

In a biomedical study, Isolation and separation of specific molecules including DNAs, proteins, and cells are prerequisites in most fields of biosciences and biotechnology. Among various bioseparation methods, magnetic nanoparticles based bioseparation is mostly documented and widely used due to its unique magnetic separation mood and promising efficiency.



In the process, the biological molecules are labeled by magnetic nanoparticles colloids and then subjected to separation by an external magnetic field, which may be applied for cell isolation, protein purification, RNA/DNA extraction, and immunoprecipitation.

Magnetic nanoparticles particles such as beads have been extensively used for separation and purification of cells and biomolecules, due to their small size, promising separation mood, and good dispersibility. One of the trends in this subject area is the magnetic separation using antibodies conjugated with beads to provide highly accurate antibodies that can specifically bind to their matching antigens on the surface of the targeted sites.

2. Diagnostics

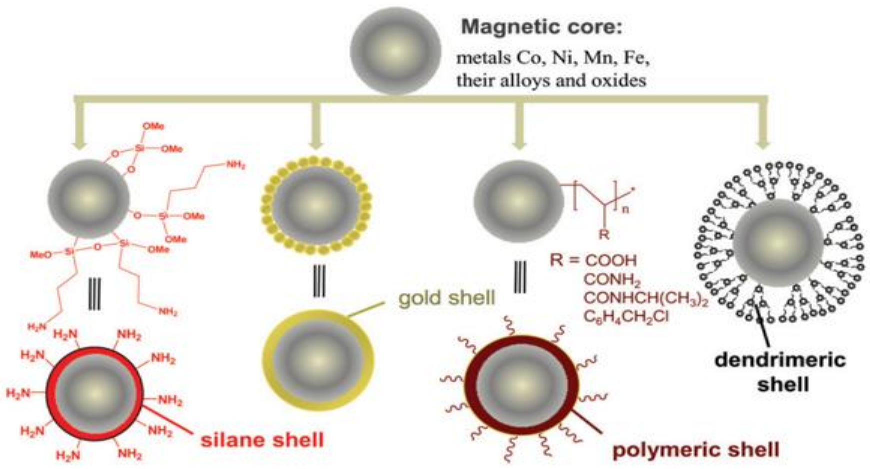
Non-invasive imaging methods have been developed by labeling stem cells using magnetic nanoparticles. Among them, Magnetic Resonance Imaging (MRI) is widely used as diagnostic tools to present a high spatial resolution and great anatomical detail to visualize the structure and function of tissues. Several kinds of magnetic nanoparticles have been developed to improve contrast agents in MRI imaging, with significant benefits of improved sensitivity, good biocompatibility and ready detection at moderate concentrations.

3. Sensors

Many types of magnetic nanoparticles-based biosensors have been surface functionalized to recognize specific molecular targets, due to their unique magnetic properties which are not found in biological systems. Due to different composition, size and magnetic properties, magnetic nanoparticles can be used in a variety of instruments and formats for biosensing with an enhancement of sensitivity and the stability.

4. Drug delivery

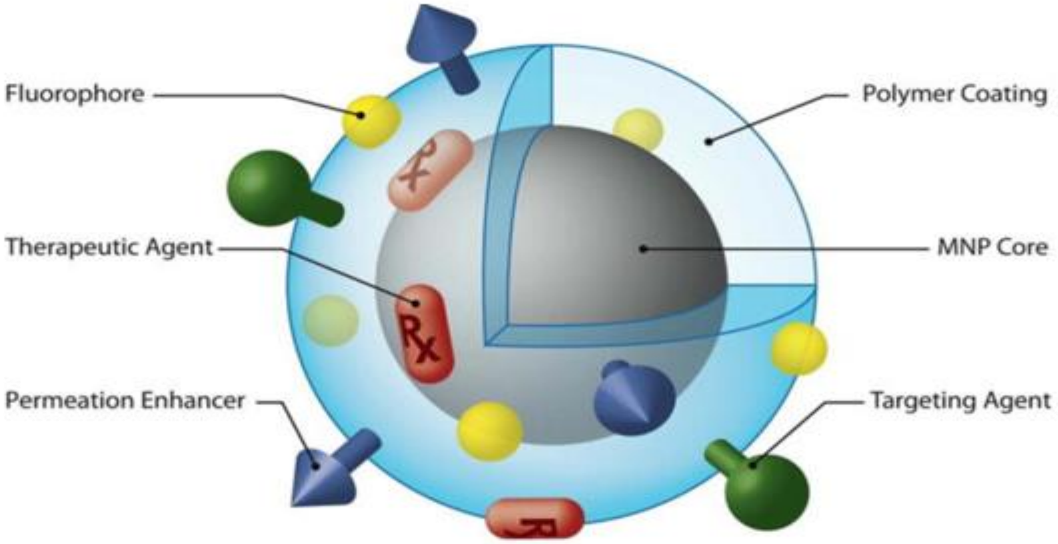
Magnetic nanoparticles have been developed and applied in localized drug delivery to tumors. The magnetic nanoparticles first act as a carrier of the drug, which are attached to its outer surface or dissolve in the coating. Once the drug coated particles have been introduced into the bloodstream of the patient, a magnetic field gradient is created by strong permanent magnet to retain the particles at the targeted region. Moreover, magnetic nanoparticles coated with a drug could be injected intravenously, transported, and retained at targeted sites, which make them highly promising system for drug delivery.**[**68**]**



Magnetic nanoparticles with various shells

5. Therapy

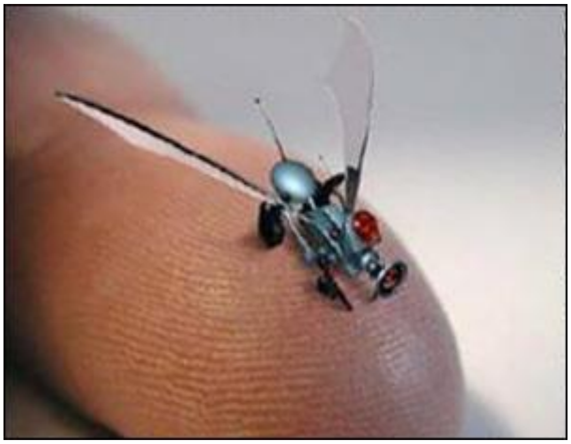
Magnetic nanoparticles have currently been explored as a technique for targeted therapeutic heating of tumors, which is called hyperthermia. Various types of superparamagnetic nanoparticles with different coatings and targeting agents are used for specific tumor sites. Magnetic particle heating can be accomplished at depths necessary for treatment of tumors located virtually anywhere in the human body. In addition, magnetic nanoparticle hyperthermia can also be used as an adjuvant to conventional chemotherapy and radiation therapy, which shows great potential.



Nano Robots

Nanotechnology can best be defined as a description of activities at the level of atoms and molecules that have applications in the real world. A nano meter is a billionth of a meter, that is, about 1/80,000 of the diameter of a human hair, or 10 times the diameter of a hydrogen atom. The sizerelated challenge is the ability to measure, manipulate, and assemble matter with features on the scale of 1-100nm. In order to achieve cost-effectiveness in nanotechnology it will be necessary to automate molecular manufacturing. The engineering of molecular products needs to be carried out by robotic devices, which have been termed nano robots.

Copyright 2001 American Dental Association

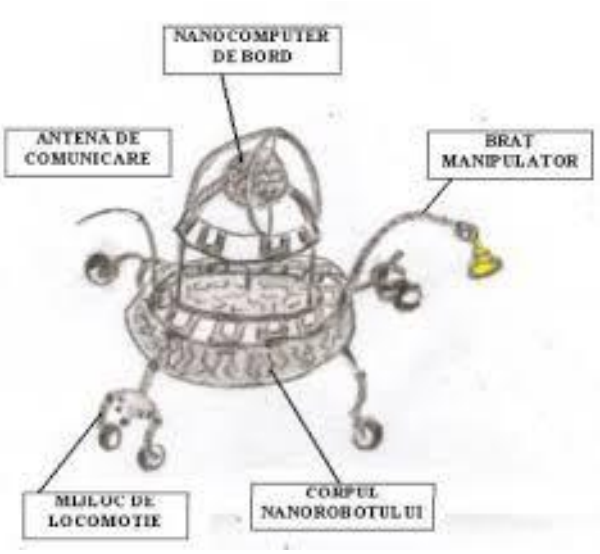


Nanorobots are also known as nanites, or nanomachines.**[**69**]** Nano-robots are the robots that are simply known as that controllable machines at the nano (10-9) meter or molecular scale, composed of nano-components. More specifically, nano robotics refer to the still largely hypothetical nanotechnology engineering discipline of designing and building nano robots.

Even though the field of nano robotics is fundamentally different from that of the macro robots due to the differences in scale and material, there are many similarities in design and control techniques that eventually could be projected and applied. Due to the modern scientific capabilities, it has become possible to attempt the creation of nano robotic devices and interface them with the macro world for control. There are countless such machines which exist in nature and there is an opportunity to build more of them by mimicking nature. Nowadays these nano robots plays a vital role in the field of dental surgery.

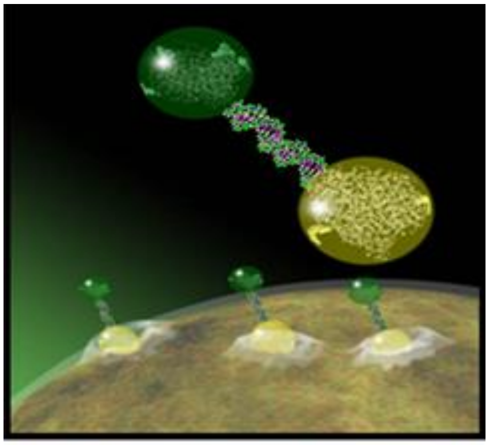
Parts of Nanorobots:

Nanorobots are planned to have a diameter of 0.5-3 microns and parts of dimension 1-10 nanometers. There are four Major parts in a Nanorobot. They are camera, pay load , capacitor, swimming tail. The chief element comprising the build of nanorobot are Carbon, Sulphur, hydrogen, oxygen, fluoride which were used for the preparation of nanoscale gears and other nano components.3 carbon will be primarily the principal element in the build of medical nanorobot because of its inert properties and strength, basically in the form of diamond or fullerene. The chemical inertness of diamond is proved by several experimental studies. Building nanorobots will involves sensors, actuators, control, power, communications and interfacing across spatial scales and between organic/inorganic as well as biotic/abiotic systems.**[**70**]**



Mechanism of Action:

The powering of Nano robots is expected to be done by metabolism of local glucose, oxygen and externally supplied acoustic energy. They can be made to work under control by on-board computers capable of performing around 1000 or more computations per second. Communication with the device can be obtained by acoustic signaling navigational network installed in the body that would provide high positional accuracy to all passing Nano robots and help in keeping track of various devices in the body. These nanorobots will be able to distinguish between different cell types by chacking their surface antigens.they are accomplished by the use of chemotacic sensors keyed to the specific antigens on the target cells. When the task of the nanorobots is completed, they can be retrieved by allowing them to effuse themselves via the usual human excretory channels. These can also be removed by active scavenger systems.**[**71**]**



Design of Nanorobots

The software NCD (nano robot control design) is a system implemented to serve as a test bed for nano robot 3D prototyping, serving as a fast development platform for medical nano robots investigation, the NCD simulations show how to interact and control a nano robot inside the body. It is an advanced nano mechatronics simulator that provides physical and numerical information for nano robot task-based modelling. The nano robot design is comprised of integrated nano electronics and components such as molecular sorting rotors and a robot arm (telescoping manipulator) derived from biological models.

The nano robot exterior shape consists of a diamonded material to which may be attached an artificial glycocalyx surface that minimizes fibrinogen (and other blood proteins) adsorption and bioactivity, ensuring sufficient biocompatibility to avoid immune system attack.

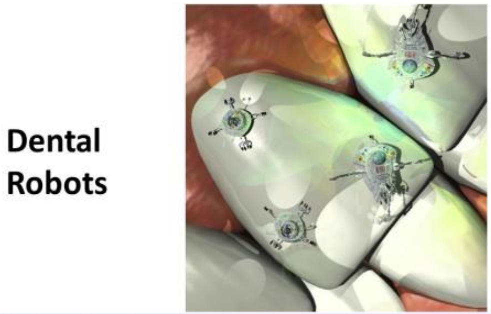
Different molecule types are distinguished by a series of chemotactic sensors whose binding sites have a different affinity for each kind of molecule .These sensors also detect obstacles which might require a new trajectory planning.

Sensor design and capabilities depend on the details of the environment and task. Thus, the nano robot requires transducers capabilities and smart sensors directly related to that specific biomedical application. In present study, the nano robot is able to detect obstacles over a range of about 1mm, and within an angular resolution equivalent to a diameter of 100nm at that range. The bio molecules are too small to be detected reliably: instead the robot relies on chemical contact sensors to detect them. This description of interaction capabilities allows evaluating different nano robot sensor based action.

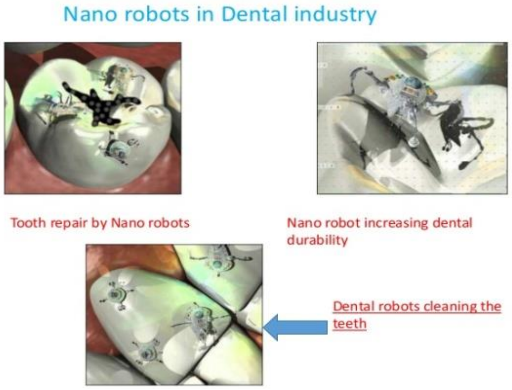
It also helps to choose the kind of low level control to maximize the information acquired for an effective real time performance. The nano robot kinematics can be predicted using state equations, positional constraints, inverse kinematics and dynamics, while some individual directional component performance can be simulated using control system models of transient and steady-state response.**[**71**]**

Nanorobots in dentistry

The growing interest in the future of dental applications of nanotechnology is leading to the emergence of a new field called Nanodentistry. Nano robots induce oral analgesia,Desensitize tooth, manipulate the tissue to re-align and straighten irregular set of teeth and to improve durability of teeth. Further it is explained that how nano robots are used to do preventive, restorative, curative procedures. Nano dental techniques involve many tissue engineering procedures for major tooth repairs. Mainly nano robotics manufacture and installation of a biologically autologous whole replacement tooth that includes both mineral and cellular components which leads to complete dentition replacement therapy. Nanodentistry has given material that is nanostructured composite.



Four remote-controlled nanorobots examine and clean the surfaces of a patient's teeth, near the gumline.



Upper enamel layers are replaced by covalently bonded artificial material such as sapphire. This material has 100 to 200 times the hardness and failure strength than ceramic. Like enamel, sapphire is a somewhat susceptible to acid corrosion. Sapphire has best standard whitening sealant, cosmetic alternative. New restorative nano material to increase tooth durability is Nano composites. This is manufactured by nano agglomerated discrete nano particles that are homogeneously distributed in resins or coatings to produce nano composites. The nano filler include an alumina silicate powder having a mean particle size of about 80nm and a 1:4ratio of alumina to silica. The nanofiller has a refractive index of 1.503, it has superior hardness, modulus of elasticity, translucency, esthetic appeal, excellent color density, high polish and 50% reduction in filling shrinkage.

They are superior to conventional composites and blend with a natural tooth structure much better.

Are NanoRobots Safe?

The nonpyrogenic nanorobots used in vivo are bulk, carbon powder and monocrstal sapphire . pyrogenic nanorobots are alumina, silica and trace elements elements like copper and zinc.

If inherent nanodevice surface pyrogeecity cannot be avoided, the pyrogenic pathway is controlled by in vivo medical nanorobots .

Nanorobots may release inhibitors, antagonistsor downmegulators for the pyrogenic pathway in a targeted fashion to selectively absorb the endogenous pyrogens , chemically modify them , then release them back into the body in a harmless inactivated form.**[**73**]**

Approaches of Nanotechnology

Nanotechnology is understood by the following 4 approaches**[**74**]**

I. The buttom up approach : Seeks to arrange smaller components into more complex assemblies, the covalent bonds of which are extremely strong. (Das et al., 2007

II. Top down approach : Seeks to produce smaller devices by using larger ones in achieving precision in structure and assembly. (Das et al., 2007) These solid state materials can also be used to create device known as N E M S (Nanoelectromechanical systems) which are used in cancer diagnosis.

III. The functional approach : Seeks to develop components of a desired functionality without regard to how they might be assembled.

IV. Biomimetic approaches: Seeks to apply biomolecules for applications in nanotechnology. (Ghalanbor et al., 2005)

The subfields anticipate what inventions nanotechnology might yield, or attempt to propose an agenda. (Kubik et al., 2006)

The applications of nanotechnology are varied. They include medicine, environment, energy, information and technology, heavy industry and consumer goods.

In the field of dentistry, the integration of nanotechnology has given rise to a new stream 'nanodentistry'. (Uysal et al., 2010) Nanotechnology has its influences in the following ways in dentistry.

Buttom up Approach

a. Nano Anesthesia

Nanotechnology uses millions of active analgesic micrometer sized dental nanorobots in a colloidal suspension for local anaesthesia On reaching the dentin, the nanorobots, within 100 seconds, are said to enter dentinal tubular holes that are 1 to 4 µm in diameter and proceed toward the pulp, guided by a combination of chemical gradients, temperature differentials and even position of navigation, all under the control of the onboard nanocomputer as directed by the dentist. (Freitas Robert, 2000)

b. Hypersensitivity cure

Reconstructive dental nanorobots selectively and precisely occlude selected tubules in minutes, using native biological materials, offering patients a quick and permanent cure for hypersensitivity caused by the changes in pressure transmitted hydrodynamically to the pulp. (Nagpal et al., 2011)

c. Dental Durability and Cosmetics

Covalently bonded artificial materials such as, sapphire or diamond in a fracture resistant nanostructured composite material that possibly include carbon nanotubes are used for replacing upper enamel layers for aesthetic purposes. (Freitas, 2000)

d. Detifrobots

Nanorobotic dentifrice (dentifrobots) delivered by mouthwash or toothpaste patrol all supragingival and subgingival surfaces at least once a day metabolizing trapped organic matter into harmless and odorless vapors, performing continuous calculus debridement and identifying and destroying pathogenic bacteria residing in the plaque and elsewhere, while allowing the 500 species of harmless oral microflora to flourish in a healthy ecosystem. (Freitas, 2000)

e. Cancer Diagnosis

Nanotechnology may permit less invasive, less uncomfortable means of identifying and quantifying the markers of disease, thus aiding in cancer diagnosis, monitoring recurrence or metastasis, and defining the locations, biologic types, and behaviors of malignancies.

The diverse techniques include.

- Physicochemical nanoscale modification i.e "nanotexturing" of surfaces on a mass spectrometry planar or micro or nanoparticle substrate is present. It has been proposed to provide size exclusion, elective capture, and resultant enrichment of selected regions of the low molecular weight proteins from body fluids and other biologic samples.

- Quantum dots, nanoscale crystals may be used as a potential reporting agent. In treatment of oral cancer, quantum dots bind to the antibody present on the surface of target cell land and when stimulated by UV light, they give rise to reactive oxygen species, thus lethal to target cells.

- Bio Barcode Assay, identify the target and amplifying the signal. A magnetic probe captures a target molecule using either monoclonal antibody or complementary oligonucleotide. Target-specific gold nanoparticles sandwich the target, thus distinguishing the target and amplifying the signal. The barcode oligonucleotides are released and detected using the scanometric method.

- Nanometer scale tubes and wires are said to help monitor local chemical, electrical, or physical property changes in cells or tissues.

- Iodinated nanoparticles that have been localized successfully to lymph nodes after bronchoscopic instillation and may be visualized precisely through the use of computerized tomography (CT).

- Nanoelectromechanical systems (NEMS) are supposed to enable the ability to monitor health status, disease, progression, and treatment outcome through non - invasive means.

- Biosensors used to investigate important biological processes at the cellular level in vivo, include – cantilever array sensor, nanotube senso r and nanobiosensors. Cantilever arrays with their extraordinary multiplexing capabilities could aid cancer diagnosis and could be engineered to bind to molecules associated with cancer, such as DNA sequences, single nucleotide polymorphisms, and proteins. (Freitas, 2000)

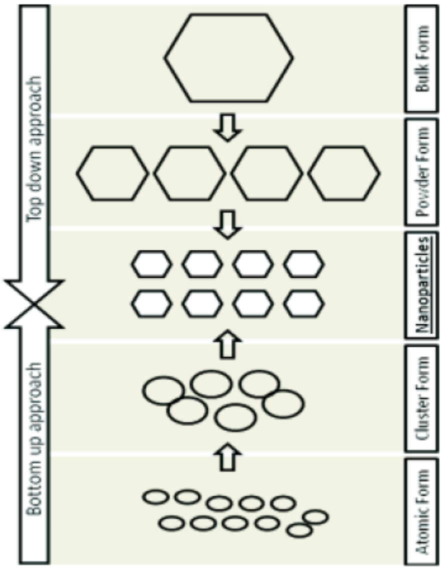
f. Therapeutic Nanotechnology

Nanotechnologic packaging of therapeutics will provide the ability to co-localize delivery of multiple and complimentary therapeutic agents. (Patil Mallanagouda , Singh Mehta Dhoom & Guvva Sowjanya, 2008). Additionally, materials that now require injection potentially could be inhaled or swallowed using nano engineered delivery devices, thus improving patient comfort and compliance

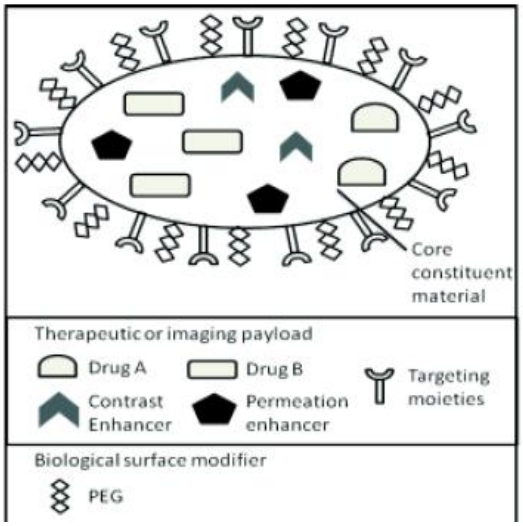
Vaccines may be made more comfortable, by using multitudes of micro- or nanometer-scale needles, to which human nerves are insensitive, rather than a painful injection.

Nanoparticulates also may allow increases in the amount of drug that reaches abnormal cells. They possess a site-specific targeting ability combined with potentially metabolism-specific targeting. It also has the ability to cloak off potentially toxic therapies. Theoretically, the requirement for less total amount of therapeutic agents may allow the safe use of some drugs that are effective but otherwise have unacceptable toxicity profiles.

Nanometer-scale features may allow the practical construction and use of fully implantable and controllable drug delivery devices. (Patil et al., 2008)



nanoparticles are the minute components used in both Top Down and Bottom Up approaches



Multifunctional Nanoparticle Illustrating The Ability to Carry One or More Therapeutic Agents, Biomolecular Targeting Through One or More Conjugated Antibodies or Other Recognition Agents, Imaging Signal Amplification ByWay of Coencapsulated Contrast Agents, And Biobarrier Avoidance Exemplified By an Endothelial Tight- Junction Opening Permeation Enhancer And By Peg For The Avoidance of Macrophage Uptake

Top Down Approach

a. Nanotechnology for Composites

Efforts to improve the clinical performance of composite filling material are focused on the following main topics:

• Reduction of the polymerization shrinkage. Nanocomposites, have a filler loading upto 95% that help reduce polymerization shrinkage,

• Improvement of the mechanical properties, especially wear resistance,

• Improvement of biocompatibility by reducing the elution of components (Patil et al., 2008) Nanofiller particles maybe of two types

• Nanometric, particles (NM) - are monodisperse non aggregate and nonagglomerated silica particles which are treated with 3 methacryloxypropyltrimethoxysilane, (MPTS - coupling agent) to prevent any agglomeration or aggregation and allow chemical bonding of the NM filler of the resin, matrix during curing. (Koneti & Dayanand, 2008)

• Nanocluster (NC's) Particles have a primary particle size of 2 to 20 nm, while the spheroid agglomerated particles have a broad size distribution, with an average size of 0.6 micrometers. (Koneti & Dayanand, 2008)

Nanoparticles with an adapted refractive index and radiopacity were obtained by synthesizing mixed oxides such as silica Zirconia nanoparticles. Moreover, well designed nano and microstructures sol gel can be utilized for producing protective and wear resistant coatings of teeth, metal alloys, and glass fillers of special compositions. According to Tussi et al, regardless of the finishing and polishing technique, the nanofilled composites exhibited the lowest pretesting surface roughness and wear. (Wei et al., 2007)

b. Nanotechnology for Glass Ionomer Cement (GIC)

Nano Ionomer is a glass ionomer cement whose formulation is based on bonded nanofiller technology. Mechanical properties of nano-ionomer are improved by the combination of fluoroaluminosilicate glass, nanofillers, and nanofiller clusters. The nanofiller components also improve some physical properties of the hardened restorative. It also shows high fluoride release that is rechargeable after being exposed to a topical fluoride source. Additionally, in vitro tests showed that the nano ionomer (Ketac N100) has the ability to create a caries inhibition zone after acid exposure. (Uysal et al., 2010)

c. Improving Endodontics

A novel root end filling material; Nanomaterial enhanced retrofil polymer (NERP) has been developed. It reveals better bond strength and adaptability to the tooth structure as compared to conventional retrofill materials. These promising results are synonymous with in vitro dental antibacterial and micro-leakage studies. Pellets of NERP loaded with an antimicrobial drug, chlorhexidine, displayed sustained drug - release capabilities and confirmed that drug-elution can be manipulated. In particular, the drug-elution studies showed enhanced release as the acidity level of the surrounding environment was reduced, a finding uniquely favorable in cases of apical infection where the environment is mostly acidic. In the latest extracted-tooth-model study, NERP materials were also found to significantly reduce the micro-leakage of bacte ria compa red to conventional mate rials, demonstrating their ability to seal effectively. (Chogle et al., 2013)

Further encorporation of nanotechnology in various solutions used for endodontic purposes aids in the prevention of agglomeration,

- Prevents agglomeration,
- They have high dentin bond strength,
- Reinforce the surface hardness of exposed dentin,
- Penetrate dentinal tubules of diameter 5 -10nm to provide additional 'nano retention'. (Mitra et al., 2003)

d. Impression Materials

Nanofillers are integrated in vinylpolysiloxanes, producing a unique edition of siloxane impression material. The material has a better flow, improved hydrophilic properties, tear strength and enhanced detail precision. The presence of the nanostructure increases the fluidity of the material, especially when pressure is applied. (Kumar & Vijayalakshmi, 2006)

e. Nano Titanium Implants

Nano Titanium is a new form of titanium metal that has been introduced. Patients should experience shorter post surgery healing times and a more reliable integration of these new implants into their body. It is highly compatible with bone and is thought to provide stronger, up to 20 times faster bonding with improved strength, biocompatibility, long life and improved wear and tear. (Albrektssonet al., 2008)

f. Nano Needles

Suture needles with nano sized stainless steel crystals have been developed. Nano tweezers are also under development which will make cell surgery possible in the near future. The characteristics in general can be said to be a combination of properties of ordinary austenitic stainless and low alloyed ferritic steels. This means that properties such as elastic modulus, mechanical properties and thermal expansion are comparable to ferritic steels (such as low alloyed carbon steels or chromium steels) while properties such as corrosion resistance is more comparable to austenitic stainless steels. (Shetty et al., 2013)

g. Biodegradable Nanofibres

Bionanotechnology, especially with the powerful electrospinning method to fabricate the nanofibrous scaffold is again believed to be a promising technology. The synthetic aligned matrix along with the advantages of synthetic biodegradable polymers, with the required nanometer-scale dimension and a defined architecture replicating the in vivo like vascular structure, may represent an ideal tissue engineering scaffold, especially for blood vessel engineering. (Mendonça et al., 2008)

h. Wound Dressing

Some medical products containing nano-particles have been raised, notably those for wound dressings. The Biosafety of nanometer-scale materials is the subject of much attention, therefore enhancing the focus on studies of the acute and chronic toxic effects of nano-particles. Selfassembly technology is a strategy for nanofabrication, which calls for designing molecules and supramolecular entities in a way that shape-complementarities cause them to aggregate into the desired structure thus acting as a recognized barrier to full and partial thickness wounds. This method is practiced widely in chemical science and biomedicine. It has been discovered that silver nano crystalline Chitosan dressing yielded in a faster healing process. (Kumar & Vijayalakshmi, 2006)

i. Bone Replacing Materials

The hydroxyapatite nanoparticles have nanocrystallites that show a loose microstructure in which nanopores are situated between the crystallites. This material structure is completed by pores in the micrometer area. Porosity values of around 60 % can be found. The surface of the pores is modified in such a manner, that it literally “hangs on” to the proteins. From the porosity in the nanometer range, most bone replacement material mainly acts on a surface on which proteins can configure. That's why the cells recognize it as body's own material. (Kumar & Vijayalakshmi,2006)

j. Major tooth Repair / Nano Tissue Engineering

Complete dentition replacement refers to replacement of the whole tooth, including cellular and mineral components.A combination of genetic engineering, tissue engineering and nanotechnology is required for the same. The pioneer for complete dentition replacement was Chan et al., who recreated dental enamel, the hardest tissue in the human body, by using highly organized microarchitectural units of nanorods. (Shetty et al., 2013)

Future for Nanotechnology

Nanotechnology faces many challenges that need to be overcome such as - precise positioning and assembly of molecular scale part, economical nanorobot mass production technique, biocompatibility, simultaneous co ordination of activities of large numbers of independent micron scale robot and social issues of public acceptance, ethics and regulation and human safety. (Kumar & Vijayalakshmi, 2006). The risk to health and environment from nanoparticles and nanomaterials and the risks posed by molecular manufacturing and social risks need further inverstigation. (Freitas, 2000).

Dental Applications:

There are various applications which Nanorobots can offer:

1) Inducing anesthesia: after instillation of colloidal suspension containing millions of active analgesic nanorobots into the patients gingiva, the nanorobots reach dentin by migrating into the gingival sulcus and pass painlessly through the lamina propria. Upon reaching the dentin, they enter the dentinal tubules upto 4 mu depth and proceed toward the pulp guided by a combination of chemical gradient under nanocomputer control. The ingress of nanorobots from tooth surface to the pulp occurs in l00 s. Once installed in the pulp, they establish control over the nerves. Then, nanorobots act according to the commands of the dentist shutting down all sensitivity in any particular tooth requiring treatment. When the dentist presses the handheld control,the selected tooth is immediately anesthesized. After the procedure is completed,the dentist orders the nanorobots to restore all sensation and egress from the tooth.**[**75,76,77**]**

Nanorobots analgesia offers greater patient comforts, reduce anxiety , no needles,greater selectivity, controllability of analgesic effect, fast and completely reversible action ,avoidance of side effects and complications.

2) Tooth repair: involves manufacturing and installation of a biologically autologous whole replacement teeth by using genetic engineering, tissue engineering that includes both mineral and cellular components,i.e ‘complete dentition replacement therapy’ should become feasible within the time and economic constraints of a typical office visit through the use of an affordable desktop manufacturing facility, which would fabricate the new tooth in the dentist’s office.

Chen et al took advantage of these latest developments in the area of nanotechnology to simulate the natural biomineralization process to create the hardest tissue in the human body , dental enamel, by using highly organized microarchitectural units of nanorod like calcium hydroxyapatite crystals arranged roughly parallel to each other.

3) Hypersensitivity cure: it is a pathological phenomenon. It is caused by pressure transmitted hydrodynamically to the pulp.Natural hypersensitive teeth have eight times higher surface density of dentinal tubules and diameter with twice as large than nano-sensitive teeth. Reconstructive dental robots using native biological materials could selectively and precisely occlude specific tubules within minutes, offering a quick and permanent cure.

On reaching the dentin,the nanorobots enter dentinal tubular holes that are 1 to 4 µm in diameter and proceed toward the pulp, guided by a combination of chemical gradients,temperature differentials ad even position of navigation, all under the control of the onboard nanocomputer as directed by the dentist. There are many pathways to travel nanorobots from dentin to pulp. Because of different tubular branching patterns, tubular density may present significant challenge to navigation.

Assuming a total path of length of about 10mm from the tooth surface to the pulp and a modest travel speed of about 100µm/second. Nanorobots can complete the journey into the pulp chamber in approximately 100 s. The presence of natural cells that are constantly in motion around and inside the teeth, including human gingival ,pulpal fibroblasts,cememtoblasts,odontoblasts and bacteria inside dentinal tubules, lymphocytes within the pulp or lamina propria suggests that such journey be feasible by cell sized nanorobots of similar mobility.**[**78,79,80**]**

4)Tooth durability and appearance: nanodentistry has given material that is nanostructured composite material, sapphire which increases tooth durability and appearance. Upper enamel layers are replaced by covalently bonded artificial material, such as sapphire. This material has 100 to 200 times hardness and failure strength than ceramic. Like enamel,sapphire is a somewhat susceptible to acid corrosion . sapphire has best standard whitening sealant,cosmetic alternative. New restorative nanomaterial to increase tooth durability is nanocomposites. This is manufactured by nanoagglomerated discrete nanoparticles that are homogeneously distributed in resins or coatings to produce nanocomposites. The nanofiller includes an aluminosilicate powder having a mean particle size of about 80 nm and a 1:4 ratio of alumina to silica. The nanofiller has a refractive index of 1.503, it has superior hardness, modulous of elasticity, translucency, esthetic appeal, excellent colour density, high polish and 50 % reduction in filling shrinkage. They are superior to conventional composites and blend with a natural tooth structure much better.

5) Orthodontic treatment: The treatment generally involves a frictional type of force which provides the desired movement. Orthodontic nanorobots would directly manipulate the tissues of periodontium, which would allow rapid and painless tooth straightening , rotating and vertical repositioning within minutes to hours. In a study published by katz, a reduction in friction has been reported by coating the orthodontic wire with inorganic fullerene like tungsten disulfide nanoparticles which are known for their dry lubrication properties.

6) Diagnosis of oral cancer

a) Nano Electromechanical Systems (NEMS):-Nanotechnology based NEMS biosensors that exhibit exquisite sensitivity and specificity for detection of abnormal cells at molecular level are being developed. They convert (bio) chemical to electrical signal. **[**81**]**

b) Oral Fluid NanoSensor Test (OFNASET):- The Oral Fluid NanoSensor Test (OFNASET) technology is used for multiplex detection of salivary biomarkers for oral cancer.it has been demonstrated that the combination of two salivary proteomic biomarkers (thioredoxin and IL-8) and four salivary mRNA biomarkers (SAT,ODZ,IL-8 and IL-1b) can detect oral cancer with high specificity and sensitivity .**[**82**]**

c) Optical Nanobiosensor:- The nanobiosensor is a unique fiberoptics-based tool which allows the minimally invasive analysis of intracellular components (Cytochrome C), which is a very important protein to the process which produces cellular energy and is well known as the protein involved in apoptosis, or programmed cell death.**[**83**]**

7) Treatment of Oral Cancer:

Nanotechnology in field of cancer therapeutics has offered highly specific tools in the form of multifunctional Dendrimers and nanoshells. The unique property of dendrimers, such as their high degree of branching , multivalence, globular structure and well defined molecular weight make them promising in cancer therapeutics . Nanoshells are miniscule beads with metallic outer layers designed to produce intense heat by absorbing specific wavelengths of radiations that can be used for selective destruction of cancer cells leaving aside intact, adjacent normal cells.

- Nanomaterials for brachytherapy: BrachySil TM delivers 32P, clinical trial .

- Photodynamic therapy: Hydrophobic porphyrins are potentially interesting molecules for the photodynamic therapy (PDT) of solid cancers or ocular diseases.**[**84,85,86,87**]**

8) Oral Hygiene and halitosis:

properly configured dentifrobots could identify and destroy pathogenic bacteria residing in the plaque and elsewhere , while allowing the 500 or so species of harmless oral microflora to flourish in a healthy ecosystem. Dentifrobots also would provide a continuous barrier to halitosis, since bacterial putrefaction is the central metabolic process involved in oral malodour.**[**88**]**

9) Periodontal tissue engineering :

Tissue Engineering concepts for periodontal regeneration are focussed on the utilization of synthetic scaffolds for cell delivery purposes. Nonbiological self-assembling nanosystems will automatically undergo prespecified assemblies much in line with known biologic systems associated with cells and tissues.

10) Surgical Nanorobotics:

A surgical Nanorobot, operated or guided by an expert dentist, are envisioned to act as on-site surgeon. Such a device are expected to perform various procedures such as detection of pathology and then diagnosing abnormal lesions by nano scale manipulations, coordinated by an onboard computer, while maintaining contact with the supervising surgeon via coded ultrasound signals.

The earliest forms of cellular nanosurgery are already being explored today . for example: a rapidly vibrating (100 Hz) micropipette with a <1 micron tip diaeter has been used to completely cut dendrites from single neurons without damaging cell viability.

Axotomy of roundworm neurons was performed by femtosecond laser surgery, after which the axons functionally regenerated. A femtolaser acts like a pair o ‘nanoscissors’ by vaporizing tissue locally while leaving adjacent tissue unharmed.

11) Bone Replacement Materials :

These can be used in maxillofacial injuries requiring bone graft, cleft patient and osseous defect in periodontal surgeries.

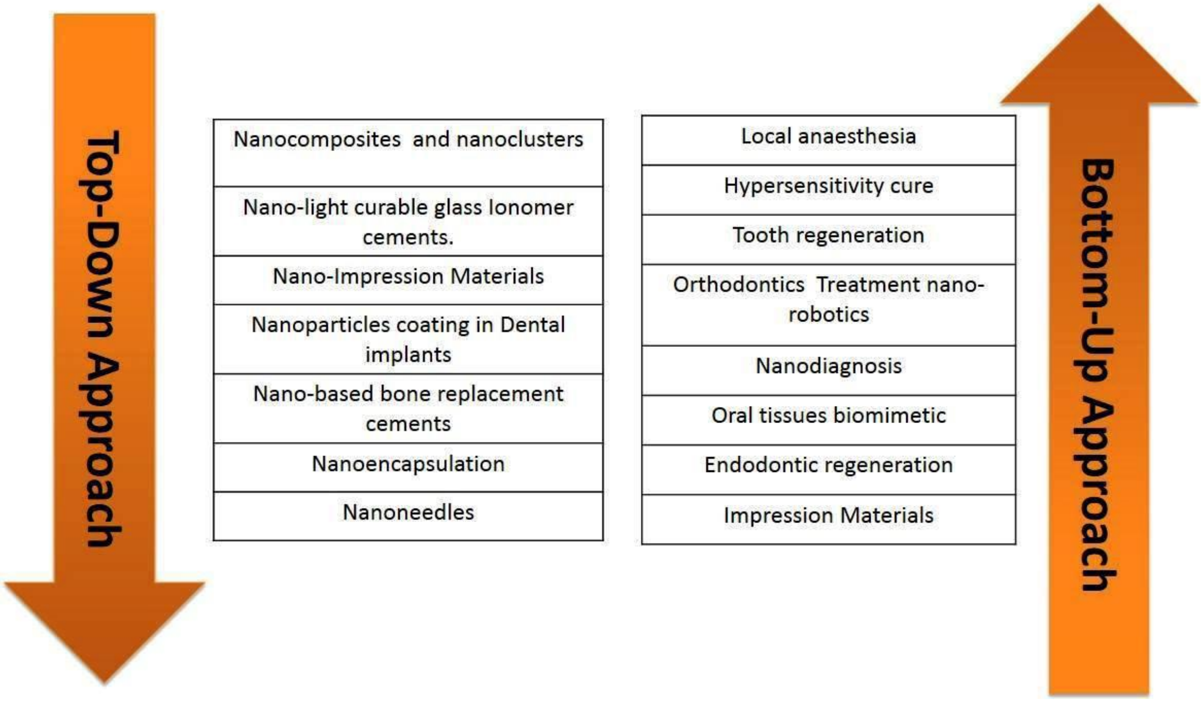
- Hydroxyapatite nanoparticles used to treat bone defects are Ostim HA.

- VITOSSO HA and TCP

- NanOSS HA

12) Personalized treatment :

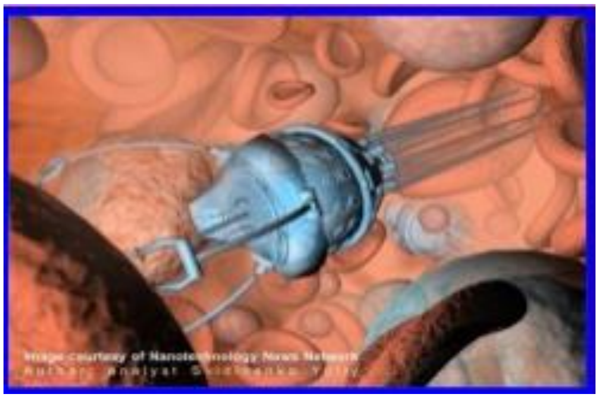
Dentists will perform routine examinations that will include use of high resolution imaging devices to better visualize the subsurface tomography of each tooth. Dentists will possess additional predictive tools to characterize bacteria underlying infections and the specific nature of the immune response will be developed , and they will be able to personalize treatments using nanoparticles drug delivery systems , that most effectively target and eliminate both the bacteria and the infection .



Breakthrough approaches of nanotechnology and their applications in dentistry

Development of Nanotechnology in the Field of Dentistry :[89-92]

1. Nanodiagnostics Nanodiagnostic devices can be used for early disease identification at the cellular and molecular levels. Nanomedicine could increase the efficiency and reliability of in vitro diagnostics, through the use of selective nanodevices to collect human fluids or tissue samples and to make multiple analyses at the subcellular level. From an in vivo perspective, nanodevices might be inserted into the body to identify the early presence of a disease, or to identify and quantify toxic molecules, tumor cells, and so forth (Freitas, 20007; Lampton, 1995).



Nanoscale Cantilevers

These are flexible beams resembling a row of diving boards that can be engineered to bind to moleculesassociated with cancer.

Nanopores

These are tiny holes that allow DNA to pass through one strand at a time. They will make DNA sequencing more efficient.

Nanotubes

These are carbon rods about half the diameter of a molecule of DNA that not only can detect the presence of altered genes but also may help researchers pinpoint the exact location of those changes.

Quantum Dots

These are nanomaterials that glow very brightly when illuminated by ultraviolet light. They can be coated with a material that makes the dots attach

specifically to the molecules to be tracked. Quantum dots bind themselves to proteins unique to cancer cells, literally bringing tumours to light.

Nano Electromechanical Systems (NEMS)

Nanotechnology based NEMS biosensors that exhibit exquisite sensitivity and specificity for analyte detection, down to single molecule level are being

developed. They convert (bio) chemical to electrical signal .

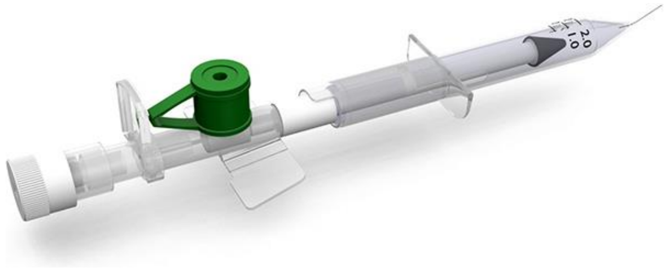
Lab-on-a-chip methods

Lab-on-a-chip (LOC) is a device which integrates several laboratory functions on a single chip. LOCs deal with the handling of extremely small fluid volumes down to less than pico liters. Assays are performed on chemically sensitized beads populated into etched silicon wafers with embedded fluid handling and optical detection capabilities.

Complex assays can be performed with small sample volumes, short analysis times, and markedly reduced reagent costs. LOC methodologies have been used to assess the levels of interleukin-1beta (IL-1beta), Creactive protein (CRP), and matrix metalloproteinase-8 (MMP-8) in whole saliva, which are potential use ofthese biomarkers for diagnosing and categorizing the severity and extent of periodontitis

2. **Diagnosis and treatment of oral cancer** Saliva is used as an inexpensive and noninvasively obtained diagnostic medium that contains proteomic and genomic markers for molecular disease identification. Exosome, a membrane-bound secretory vesicle, is one such marker whose level is elevated in malignancy. This marker has been studied by using atomic force microscopy, which employs nanoparticles. The nanoelectromechanical system, oral fluid nanosensor test, and optical nanobiosensor can also be used for diagnosing oral cancer7. Nanoshells, which are miniscule beads, are specific tools in cancer therapeutics. Nanoshells have an outer metallic layer that selectively destroys cancer cells, while leaving normal cells intact. Brachytherapy is an advanced form of cancer treatment. Still under trial are nanoparticle-coated, radioactive sources placed close to or within the tumor to destroy it. Other uses of nanovectors include drug delivery across the blood–brain barrier in the treatment of Alzheimer's and Parkinson's diseases (Song et al., 20049; Wong, 200610)

3. Nanoanesthesia When nanotechnology or nanorobots are used to induce anesthesia, the gingiva of the patient is instilled with a colloidal suspension containing millions of active, analgesic, micron-sized dental robots that respond to input supplied by the dentist. Nanorobots in contact with the surface of the crown or mucosa can reach the pulp via the gingival sulcus, lamina propria, or dentinal tubules. Once in the pulp, they shut down all sensations by establishing control over nerve- impulse traffic in any tooth that requires treatment. After completion of treatment, they restore this sensation, thereby providing the patient with anxiety-free and needleless comfort. The anesthesia is fast-acting and reversible, with no side effects or complications associated with its use (Freitas, 2000)



Nanoanaesthesia

4. Nanosolutions Because they produce unique and dispersible nanoparticles, nanosolutions can be used as bonding agents. Homogeneity is ensured, because the adhesive is mixed perfectly every time. Nanoparticles have also been used as sterilizing solutions in the form of nanosized emulsified oil droplets that bombard pathogens (Nagpal et al., 2011)

5. Impression materials: Nanofillers are integrated into vinylpolysiloxanes, producing a unique siloxane impression material that has a better flow, improved hydrophilic properties, and enhanced precision detail (Kumar and Vijayalakshmi, 2006)

Trade name: Nanotech Elite H-D

nano impression material

6. Bone replacement materials: Bone is a natural nanostructure that is composed of organic compounds (mainly collagen) and reinforced with inorganic ones. Nanotechnology aims to emulate this natural structure for orthopedic and dental applications and, more particularly, for the development of nanobone. Nanocrystals show a loose microstructure, with nanopores situated between the crystals. The surfaces of the pores are modified such that they adsorb protein, due to the addition of silica molecules. Bone defects can be treated by using these hydroxyapatite nanoparticles (Kumar and Vijayalakshmi, 2006)13. Hydroxy apatite nanoparticles used to treat bone defects are14: • Ostim HA (Osartis GmbH, Germany) • Vitosso (Orthovita, Inc) HA + TCP (tricalcium phosphate) • NanOSSTM HA (Angstrom Medica)

Bone defect can now be treated with hydroxyapatite nanoparticles

7. Nano-ceramics

The good resistance to microcrack propagation is related to the strengthening effect of the nano-ceramic particles.

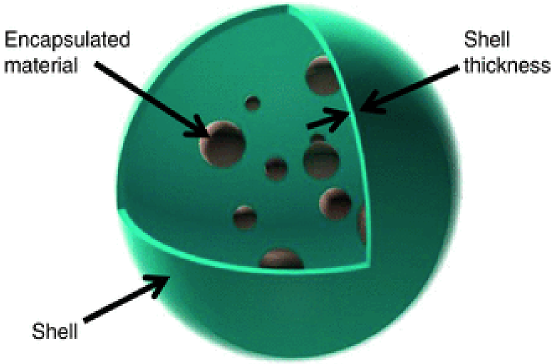
Nanofillers - Enhances polishing ability and reduces wear.

- Nanopigments - Adjust the shade of the restoration to the surrounding teeth (chameleon effect).
- Nanomodifiers - Increases the stability of the material and prevent sticking to instruments.

Nanoceramic

Nanoceramic

8. Nanoencapsulation: Targeted release systems that encompass nanocapsules are under trial for inclusion in vaccines and antibiotics **(Kumar and Vijayalakshmi, 2006). Controlled drug release has been best experimented in nanomaterials with hollow spheres, nanotubes, core-shells structure and nanocomposite.**



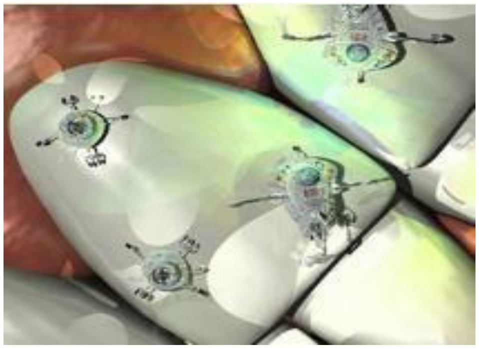
Nanoencapsulation

9. Dentine tubule blocking to alleviate hypersensitivity: Hypersensitivity is caused by changes in the pressure transmitted hydrodynamically to the pulp. The dentinal tubules of a hypertensive tooth have twice the diameter and eight times the surface density of those in nonsensitive teeth. These characteristics have led to the use of nanorobots that selectively and precisely occlude tubules in minutes, by using local, native materials, thus offering patients a quick and permanent cure (Nagpal et al., 2011)

Hypersensitivity cure

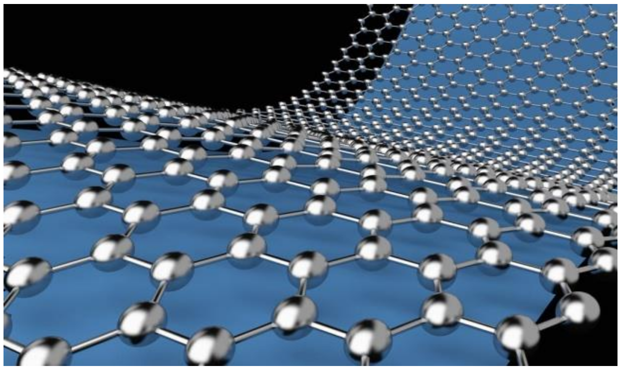
10. Nanorobotic dentifrices (Dentifrobots): Nanorobotic dentifrices, when delivered either by mouthwash or tooth paste, can cover all subgingival surfaces, thereby metabolizing trapped organic matter into harmless and odorless vapors. Properly configured dentifrobots can identify and destroy pathogenic bacteria that exist in the plaque and elsewhere. These invisibly small dentifrobots are purely mechanical devices that safely deactivate themselves when swallowed.

Nanorobots provided by mouthwash or toothpaste could perform continuous calculus debridement and metabolize trapped organic matter into odourless and inert vapors by hovering on supragingival and subgingival surfaces. These mechanical devices crawling at 1 to 10 microns/sec would be inexpensive and would be programmed in such a manner that they would deactivate themselves if swallowed.



Nanodentifrice

11.Orthodontics: Orthodontic robots allow painless tooth uprighting, rotating, and vertical repositioning, as well as rapid tissue repair. A new stainless-steel wire that uses nanotechnology is being studied that combines ultra-high strength with good deformability, corrosion resistance, and surface finish.



Orthodontic Wire

12. Nonsurgical devices:

A surgical knife from microstructured silicon with a diamond layered tip has been developed. Diamond is a material that is chemically rigid, and silicon is non-magnetic and biocompatible.

Trade name : Sandvik Bioline, RK 91TM needles

Advantages :

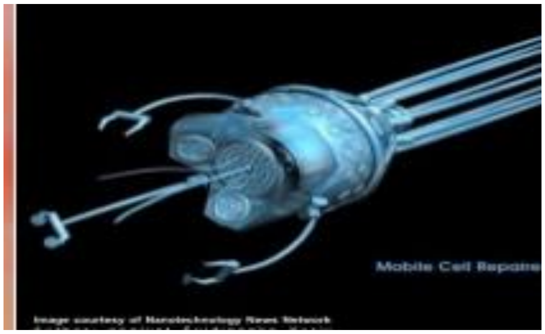
*Shaper incisions

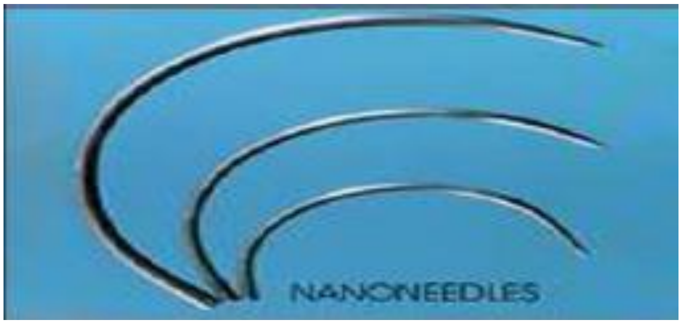
* Kower penetration pressure

Nanosized stainless steel crystals incorporated in suture needles have been developed. Nanotweezers are also under development which aims in making cell surgery possible in the near future.

13. Nanoneedles:

Nanosized stainless-steel crystals incorporated into suture needles have been developed. Cell surgery may be possible in the near future with nanotweezers, which are now under development.





Suture Needle With Nano Sized Crystal NeedlesNanoneedles

14. Nanocomposites:

Microfillers in composites and microcore materials have long been in use. Although the filler particle size cannot be reduced below 100 nm, nanocomposite particles are minute enough to be synthesized at the molecular level. These nanoparticles improve the compressive strength of the material. Filler particles of submicron size, such as zirconium dioxide, are also necessary to improve polishability and esthetics. However, when particles of this size are used, the material may be more prone to brittleness and cracking or fracturing after curing.

Nanocomposites

Composite with nanofillers has two types of nanofillers – nanomeric and nanocluster type

Trade name: Filtek Supreme universal restorative purenano.

Advantages :

*High filler loading

*Desirable handling characteristics

*Superior physical properties like modulus of elasticity and flexural strength ,etc

*High polish retention because of nanosize fillers which even if get plucked away by tooth brush abrasion , leave the surface with defects smaller than the wavelength of light.

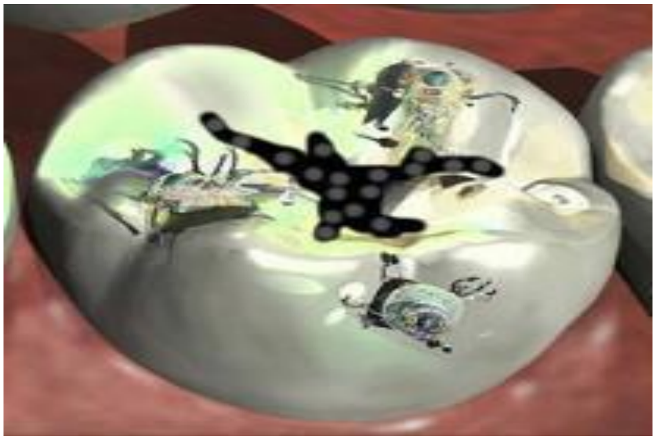
*Higher translucency giving it more lifelike appearance

*Fifty percent reduction in curing shrinkage.

To address this issue, hybrid composites and composites containing a wider distribution of filler particles have come into use. Although these composites display a better balance of strength and esthetics, they are weak due to nanoparticle clumping or agglomeration. This problem can be overcome by incorporating a proprietary coating process during the particle manufacturing procedure, thereby eliminating weak spots and providing consistent strength throughout the entire "fill" of the core build-up. Additionally, the even distribution of nanoparticles results in a smoother, creamier consistency and improves flow characteristics. Once the material is cured to its hardened state, these properties contribute to the dentin-like cutability and polishability of the material (Kumar and Vijayalakshmi, 200613; Abhilash, 2010)15.

15. Major tooth repair/nanotissue engineering:

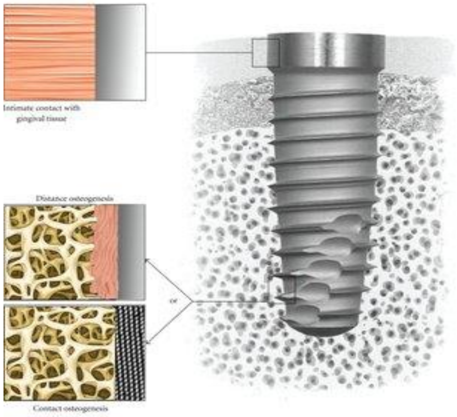
Replacement of the whole tooth, including the cellular and mineral components, is referred to as complete dentition replacement. This therapy is possible through a combination of nanotechnology, genetic engineering, and tissue engineering. Complete dentition replacement was the basis for research by Chan et al., who recreated dental enamel, the hardest tissue in the human body, by using highly organized microarchitectural units of nanorods.



Nanorobots in tooth repair

16. Dental implants:

Structure, chemistry, and biocompatibility The determining factors for successful osseointegration are surface contact area and surface topography. However, bone bonding and stability also play a role. Bone growth and increased predictability can be effectively expedited with implants by using nanotechnology. The addition of nanoscale deposits of hydroxyapatite and calcium phosphate creates a more complex implant surface for osteoblast formation (Albrektsson et al., 200816; Goene et al., 200717). Extensive research on the effects and subsequent optimization of microtopography and surface chemistry has produced ground-breaking strides in material engineering. These new implants are more acceptable, because they enhance the integration of nanocoatings resembling biological materials to the tissues.



Dental implants

17. Non sterilizing solution :

Gandly enterprises Inc, Florida, has introduced a new disinfectant based on super science of nanoemulsion technology which uses nanosized emulsifier droplets of oil that bombard the pathogens, e.g. EcoTru disinfectant

Advantages :

* Broad spectrum

* Hypoallergic

* Noncorroding

* Does not stain fabric

* Require no protective clothing

* Environment friendly

* Compatible with various impressions

18.Nanoadhesives :

These are unique and dispersible nanoparticles which prevent agglomerations and these are produced from nanosolutions.

Advantages:

*Higher dentin and enamel bond strength

*High stress absorptions

*Longer shelf life

*Durable marginal seal

*No separate etching required

*Fluoride release

Nanoadhesives

19.Application of Carbon Nanotubes (CNT) in oral regenerative medicine

There is no doubt that dentistry is one of the branches of medicine most interested in the application of new knowledge acquired from the recent advances in tissue engineering and, particularly, in the field of nanotechnology. Important areas such as implantology, periodontics, and oral and maxillofacial surgery can benefit tremendously from the development of new nanomaterials. In the past few years, CNT combined with biopolymers have been novel potential biomaterials that may aid in the restoration of bone defects in dentistry.

Currently, much information about the synthesis, characterization, and properties of CNT is available; however, more in vitro and in vivo studies are needed for a better comprehension of their effects on bone repair/regeneration. In 2010, Mendes et al18. evaluated the effects of single-walled CNT (SWCNT) associated with sodium hyaluronate (HY-SWCNT) on bone repair/

regeneration of tooth sockets in rats. Treatment of sockets with this nanomaterial increased the formation of bone trabeculae approximately 3-fold and decreased the number of cell nuclei, thus indicating that the healing process was advanced in comparison with that in control sockets.

Also, the expression of type I collagen was increased by 46% in treated sockets after 7 days of tooth extraction. This is an important finding, since, during the bone healing process, the collagen fibrils form osteoid, which allows for the deposition of crystals of carbonated hydroxyapatite responsible for mineralization of the bone matrix (Bouletreau et al., 2002)19. Thus, an augmented expression of collagen type I in HY-SWCNT-treated sockets further suggests that the healing process is accelerated in these sockets (Mendes et al., 2010)18.

No evidence of toxicity was observed in this study (Mendes et al., 2010) . Similar methodology was used to investigate the effects of HY-SWCNT on bone repair/regeneration of tooth sockets of rats under conditions in which bone repair/regeneration was hindered. It is well-known that diabetes alters bone metabolism by reducing both neoformation and resorption, prolonging the process of bone tissue repair/regeneration. Thus, the effects of HY-SWCNT were tested in rats with type I diabetes, induced by streptozotocin (Sá et al., 2013)20. It was found that, 14 days after tooth extraction, the bone repair/regeneration was approximately 3.3-fold higher in tooth sockets of diabetic rats treated with the nanomaterial.

The treatment markedly increased the formation of bone trabeculae and reduced the number of cell nuclei, reaching values similar to those observed in non-diabetic rats. Therefore, the treatment with HY-SWCNT was able to restore the bone repair/regeneration process in tooth sockets of diabetic rats (Sá et al., 2013).

In summary, both of the above-described studies (Mendes et al., 2010; Sá et al., 2013) verified that HY-SWCNT have great potential use for bone regenerative procedures in dentistry, in normal and adverse metabolic states. Corroborating these findings, Usui et al. (2008)21 conducted a series of experiments implanting MWCNT into different types of bone in mice. First, they implanted MWCNT subperiosteally into the skull to evaluate bone-tissue compatibility. At 1 and 4 wks post-surgery, there were no significant signs of incompatibility. These authors then implanted MWCNT into tibial defects to examine their influence on bone healing during 4 wks and found a bone formation pattern similar to that of the control group, suggesting that the nanomaterial did not inhibit bone regeneration. More importantly, MWCNT particles promoted immediate HA crystallization on their surfaces, acting as a core for initial HA crystallization.

Application of Nanotechnology in dentistry with available products.

Discipline	Available Materials
Restorative Dentistry	Ketac™ (3M ESPE, St. Paul, MN, USA), Ketac N100; Nano-ionomers (3M ESPE), Filtek Supreme XT (3M ESPE), Fuji IX GP (GC, Leuven, Belgium), Nano-primer, Premise™ (Kerr/Sybron, Orange, CA, USA), Adper™ Single bond plus Adhesive (3M ESPE), Ceram X™ (DENTSPLY International, Milford, CT, USA).
Regenerative Dentistry and Tissue Engineering	Ostim® (Osartis GmbH, Elsenfeld, Germany), VITOSSO™ (Orthovita-Inc, Malvern, PA, USA), Nano-Bone® (ARTOSS, Rostock, Germany).
Periodontics	Arestin® (Valeant, Bridgewater, MA, USA), Nanogen® (Orthogen, Springfield, IL, USA).
Preventive Dentistry	NanoCare® Gold (Nano-Care, Saarwellingen, Germany).
Orthodontics	Ketac™ N100 Light Curing Nano-Ionomers (3M ESPE), Filtek Supreme Plus Universal (3M ESPE).
Prosthodontics	Nanotech elite H-D plus (Zhermack, Badia Polesine, Italy), GC OPTIGLAZE color® (GC).
Oral Implantology	Nanotite™ Nano-coated implant (BIOMET 3i, Palm Beach Gardens, FL, USA).

Endodontics	AH plus™ (DENTSPLY International), Epiphany (Pentron Clinical Technologies, Wallingford, CT, USA), Guttaflow® (Coltène, Altstätten, Switzerland).

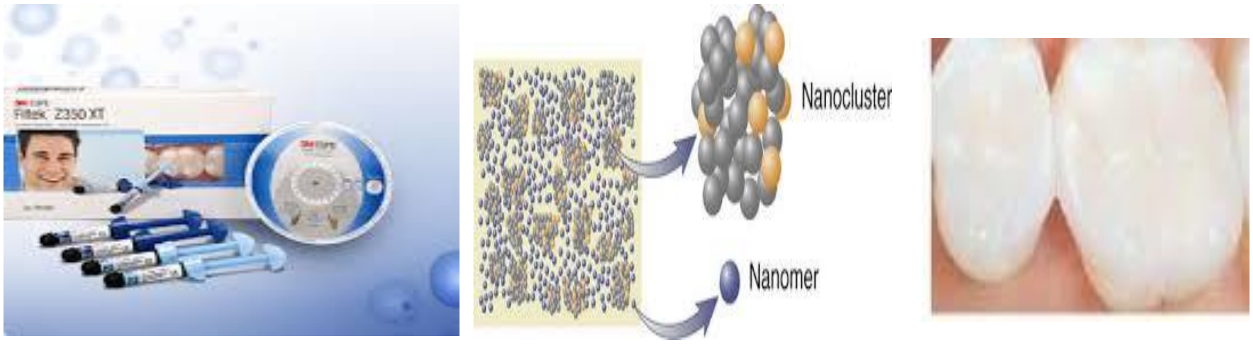
Development of Nanotechnology in the Field of Conservative Dentistry and Endodontics

Advances of Nanotechnology in Conservative Dentistry[93,94,95]

(a) Nanocomposite

One of the most significant contributions to dentistry has been the development of resin based composite technology. Adhesively bonded composites have the advantage of conserving sound tooth structure with the potential for tooth reinforcement, while at same time providing cosmetically acceptable restorations. However, no composite material has been able to meet both functional needs of posterior class I or II restorations and superior esthetics required for anterior restorations. There was a need to develop a composite dental that could excellent mechanical properties suitable for high stress – bearing restoration as well as superior polish retention. Nanoproducts Corporation has successfully manufactured nonagglomerated discrete nanoparticles that are homogeneously distributed in resins or coatings to produce nanocomposites. The nanofiller used include an alumino silicate powder having a mean particle size of 80 nm. Due to small particle sizes nanofillers are capable of increasing the overall filler level as high as 90% to 95% by weight. Since polymerization shrinkage is mainly due to the resin matrix, the increase in filler level results in a lower amount of resin in nanocomposites and will also significantly reduce polymerization shrinkage and dramatically improve the physical properties of nanocomposites. The nanocomposite is composed of three different types of filler components: nonagglomerated discrete silica nanoparticles, barium glass, and prepolymerized fillers.

The development in the use of nanocomposites patented in response to the persistent and discouraging issues of polymerization shrinkage, strength, microhardness, and wears resistance essential in posterior occlusal applications . Bowen developed the resins **[**Bisphenol A-Glycidyl Dimethacrylate (Bis-GMA)**]** and used silane couplers. Around the same era, words like “nano” were coined by the noble laureate Sir Richard Feynman in 1959 . This discovery was a landmark for advances in dental composites. Since then, composite fillings became an essential component of the restorative armamentarium. The last decade has witnessed rapid advances in dental restorative materials including the resin-based composites. The introduction of nanotechnology led to the discovery of nano-filler particles. All efforts were and are being made to achieve considerable advances in physical properties and tackle issues like polymerization shrinkage, wear resistance, micro hardness and achieve patient satisfaction in terms of the aesthetic appearance .



Nanocomposites

Composition

Nanocomposites are composed of two or more materials that include a matrix material and nanoscale particles. The matrix should be a biocompatible polymeric, metallic, or ceramic material. In nanocomposites, it is possible to operate the mechanical properties by incorporating secondary nanoparticles to obtain the same characteristic features of natural bone . The properties of nanostructured materials are completely controlled by their synthesis method, processing means and their chemistry . It has been acknowledged that the intrinsic molecular identification of the molecules is governing the formation, morphological development and crystallography of the nanocomposites .

Evolution of Organic Resin Matrix

Conventional Resin Based Composites (RBC) were based on organic polymer matrix mainly Bis-GMA and triethylene glycol di-methacrylate (TEGDMA). Due to the hydrogen bonding interactions that are present in between hydroxyl groups and monomer molecules, Bis-GMA becomes very viscous. In order to obtain working viscosity they are mixed with more fluid monomer. In some instances Bis-GMA is combined with tri-ethylene glycol di-methacrylate (TEGDMA) or urethane di-methacrylate (UDMA) or even in some cases by ethoxylatedBisphenol-A-dimethacrylate (Bis-EMA). In order to tackle issues of shrinkage, aging and other environmental factors such as temperature changes and moisture, Bis-GMA is replaced with UDMA or other dimethacrylates .

Most of the existing methacrylate resin shrinks depending on the number of polymerizable units. This shrinkage is related to monomer percentage. Two methodologies have been used to reduce polymerization shrinkage; either by reducing the reactive sites or using different types of resins. By increasing the filler loading or increasing the molecular weight per reactive group will reduce the density of reactive sites per volume .

The properties of nanocomposites (good translucency, contouring and surface finish) are excellent and can restore lost or damaged dental tissues . Current research is now being focussed on reducing the polymerization shrinking. The addition of using monovinyl methacrylate monomers into dental resin was introduced by Decker, and reported enhanced polymerization kinetics and improved mechanical properties. They were made up of secondary and tertiary functionalities including urethanes, carbonates or cyclic carbonates. They were also referred to as ultra-rapid monomethacrylates. Recently researchers are investigating options of adding acidic functional groups in monomers .


(a) (b)

Clinical applications of tooth colored nanocomposite restorative materials (a) Root treated and unrestored premolar tooth; (b) Crown build up with a post and core using a modern nanocomposite restorative material

A Paradigm Shift of Nano Fillers to Clusters to Hybrids

Carbon nanotubes have superior and exceptional mechanical properties as well as unique bioactivity . On the other hand carbon nanotubes lack some essential properties such as hydrophobicity and chemical inertness, which in turn limit their applications . Reinforcing dental composite with carbon nanotubes could help reduce such defects and provoke the advantages gained by excellent mechanical and biological characteristics . Inorganic component of dental composites is made up of filler particles and comprised of quartz or engineered glass particles.

Their purposes are to increase strength, modulus of elasticity, reduce polymerization shrinkage and have positive effects on coefficient of thermal expansion and water absorption. Nanohybrid or nanofilled composites are two types of materials referred to the terminology of nanocomposites .

In the process of evolution of dental composites, the alteration of filler size, shape, morphology and loading efficiency still remains a landmark. Various methods adapted to synthesize nanofillers are, flame pyrolysis, flame spray pyrolysis or sol-gel processes. Since the dimensions of these filler particles are below that of visible light, it is impossible for them to either scatter or absorb visible light. This phenomenon plays a key role in getting excellent aesthetic properties and can be used for anterior teeth restorations. Filler loading efficiency can be greater as the size is very small.

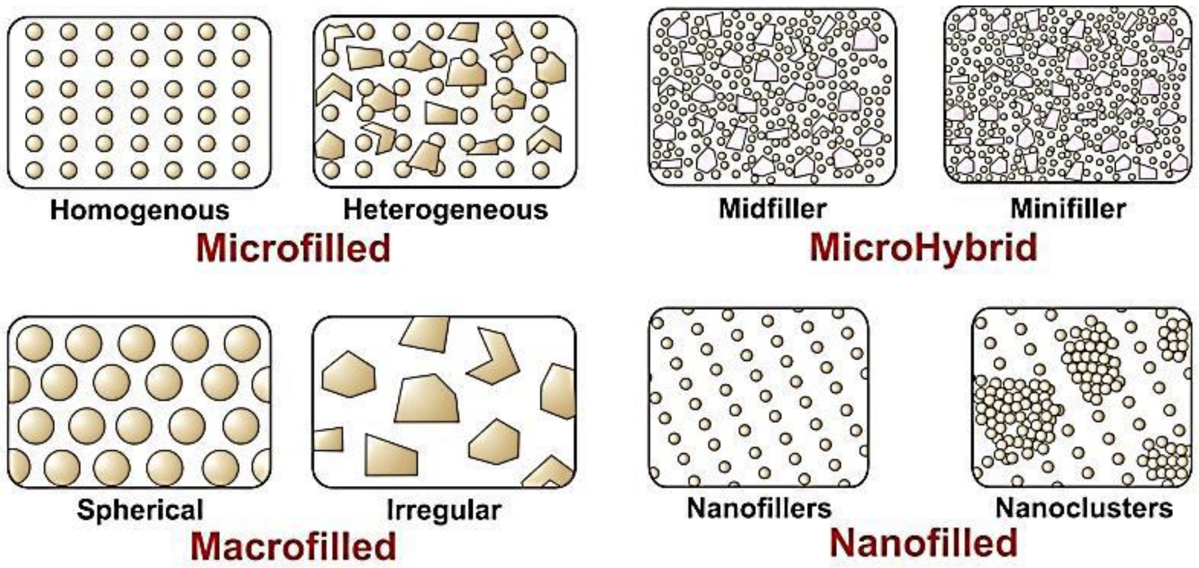
A direct relationship exist in between the filler loading and surface area of filler particles, this has an effect on the wettability of fillers. What nano based filler particles are doing is they help to improve the continuity in between the macroscopic (40 nm to 0.7 nm) natural tooth structure and nano-sized filler particle. This eventually results in a more natural and advanced interface. A homogenous and non-homogenous distribution of nano sized fillers and presence of nanoclusters results in composites with different bulk and surface properties that can be tailor made according to the site of application.

Aesthetic applications of resin nanocomposite restorative materials

(a) Preoperative labial aspect of defective maxillary anterior segment with recurrent decay and discoloration;

(b) Composite layering technique adapted to restore decayed tooth structure and midline;

(c) Postoperative appearance of midline correction using a nanocomposite dental restorative material.



Classification of dental composites on the basis of particle size and structure

Nanofills and nanohybrids are the two different types of more commonly available nanocomposites. Nanofills are dominated by the presence of 1 to 100 nm size particles mainly and nanohybrids are comprised of larger particles ranging from 0.4 to 5 µm, hence they are not truly nanofilled and are called hybrids. For example, NANOSIT™ (Nordiska Dental, Angelholm, Sweden) is a nanohybrid composite comprised of inorganic particles ranging from 7 nm to ≤2000 nm.

The uniformity of particle distribution in nanofillers ranges from 5 to 20 nm in a commercially available product 3M ESPE (Filtek™ Supreme Plus, 3M ESPE, St. Paul, MN, USA). Similarly, such interface (hybrid materials) enables increased filler loading and improved adaptability of dental composites. In case of nano-filled composites, it is extremely difficult to control the particle size precisely hence particle size range is used.

Various sized nanoparticles facilitate better interface and loading. Comparable results are obtained using nanohybrid and cluster materials.

One of the key purposes of using nanomeric particles is to reduce the particle size than the wavelength of visible light (400 nm to 800 nm). This helps in obtaining highly translucent materials, high surface area to volume ratio and molecular interactions as the polymer size range is usually in the same dimensions. One of the two types of nanomeric particles are nano-agglomerated particles made up of silica or zirconia, surface coated with coupling agent to enhance bonding. Highly filled composites if made using nanomers of the same size have a poor effect on rheological properties . In order to overcome this drawback nanoclusters were synthesized by lightly sintering nanomeric oxides resulting in controlled particle size distribution.

Nanoclusters act as a bunch of grapes with an average size range of 0.6 µm. These nanoclusters are also surface treated with silane to improve chemical bonding and adhesion with the organic resin matrix. Filtek™ Supreme Plus (3M ESPE) has pioneered the combination of nanoclusters and nanoparticles to obtain better wear resistance. A considerable improvement in the wear properties was observed using the three body wear test performed on an oral wear simulator.

Coupling Agents

In order to achieve a strong covalent interaction in between the organic matrix and inorganic fillers, coupling agents are used. The coupling agents tend to promote bonding or adhesion between the filler particles and matrix and helping in the transfer of load and stresses. A commonly used coupling agent is gamma methacryloxy propyl trimethoxysilane (MTPS). One side of the coupling agent tends to bond with hydroxyl groups of silica particles and other is copolymerized with polymer matrix . Other agents that are added in minor quantity are initiators for light activation, accelerators, pigments for enhancing color and hue. Most commonly used visible initiator is camphoquinone (CQ), its absorption spectrum lies in between 450 and 500 nm wavelength.

(b)Ormocers

A new organically modified ceramics based on sol-gel synthesis called Ormocers are widely used in nanocomposite restorative systems . The particles are silicones, organic polymers, and ceramic glasses that are applicable to dental composites and the nanoparticle fillers are ZrO2.

(c)Nanomaterials in adhesives (nanofilled bonding agents)

Adhesively bonded joints (ABJs) generally comprise of at least two joining

components (adherends) with a layer of adhesive in between. The adhesive layer is considered to be an important part of a joint system, as it is the agent that accommodates the transfer of load from one adherend to another. ABJs are being widely used in industry owing to their many advantageous attributes compared to conventional mechanically fastened joints. Some of the advantages of adhesive bonding over alternative assembly techniques, especially when joining fiber- reinforced polymer (FRP) composites, are shown below :

- Stresses are more evenly distributed over the entire bond region, thereby

minimizing high localized stress concentrations.

- More superior fatigue resistance than mechanically fastened joints.

- Excellent resistance to mechanical vibration.

- Better compliance to critical tolerances can be achieved compared to

mechanical fastening methods.

- Produces leak-free joints.
- Provides weight and cost savings.

Nanoadhesives

The most common NPs used in reinforcing adhesives are classified based on their type; therefore, a brief description of each group is provided below**[**96**]**

Carbon-based NPs

Among the various types of NPs, the excellent capability of carbon NPs in ameliorating different properties of resins or matrices has persuaded researchers to perform extensive investigations into the behavior of carbon NP reinforced polymers. There are three common configurations of carbon nanofillers, including zero dimensional or spherical particles such as nano-diamond (ND) particles, one-dimensional or cylindrical fillers such as carbon nanotubes (CNTs) and carbon nanofibers (CNFs), and two-dimensional nanofillers such as graphene nanoplate- lets (GNPs). The ND particles with their well-established superior tribological properties have been widely used for surface modification of different materials . In addition, it has been shown that inclusion of CNTs and CNFs into polymers leads to notable increase in the mechanical properties , electrical properties , and thermal properties of the resulting nanocomposites. Besides, the nanocomposites reinforced with GNPs are postulated to offer remarkable thermal , mechanical , and electrical properties .

All these impressive features have encouraged the researchers to explore the reinforcing effect of nanomaterials when included in different polymer matrices. The main disadvantages of carbon nanomaterials are known to be: (a) the incon-sistency in the quality of carbon NPs, especially in their mass-produced form, and (b) their cost.

Metal-based NPs

Metallic NPs have fascinated scientists for over a century, mainly due to their utilization in biomedical sciences and engineering . Today, these materials can be synthesized and modified to obtain various chemical functionalities. Metallic anomaterials can be formed from most metallic elements of the periodic table such as nano-gold, nano-silver and metal oxides (e.g., alumina (Al_2O_3) or zirconia (ZrO_2)) NPs. Although the metal based NPs have been mainly investigated for their electrical , optical and magnetic properties , it has been shown that the mechanical properties can also be improved by inclusion of metallic NPs into polymers .

Although the interest in the optical and electrical properties of metallic NPs has had a long history a number of recent experiments have renewed the interest in using metallic NPs for optical applications. This has also fostered better theoretical and experimental understandings of the key factors and mechanisms governing these properties . Moreover, some metallic NPs have certain unique properties that are of clinical interest. For instance, nano-silver particles have anti-bacterial properties, which have made them one the most commercialized metallic nanoparticles in healthcare . This feature of nano-silver has also rendered it as a potential candidate for inclusion in adhesives used for biomedical applications.

POSS

Polyhedral oligomeric silsesquioxanes (POSS) are nanostructures with the empiri cal formula $RSiO_{1.5}$, where R may be a hydrogen atom or an organic functional group . POSS nanostructures have diameters in the range 1–3 nm. In the last decade, POSS NPs have attracted considerable attention, mainly owing to their small dimensions, and easy incorporation into polymeric materials, thus providing excellent reinforcing attributes to polymers. POSS is also being used as a facilitator for other NPs to improve their dispersion ability.

(d)Nanomaterials in coating agents

Nanotechnology applications in coatings have shown remarkable growth in recent years. This is a result of two main factors: 1) increased availability of nano-scale materials such as various types of nanoparticles, and 2) advancements in processes that can control coating structure at the nanoscale. Another important reason for this growth is the potential of nanotechnology to address many performance challenges presented by the vast range of products and structures that coatings are an integral part of. Applications of coatings include interior and exterior house paints, interior fUrnishings, glass and façade coatings for high-rise buildings, all types of transportation vehicles and structures (automobiles, airplanes, bridges, road markings, marine vessels, spacecrafts, etc.), and a wide variety of industrial and non-industrial maintenance coatings.

At a much smaller scale, coatings are used in numerous electronic products (both consumer and industrial electronics) and biomedical products. Coating layer thicknesses can vary from hundreds of micrometers (e.g., anti-skid coating on the deck of an aircraft carrier) to less than 100 nm (e.g., insulating coatings in microchips).

Coatings play one or more of three key roles in these applications: 1) improve product's esthetic appeal, 2) protect the substrate from a wide range of abuses (e.g., damage due to scratches or impact, corrosion, long term weathering, and bio-fouling), and 3) provide specialized functionality to the product (e.g., conductivity, insulation, water repellency, and heat reflection). It is in the latter two roles where nanotechnology has opened up exciting possibilities to improve performance attributes of coatings and the associated products.

Nanoparticle-Based Composite Coatings Incorporation of preformed nanoparticles into organic coating formulations is one of the most straightforward approaches to preparing nanocomposite coatings. Increased availability of inorganic oxide nanoparticles targeted for various property improvements of organic coatings has tremendously helped coating formulating companies to introduce nanotechnology products.

Nanocomposite Coating Performance

Scratch Resistant, Nanocomposite Clear Coatings

Until the recent advancements that led to the availability of a wide range of inorganic nanoparticles, silica has been the choice material for reinforcing clear coatings for applications such as automotive top-coats, floor wear layers, acrylic eye-glass lenses, and scratch resistant polycarbonate sheets for various applications. Colloidal silica has been available for decades from at least a dozen companies around the world in the particle sizes range from about 2 to 100 nm, in aqueous and non-aqueous media. The refractive index (RI) of silica which is 1.46 closely matches the refractive index of common organic binders in coatings, and therefore, high silica loading levels can be achieved without causing haziness problems in coatings. In 1976, Dow Chemical has claimed use of colloidal silica in abrasion resistant coatings for acrylic lenses

Anticorrosion and Barrier Coatings

The role of nanocomposites in barrier films for packaging applications has been reviewed along with a comprehensive list of other approaches (60). Products in the market today include polyamide, PET, and PP composite films containing nanoclays. An elastomeric barrier coating introduced in 2001 for Wilson's Double Core tennis balls was claimed to be the first nanocomposite coating for such a product. One to two micron thick coating of this nanocomposite is claimed to be as effective as a 12 micron thick layer of ethylene vinyl alcohol (EVOH) copolymer as an oxygen barrier for PET.

Coating agents

Nanocomposite Coatings for Controlling UV, IR, and Other Radiation Coatings play a critical role in controlling the effects of electromagnetic radiation (UV, Visible, IR, other) on many surfaces. The specific electromagnetic frequency range of interest is a factor that determines the coating formulation ingredient selection. Controlling the interactions with the visible light to affect the color and appearance through the right choice of ingredients is the best example of this. Various organic and inorganic pigments are selected for this purpose. Ti02 (RI=2.5-2.7) is the most effective white pigment; its hiding power is highest at about 250 nm particle size.

Advances of Nanotechnology in Preventive Dentistry

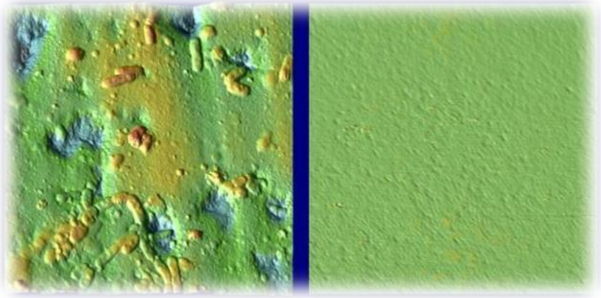
(a)Caries prevention fillers

To increase mineral content to control dental caries, calcium and phosphate ion-releasing fillers have been developed, such as nanoparticles of dicalcium phosphate anhydrous (DCPA) and tetracalcium phosphate **[**TTCP: Ca (PO) O**]**-whiskers . Recent studies by Xu et al. have evaluated the incorporation of nanosized CaPO4 particles with resin bonded composites, with a resulting improvement in stress-bearing capacity, as well as ion release that could inhibit caries. Further investigation of this model using dicalcium phosphate anhydrous incorporated with nanosilica-fused whiskers found that it increased the strength of the resin bonded composites by as much as threefold while releasing CaPO4. This release was greater with decreasing CaPO4 particle size.

The authors hypothesize that such a system could provide a desirable combination of caries prevention and increased restoration strength.

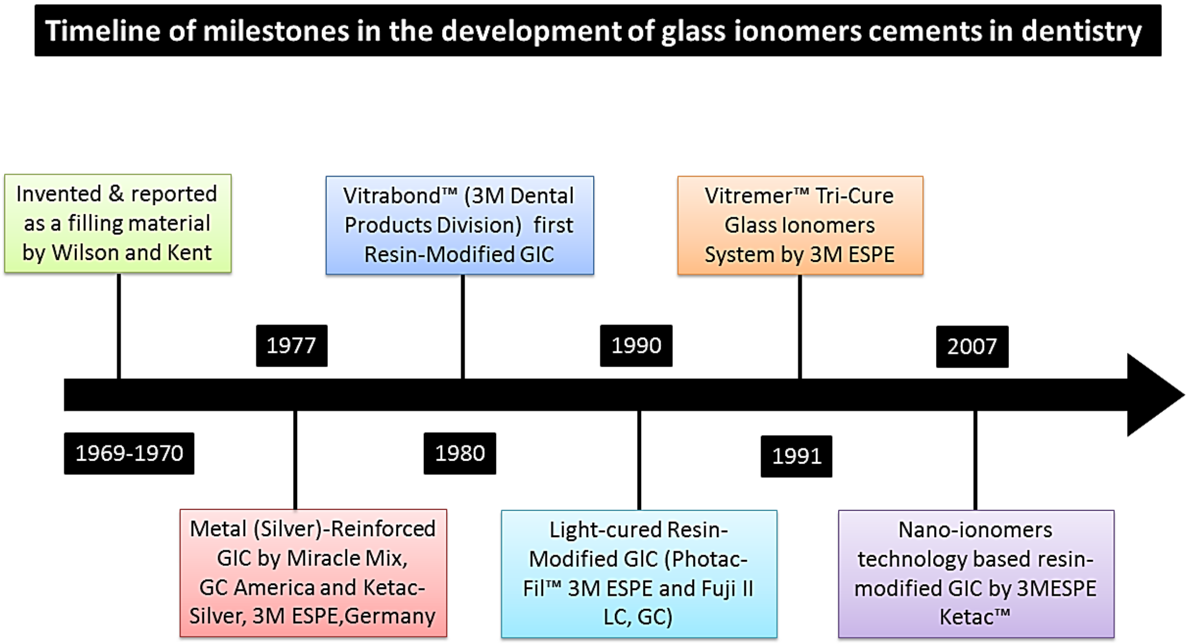
(b)Nanofilled Resin Modified Glass Ionomer (Nano-Ionomers)

Dental cements are materials in dentistry that are used frequently. There is no universally accepted cement that fulfills all applications; there are a variety of cements whose properties and manipulation lead them to be an appropriate choice for a given application. The retention of restorations on prepared teeth is a major function of dental cements. Long-term cementation is required for permanent restorations such as crowns and bridges. Strong cements, such as compomer, glass ionomers, hybrid ionomers, zinc phosphate, zinc poly-carboxylate, or resin-based cement, are used for the long term cementation .



Nano- ionomers

Glass ionomers were introduced by Wilson and Kent in the 1970s as dental filling material . The timeline of milestone in the development of glass ionomers cement in dentistry is described in The powder is composed of mainly fluoro-alumino-silicate (FAS) glass particles and ions such as strontium, calcium and lanthanum. The liquid is a copolymer of acrylic acid and itaconic acid or maleic acid and supplied as a viscous fluid. Acid base reaction takes place while powder and liquid are mixed and initial set takes place in 3–4 min . Glass ionomers are being used widely because of its excellent properties such as chemical bonding to the tooth structure, biocompatibility and fluoride release. On the other hand, there are a number of shortcomings for this group of materials such as poor aesthetic, prolonged setting reaction, compromised mechanical properties and weaker bond strength . In order to improve the properties and to overcome these shortcomings, active research is in progress, such as in the addition of cellulose fibers, hydroxyapatite and fluoroapatite and nanotechnologies.



Timeline of milestone in the development of glass ionomer cements and nano-ionomers for dental restorations

For the restoration of primary teeth and small cavities in permanent teeth a new nano-filled Resin Modified Glass Ionomer (RMGIC) restorative material has been introduced It is based on a prior Resin Modified Glass Ionomer (RMGIC) with a simplified dispensing and mixing system (paste/paste) that requires the use of a priming step, but no separate conditioning step. Its primary curing mechanism is by light activation, and no redox or self curing occurs during setting . Apart from the user-friendliness, the major innovation of this material involves the incorporation of nano-technology, which allows a highly packed filler composition (69%), of which approximately two-thirds are nanofillers.

Chemistry of nanoionomer is based on the methacrylate modified polyalkenoic acid, which is capable of both crosslinking via pendate methacrylate groups as well as the acidbase reaction between the Fluoroaluminosilicate Glass (FAS) and the acrylic and itaconic acid copolymer groups. It contains surface treated nanofillers (approx 5 nm to 25 nm) and nanoclusters (approx 1 µ to 1.6 µ). Filler loading is approx. 69% by weight of which the relative proportion of two filler types (FAS and combination of nanofillers) are approx 2/5 and 3/5 respectively. All nanofillers are further surface modified with methacrylate silane coupling agents to provide covalent bond formation into free radically polymerized matrix .

More recently, nanotechnologies have been applied to the resin modified glass ionomers in the form of nanoparticles (nanomers) and nanoclusters in fluoroaluminosilicate (FAS) glass. These nanoionomers (Ketac™ Nano; 3M ESPE) have been available for clinical use since 2007 . The addition of nanoparticles resulted in the aesthetic improvement of the final restoration and polishablilty . It is important to mention that fluoride release property is not affected by addition of nanoparticles due to the high surface area.

In a recent study, the Knoop hardness of Ketac™ Nano was observed to be lower (39 KHN) than resin modified (Vitremer) glass ionomers (69.9 KHN). The Knoop hardness of Ketac™ Nano (48 KHN) is not fulfilling the American Dental Association (ADA) specifications for restoration hardness; hence cannot be recommended for high stress bearing areas. The manufacturer (3M ESPE) has recommended its use for class I, class III, class V, under the composite and primary teeth. Tancan, et al. reported shear bond strength (SBS) of nanoionomer and nanocomposites is good as compare with conventional GICs orthodontic bracket bonding.

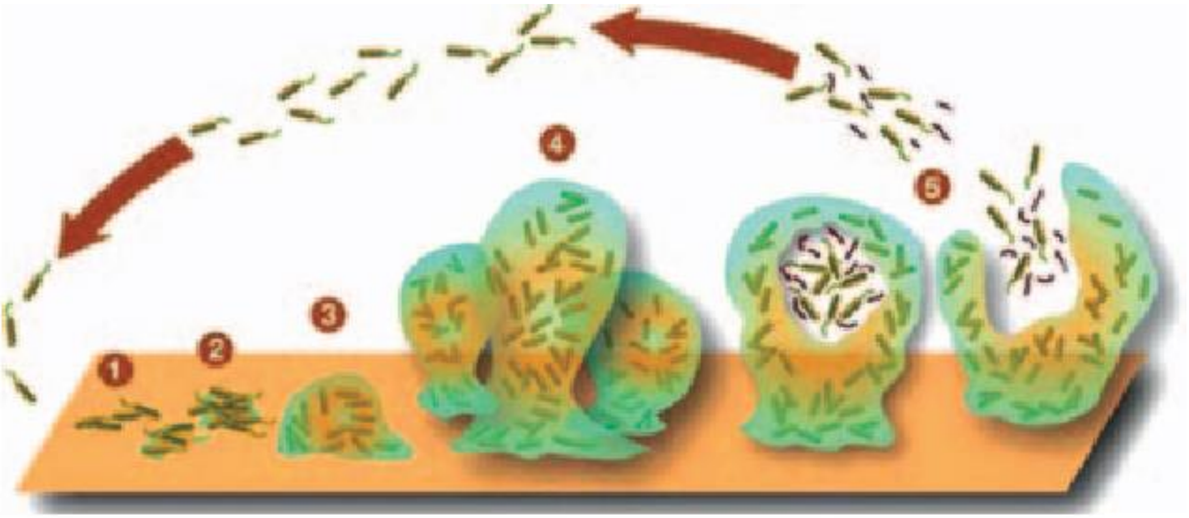
Another development is the introduction of a new nanomaterial called Equia® System. Inorganic silica nanofillers (40 nm size) are dispersed in liquid and reinforce the resulting polymer matrix. Adding 15 wt. % silica nanofillers resulted in good wear resistance and reduction in the initial setting time. Due to better resistance dissolution, disintegration and wear, these materials were observed to maintain polished surface for a longer period of time . There is an enhancement of optical properties and translucency compared to conventional glass ionomers and aesthetic appearance is improved remarkably and claimed as good as of natural teeth . Friedl et al. present a retrospective study on new glass ionomers cements to evaluate their performance and concluded Equia® System is good for posterior filling materials .

The effects of additives such as nanoscale hydroxyapatite (HA) and fluoroapatite (FA) on properties of glass ionomers is a hot topic for researchers. Hydroxyapatite crystals are well known for their biocompatibility and have made a major contribution in the chemical structure of natural enamel and dentin. The bond strength of resin modified glass ionomers to the tooth structure was measured 8–12 MPa . The bond strength was increased with addition of micro HA (5–10 μm) and whereas Nano-HA (100–150 nm) further improved the bond strength. This improved strength is probably related to the availability of a higher surface area for bonding to tooth structure in case of Nano-HA. This high surface area also increases the surface finish and solubility of Nano-HA that helps filling the demineralizing micro-pores in the tooth structure . Similarly, Nano-HA and Nano-FA prepared using ethanol based sol-gel methods were added to Fuji II glass ionomers .

The modified nano-filled glass ionomers exhibited better mechanical properties such as compressive strength, diametral tensile strength and biaxial flexural strength. Modification of existing glass ionomers using nanomaterials is an active area of current research. A number of other materials such as alumina, alumina/titania, zirconia and yttria stabilized zirconia. There are very high expectations from this on-going research on nanomaterials in relation to glass ionomers. As a result, it can be hoped that there will be an addition of new dental materials in the near future or the properties of existing glass ionomers will be improved significantly .

(c)Nanomaterials for Managing Oral Biofilms

Nanotechnology has been used to study the dynamics of demineralization/remineralization process in dental caries by using tools such as atomic force microscopy (AFM) which detect bacteria induced demineralization at an ultrasensitive level. Using AFM the correlation between genetically modified Streptococcus mutans scale morphology has been assessed. The nanoscale cellular ultra structure is a direct representation of genetic modifications as most initiate changes in surface protein and enzyme expression, where host- cell nutrient pathways and immune response protection likely occur. The surface proteins and enzymes, common to S. mutans strains are a key contributor to the carcinogenicity of these microbes. New silver nanotechnology chemistry has proven to be effective against biofilms. Silver works in a number of ways to disrupt critical functions in a micro-organism.



For example it has a high affinity for negatively charged side groups on biological molecules such as sulphydryl, carboxyl, phosphate and other charged groups distributed throughout microbial cells. Silver attacks multiple sites within the cell to inactivate critical physiological functions such as cell wall synthesis, membrane transport, nucleic acid (RNA and DNA) synthesis and translation, protein folding and function and electron transport. For certain bacteria as little as one part per billion of silver may be effective in preventing cell growth. Recent studies show that ionic plasma disposition silver antimicrobial nanotechnology is effective against pathogens associated with bio-films including E. coli, S. pneumoniae, S. pneumoniae, S. aureus and A. niger .

Advances of Nanotechnology in Endodontics

(a)Disinfection of Root Canals

Nanoparticulate based disinfection in endodontics The most efficient disinfection of root canals with nanoparticles has gained popularity in the recent years. This is mainly due to the broad spectrum antibacterial activity . The nanoparticles evaluated in endodontics include Chitosan, zinc oxide and silver . The efficacy of chitosan and zinc oxide nanoparticles against Enterococcus fecalis has been attributed to their ability to disrupt the cell wall. In addition, these nanoparticles are also able to disintegrate the biofilms within the root canal system . Silver nanoparticles are being evaluated for use as root canal disinfecting agents. It has been shown that 0.02% silver nanoparticle gel is able to kill and disrupt Enterococcus faecalis biofilm . Another revolutionary introduction in the field of endodontics, the fundamental basis of which lies in nanotechnology, is bioactive glass (SiO2-Na2O-CaO-P2O5. The use of SiO2-Na2O-CaO-P2O5 has been suggested for root canal disinfection . The antimicrobial effect of bioactive glass is due its ability to maintain an alkaline environment over a period of time. The efficacy of 45S5 bioactive suspension-nanometric/micrometric hybrid as an antimicrobial agent showed that a ten-fold increase in silica release and 3 units of pH elevation was found with the nanometric bioactive glass .

(b)Endodontic Sealer

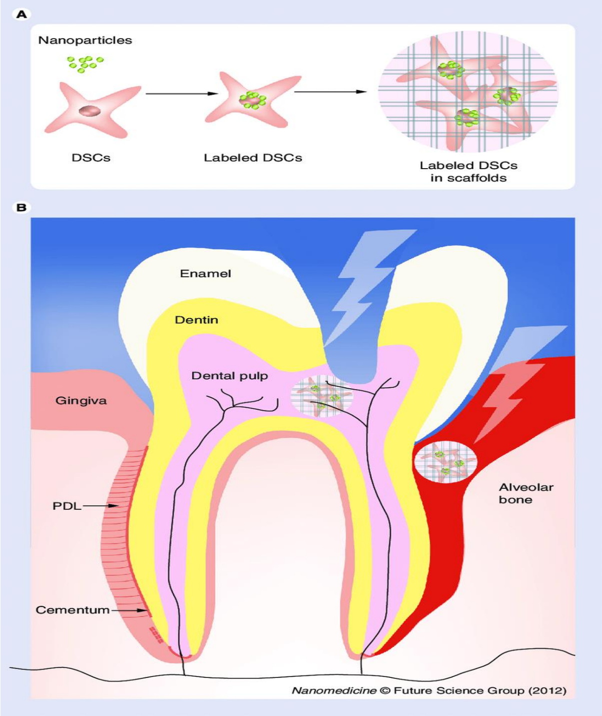
The applications of nanotechnology are not limited to filling materials but have been extended to endodontic applications. A bioceramic based nanomaterials (EndoSequence BC sealer) composed of calcium silicate, calcium phosphate, calcium hydroxide, zirconia and a thickening agent, has been developed recently. Nanoparticles have improved the handling and physical properties. During the hydration reaction in the root canal, a nanocomposites structure of calcium silicate and hydroxyapatite is formed. The hydration reaction and setting time is affected by the availability of water and setting time may be prolonged in overly dried canals. Nano sized particles facilitate delivery of material from 0.012 capillary needle and adopt to irregular dentin surfaces. It sets hard in a matter of a few hours providing excellent seal and dimensional stability. Upon setting, it forms of hydroxyapatite; providing biocompatible and bioactivity. The highly alkaline pH (12.8) gives antimicrobial properties as well .

Endodontic sealer

Another example is a silicon based sealer (Gutta-Flow Sealer) with an addition of gutta-percha powder and silver nanoparticles. This material is available in the form of uni-dose capsule that can be mixed and injected . This nano-sealer has good biocompatibility, dimensionally stable and sets within half an hour. This material has been reported to improve the sealing capability and better resistance to bacterial penetration. For infection point of view, the antibacterial activity of endodontic sealers can be very beneficial. Recently, antibacterial quaternary ammonium polyethyleneimine (QPEI) nanoparticles have been incorporated into existing sealers such as AH plus, Epiphany and Guttaflow . Resin composites containing QPEI nanoparticles resulted in prolonged antibacterial activity without compromising the mechanical properties . In order to obtain similar antibacterial effect in endodontic sealers, 0-2 wt% QPEI nanoparticles were added in to the commercially available sealers . The addition of QPEI nanoparticles is very stable, leaching no byproducts in the surrounding and there was no effect on the biocompatibility; however, the antibacterial properties remained excellent.

(c)Materials for endodontic regeneration

Teeth with degenerated and necroses pulps are routinely saved by root canal therapy. Although current treatment modalities offer high levels of success for many conditions, an ideal form of therapy might consist of regenerative approaches, in which diseased or necrotic pulp tissues are removed and replaced with healthy pulp tissues to revitalize teeth. In their study, Fioretti et al. showed that a-MSH (melanocortin peptides) possess anti-inflammatory properties and also promote the proliferation of pulpal fibroblasts. They reported the first use of nanostructured and functionalized multilayered films containing a-MSH as a new active biomaterial for endodontic regeneration.



Nanomedicine © Future Science Group (2012)

The applications of nanoscale scaffold materials for tooth tissue regeneration are well established. For pulp regeneration, pulp stem cells were purified in the laboratory and grown in sheets on scaffolds. The scaffolds used were composed of nanofibers of biodegradable collagen type I or fibronectin . Self-assembling polypeptide hydrogels have been used for pulp tissue regeneration.

There is formation of a nanofiber mesh that supported the growing cells . Puramatrix (containing amino acids repeats of alanine, arginine and aspartate) has been proven to enhance cell growth . Natural silk based nanomaterials are being used for various tissue regeneration applications and have promising scope for dental applications . Injectable self-assembly collagen I scaffold loaded with exfoliated teeth stem cells resulted in the formation of pulp like tissue and functional odontoblasts .

Collagen type I is the most abundant fibrous protein found in the form of nanofibers in dentin (~80%–90% of organic matrix) and bone . Odontogenic differentiation and mineralization was promoted in the presence of type I collagen scaffolds . The tissue regeneration approached are not in practical implementation at present, however further research is expected to overcome the challenges to fancy tissue engineering products available for clinical applications in near future.

Challenges faced by nanodentistry

1. Engineering challenges

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

2. Biological challenges

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

3. Social challenges

- Ethics
- Public acceptance
- Regulation and human safety

Engineering challenges:

There is a problem in the feasibility of mass production technique. Precise positioning and assembly of molecular scale part is a challenge for them. Manipulating and coordinating activities of large numbers of independent microscale robots simultaneously is a difficult task. Even though the field of nanorobotics is fundamentally different from that of the macro robots due to the differences in scale and material, there are many similarities in design and control techniques that eventually could be projected and applied. Due to the modern scientific capabilities, it has become possible to attempt the creation of nanorobotic devices and interface them with the macro world for control. There are countless such machines which exist in nature and there is an opportunity to build more of them by mimicking nature. Now a days these nanorobots play a vital role in the field of Bio Medicine & dentistry, especially in the treatment of cancer. It also helps to remove the defected part in our DNA structure and some other treatments that have the greatest aid to save human lives.

Biological challenges:

It is essential to develop bio friendly nanomaterial and ensure compatibility with all intricate of human body. In general, smaller particles are more bioactive and toxic. Their ability to interact with other living systems increases because they can easily cross the skin, lung, and in some cases the blood/brain barriers. Once inside the body, there may be further biochemical reactions like the creation of free radicals that damage cells. While the body has built- defense for natural particles it encounters, the danger of nanotechnology is that it is introducing entirely new type of particles. Some experts believe that the body is likely to find toxic. Social challenges: Highest at risk are workers employed by manufacturers producing products that contain nanoparticles. The National Institute for Occupational Safety and Health (NIOSH) reports over two million Americans are exposed to high levels of nanoparticles. NIOSH publishes safety guidelines and other information for those employed in the nanoindustry**[**97**]**.

Problems for Research in Nanotechnology in India:

The production and application of Nanorobots in India might find the following problems:**[**106**]**

- Poor and slow strategic decisions
- Inappropriate funding
- Lack of involvement of private agencies
- Inadequate trained manpower and problem of retaining them

Nano-Hazards

Since nanotechnology is a very recent discovery and is only just being put in to use, there are issues that need to be addressed. As long term effects of nanotechnology are unknown, therefore, potential hazards caused by the nanotechnology might not show for many years. Various factors govern the amount of free Nanoparticles in nature such as their physico-chemical properties, quantity, and time of exposure. Nanomaterials released in the environment can be further modified by, Temperature, pH, different biological conditions, and presence of other pollutants. In this interaction , nanomaterials can alter atmosphere, soil and water and prove to be harmful to human health and the environment.**[**98**]**

Review of Literature

1. Alagarasi ; INTRODUCTION TO NANOMATERIALS;2011

this article reviewed that Nanomaterials are cornerstones of nanoscience and nanotechnology. Nanostructure science and technology is a broad and interdisciplinary area of research and development activity that has been growing explosively worldwide in the past few years. It has the potential for revolutionizing the ways in which materials and products are created and the range and nature of functionalities that can be accessed. It is already having a significant commercial impact, which will assuredly increase in the future.**[**6**]**

2. R.B.Durairaj, Shanker.J, and Dr.M.Sivasankar ; Nano Robots In Bio Medical Application; IEEE – ICAESM 2012

This article describeed that the nano-robots are the robots that are simply known as that controllable machines at the nano (10-9) meter or molecular scale, composed of nano-components. More specifically, nano robotics refer to the still largely hypothetical nanotechnology engineering discipline of designing and building nano robots.

Even though the field of nano robotics is fundamentally different from that of the macro robots due to the differences in scale and material, there are many similarities in design and control techniques that eventually could be projected and applied. Due to the modern scientific capabilities, it has become possible to attempt the creation of nano robotic devices and interface them with the macro world for control. There are countless such machines which exist in nature and there is an opportunity to build more of them by mimicking nature.

Nowadays these nano robots plays a vital role in the field of Bio Medicine. Especially in the treatment of cancer, Cerebral Aneurysm, kidney stones removal, also to remove the defected part in our DNA structure and some other treatments that have the greatest aid to save human lives. This paper guides to the recent research on nano robots in the Bio medical applications.**[**71**]**

3. Rita Chandki , M. Kala , Kiran Kumar N. , Biji Brigit , Priyank Banthia , Ruchi Banthia; 'NANODENTISTRY': Exploring the beauty of miniature; J Clin Exp Dent. 2012;4(2):e119-24.

This article reviewed the current status and the potential clinical applications of nanotechnologyin dentistry.Feynman's early vision in 1959 gave birth to the concept of nanotechnology. He saw it as an unavoidable development in the progress of science and said that there is plenty of room at the bottom. Since then, nanotechnology has been part of mainstream scientific theory with potential medical and dental applications. Numerous theoretical predictions have been made based on the potential applications of nanotechnology in dentistry, with varying levels of optimism. While a few layers of nanotechnologic capability have become a reality for oral health in the last decade, many of these applications are still in their puerile stage .The most substantial contribution of nanotechnology to dentistry till date, is the more enhanced restoration of tooth structure with nanocomposites. The field of nanotechnology has tremendous potential, which if harnessed efficiently, can bring out significant benefits to the human society such as improved health, better use of natural resources, and reduced environmental pollution. The future holds in store an era of dentistry in which every procedure will be performed using equipments and devices based on nanotechnology. **[**107**]**

4. Rohit Kumar, Omprakash Baghel, Sanat Kumar Sidar; Applications of Nanorobotics; ISSN 2278 – 0882 Volume 3, Issue 8, November 2014

The purpose of this paper is to review the phenomenon of nanorobotics at a might apply to micro and nano scale robotics is called nanorobotics. These miniature robots have unique advantages such as accessing to unprecedented and small areas, increased flexibility, functionality and robustness, and being low cost), adaptive and distributed. Nanorobotics is the technology of creating machines or robots at or close to the microscopic scale of a nanometer (10−9 meters). More specifically,. As no artificial non-biological nanorobots have yet been created, they remain a hypothetical concept.**[**108**]**

5. Sneha Sundar Rajan , Shashi Rashmi Acharya And Vidya Saraswathi ; Nanodentistry; Indian J.Sci.Res. 4(2) : 233-238, 2013

Nanotechnology is a phenomenon present since the late 1950's and is currently finding a strong ground in the field of dentistry. Nanotechnology when integrated into dentistry gives rise to a new stream nanodentistry. The purpose of this paper is to review nanodentistry in its current form categorizing broadly into bottom up approach and top dowm approach hence covering various applications of nanotechnology ranging from the nanorobots in nano anesthesia to its varied use in dental materials and implants. Nanotechnology is an empire in the rising and though it faces many challenges such potential toxicity of nanoparticles, risks due to malicious and unwise use of molecular manufacturing, it still offers great potential for innovations in dentistry.**[**102**]**

6. Dr. Mehra P, Dr. Nabhi K; A Nanorobotics - The Changing Face of Dentistry; Index Copernicus Value (2013): 6.14 | Impact Factor (2014): 5.611

Nanotechnology is the manipulation of matter on the molecular and atomic levels. It has the potential to bring enormous changes into the fields of medicine and dentistry. A day may soon come when nanodentistry will succeed in maintaining near-perfect oral health through the aid of nanorobotics, nanomaterials and biotechnology. However, as with all developments, it may also pose a risk for misuse. Time, economical and technical resources, and human needs will determine the direction this revolutionizing development may take. This article reviewed that the current status and the potential clinical applications of nanotechnology, nanaomedicine and nanodentistry.**[**105**]**

7. Sumit Mohan ,Anuraag Gurtu , Anurag Singhal and Ankita Mehrotra; Nanotechnology : Its Implications in Conservative Dentistry and Endodontics; Journal of Dental Sciences & Oral Rehabilitation 2013; July – September

Feynman postulated concept of nanotechnology as an unavoidable development in the progress of science. Since then, nanotechnology has been part of mainstream scientific theory with potential medical and dental applications. Numerous theoretical predictions have been made based on the potential applications of nanotechnology in dentistry. The most substantial contribution of nanotechnology to dentistry is the more enhanced restoration of tooth structure with nanocomposites. The field of nanotechnology has tremendous

potential, which if harnessed efficiently, can bring out significant benefits to the human society such as improved health, better use of natural resources. The future holds in store an era of dentistry in which every procedure will be performed using equipments and devices based on nanotechnology. This article reviews the potential clinical applications of nanotechnology in conservative dentistry and endodontics.**[**109**]**

8. Roshan Noor Mohamed,Sathyajith Naik,Poornima Parameswarappa ;Nanodentistry: The next big thing is small,Article · April 2014

This study reviewed that Nanotechnology has revolutionized the field of dentistry with tremendous potential to provide a comprehensive oral health care using the nanomaterials, advanced clinical tools and devices. The new era of dentistry will encompass precisely regulated analgesia, tooth renaturalization, complete cure for hypersensitivity and rapid orthodontic treatment. Many novel nanotechnology products are on the way, and new treatment modalities are also proposed. Nanotechnology has increased the hope for better oral health care delivery and improved maintenance through the ongoing research in diagnosis, cure and prevention of oral diseases. This review article provides an insight about the importance and possible applications of nanotechnology in the field of dentistry.**[**1**]**

9. Deepak Ranjan Dalai1, D. J. Bhaskar, Chandan Agali R., Nisha Singh, Devanand Gupta, Swapnil S. Bumb; Futuristic Application of Nano-Robots in Dentistry; International Journal of Advanced Health Sciences | July 2014 | Vol 1 | Issue 3

This review article described that the Nanorobots which are considered as the most useful gift of nanotechnology to medical sciences, having size of few nanometers (10-9)meters are produced by a modern technology called Nanorobotics. These micron-sized devices aid in précised interaction with objects of nanoscale and manipulate with high power resolution. The advents of nanotechnology involve the application of nanorobots in various aspects of dentistry like, Local Anesthesia, Dentition Re-naturalization, and permanent Hypersensitivity cure, complete Orthodontic Realignments during single office visit, and continuous oral health maintenance using mechanical dentifrobots.It is envisoned that Dental Nanorobots could be constructed to destroy caries-causing bacteria or to repair tooth blemishes. Eventhough research work and clinical trials on Nano robots are in the early stage, researchers are quite optimistic regarding the use the these microrobots in dentistry.**[**106**]**

10.Sivaramakrishnan SM and Neelakantan P; Nanotechnology in Dentistry - What does the Future Hold in Store?; Dentistry 2014, 4:2

This reviewed article provides a comprehensive discussion of the present and future of nanotechnology in dentistry.

The medical and dental field has seen several technological revolutions that have changed clinical practice. One concept which has and holds further promise in bringing about a paradigm shift in the field of diagnostics and management is nanotechnology. Nanotechnology has several applications in dentistry, from diagnosis of pathological conditions to local anaesthesia, orthodontic tooth movement and periodontics. Biomaterials science has also greatly benefited by this technology.**[**112**]**

11. Amit Kumar; Nanotechnology Development in India: An Overview; 2015

Nanotechnology has been heralded as a revolutionary technology by many scholars worldwide. Being an enabling technology, it has the potential to open up new vistas in the field of R&D in various multiple disciplines and have wide domain of sectoral applications, ranging from healthcare/medicines, electronics, textiles, agriculture, construction, water treatment, and food processing to cosmetics. Much of these applications are very much pertinent for a developing country like India. In this context, the government has been playing a pioneering role in fostering and promoting nanotechnology R&D in India since early 2000s. This discussion paper attempts to capture the nanotechnology development in India by highlighting the various initiatives undertaken by the government to promote basic R&D in it, the major actors involved and the state of regulatory framework existing in the country. It also looks into these aspects vis-à-vis certain global initiatives/trends.**[**113**]**

12. Shreemoy Dash, Sowmya Kallepalli; influence of nanotechnology in operative dentistry and endodontics –think "BIG" act "SMALL"; Journal of Advanced Medical and Dental Sciences Research |Vol. 3|Issue 4| October- December 2015

Thia article reviewed that today the revolutionary development of nanotechnology has become the most demanding discipline in the field of science and technology. It forms the basis of novel methods for disease diagnosis and prevention.

The evolution of nanotechnology will help dentists with oral health care services less stressful and more acceptable to the patients. However, patient awareness and education are important to make them understand the developments in this field and the options available in the treatment. This review article provides an insight about the role of nanotechnology and its applications in Operative Dentistry andEn dodontics.**[**103**]**

13. Zohaib Khurshid , Muhammad Zafar , Saad Qasim , Sana Shahab , Mustafa Naseem and Ammar AbuReqaiba; Advances in Nanotechnology for Restorative Dentistry; Materials 2015, 8, 717-731; doi:10.3390/ma8020717

This review described the basic concept of nanomaterials, recent innovations in nanomaterials and their applications in restorative dentistry. Advances in nanotechnologies are paving the future of dentistry, and there are a plenty of hopes placed on nanomaterials in terms of improving the health care of dental patients. Rationalizing has become a new trend in the world of science and technology. Nanotechnology has ascended to become one of the most favorable technologies, and one which will change the application of materials in different fields. The quality of dental biomaterials has been improved by the emergence of nanotechnology. This technology manufactures materials with much better properties or by improving the properties of existing materials. The science of nanotechnology has become the most popular area of research, currently covering a broad range of applications in dentistry.**[**93**]**

14. Sachdeva S,Kapoor P, Tamrakar AK,Noor R; Nano-composite dental resins: an overview; Annals of Dental Specialty Vol. 3; Issue 2. Apr – June 2015 |

This article reviewed that dental composite resins, due to their superior esthetic and shade matching properties, have been widely used as the material of choice for restoring anterior teeth. However, their application in the posterior stress bearing areas has remained questionable due to the lack of adequate physical & mechanical properties. The recent advent of nanotechnology has enabled manipulation of these conventional dental composites at a nanoscale level resulting in the newer and advanced materials called Nanocomposites. In these nanocomposites, the resin matrix is reinforced with the nanosized filler particles, resulting in significantly improved mechanical properties. The resultant improvement in physical properties, coupled with superior esthetics, has made nanocomposites as the ideal material of choice in anterior as well as posterior class-I & II situations. This paper attempted to give an overview on the applications and properties of nanocomposites.**[**104**]**

15. S A P Rasheed1, Mathews Jude2, Kevin Suresh3, Suneethi Dey4, Shubhalakshmi Sunil5, Dan Varghese6; Nanotechnology and Its Applications in Dentistry; International Journal of Advanced Health Sciences • Vol 2 Issue 9 • January 2016

This article reviewed that "Nano" is a word derived from Greek meaning "dwarf." One Nano is 10−9 of a meter. It is a scientific approach of altering, manipulating the properties of atoms on a nanometer scale. Nanotechnology involves commonly two approaches that are the Bottom Up approach and Top Down approach. It is possible to maintain a near perfect oral health using nanomaterials, nanorobotics and through the advances in the field of biotechnology. The wider application of nanotechnology in the field of dentistry leads to the emergence of a new field called nanodentistry. It can be used for administering local anesthesia and can also be used to manipulate periodontal tissues in the future thereby allowing a rapid and painless correction of malaligned tooth and that too in a very short time which will save time and less painful compared to the conventional orthodontic treatment. Vinyl poly-siloxane incorporated with nanofillers produce high-quality addition silicone impression materials with better flow, adhesiveness, and improved hydrophilic properties. Failure of implants mainly occurs due to insufficient bone formation around the biomaterial placed, which can be overcome by coating the dental implants with nanoparticles.

Dental robots can be used to occlude the dentinal tubules selectively thereby preventing the dentin hypersensitivity permanently within minutes. It can be used in the local delivery of drugs. Mouthwash or toothpaste incorporated with nanorobots prevents the accumulation of calculus by metabolizing trapped organic matter and converts it into odorless and harmless vapors and can be used for replacement of damaged enamel layers. Incorporating nanoparticle in the disinfectant has found to be useful in increasing the efficacy. So that, the rebuilt tooth structure cannot be distinguished from the original structures.**[**2**]**

16. Munish Goel, Neeraj Sharma, Sheenam Garg and Anish Garg;; Nanodentistry - "Unbounding The Future"; April 11, 2016

This ar¬ticle highlighted the potential application of nanotechnology in dentistry and their impact on clinical dental practice.

Nanotechnology, or nanoscience, refers to the research and development of an applied science at the atomic, molecular, or macro¬molecular levels i.e., molecular engineering & manufacturing . In the long term, nanomedicine will allow instant pathogen identi¬fication and examination, in vivo individual cell surgery and improvement of natural physiological function. Nanotechnology holds a promise for advanced diagnostics, targeted drug delivery and biosensors . The maintenance of comprehensive oral health care with the use of nanomaterials, biotechnology, and ultimately dental nanorobotics will be made possible by nanodentistry. Current research focuses on manufacturing of nanostructure, nanomotors and various means to assemble them together in larger structures. **[**110**]**

17. Pankaj Gupta, Heeresh Shetty; Nanotechnology: Its Role in Restorative Dentistry and Endodontics;2016

This article reviewed that Nanotechnology has made its way into various fields of medicine and dentistry in a positive way. The current communication gives an insight into the various applications of nanotechnology in restorative dentistry and endodontics**[4]**

18. Ramandeep Singh Gambhir, G. M. Sogi1, Ashutosh Nirola2, Rajdeep Brar, Tegbir Sekhon,Heena Kakar Nanotechnology in dentistry: Current achievements and prospects; January 16, 2017, IP: 47.11.2.162**]**

The present article focuses on the current status and the future implications of nanotechnology in dentistry Nanotechnology offers advances particularly in each and every field of human activity such as electronics, industry, telecommunications, environmental science, etc., The field of nanotechnology has got remarkable potential that can bring considerable improvements

to the human health, enhanced use of natural resources, and reduced environmental pollution. Since 1990s, nanotechnology has been exploited for potential medical and dental applications. Nanotechnology holds promise for advanced diagnostics, targeted drug delivery, and biosensors. Dentistry is undergoing yet another change to benefit mankind, this time by transforming itself to the nanodentistry. A variety of nanostructures such as nanorobots,nanospheres, nanofibers, nanorods, etc., have been studied for various applications in dentistry and medicine. Preventive dentistry has also utilized nanodentistry to develop the nanomaterials for inclusion in a variety of oral health-care products. However, due t insufficient evidence on potential hazards on human health and environment, nanotechnology has become a controversial issue. It is documented that nanomaterials can enter the human body through several routes and can pose a threat to human health by interacting with the DNA.**[**111**]**

19. Dr. Priyal N. Shah, Dr. Sonali Kapoor; Nano-Biomaterials and Their Biocompatibility in Restorative Dentistry: A Review; Volume 6 Issue 4 ǁ April 2017 ǁ PP. 01-06

This article described that the Human healthcare is facing a major uprising in the wake of ongoing technological expansions in the field of nanotechnology. Incorporation of nanotechnology into dentistry will make possible the maintenance of near perfect oral environment by using nanomaterials, including tissue engineering, and ultimately, dental nanorobots. New potential treatment prospects in dentistry may include: dentition renaturalization and permanent hypersensitivity cure, local anaesthesia, complete orthodontic realignments during a single office visit, covalently bonded diamondised enamel, and oral health maintenance using mechanical dentifrobots, to destroy bacteria in the mouth that cause dental caries or even repair spots on the teeth where decay has set in, by use of computer to direct these tiny workers in their tasks.

Nanodentistry still faces many significant challenges in realizing its tremendous potential. There are larger social issues of public acceptance, regulations, ethics and human safety that must be taken into consideration before molecular nano-technology can enter the modern medical armamentarium. However, there is equally powerful motivation to surmount these various challenges such as the possibility of providing high quality dental care to 80% of the population that at present receives no noteworthy dental care. Time, financial and scientific resources, specific advances and human needs will conclude which of the applications to be realized first!**[**94**]**

20. Priyanka parman ; Nanodentistry: Meaning, Advantages and Disadvantages;2018

She reviewed and told that Extending nanotechnology into the field of dentistry thereby makes Nanodentistry an emerging field with significant potential to yield new generation of clinical tools, mate¬rials and devices for oral health care. Nanodentistry is said to be the future of dentistry where all procedures are to be per¬formed using Nano robots that may become a replacement to the present day dental assis¬tants, technicians & hygienists.

The discovery of Nano dental materials such as Nano powders and Nano composites reinforced with Nano fillers are the most rapidly developing group of materials with excellent prospective for application in the field of dentistry.

Nanostructured yttrium stabilized zirconium oxide ceramics is widely used for fabrication of crowns, bridges, inlays and other dental el¬ements for which high strength, durability and better aesthetics are required. Nanoparticles of varying composition and chemistry have been engineered to prevent the biofilm from attaching to the tooth’s surface which is the prime cause for development of plaque and calculus.

Some nanomaterial’s have also been developed to help with the remineralisation of the teeth after significant decay. Precisely, it brings forth a new era of local anesthesia’s, dentifrices (tooth paste), better treatment mo-dalities in the management of gum problems, dental caries, tooth hypersensitivity and oral cancer by the usage of morphological, biophysi¬cal and biochemical properties of the oral cav¬ity.The diagnosis of the associated problems will become easier due to smaller diagnostic machinery and Nano-devices with ultimate cor¬rectness in the results within shortest span of time. It also promises to reduce the span of cosmetic procedures with faster healing and improved aesthetics.

The painful procedures, mortality and morbidity rates thus associated will be reduced spontaneously in the future. With such possible innovations any disease can be relevantly treated at any stage with great efficacy.**[**5**]**

Conclusion

Nanodentistry has strong potential to revolutionize dentistry to diagnose and treat diseases. Dr. Gregory Fahy described nanorobots as “living organisms, naturally existing, fabulously complex systems of molecular nanotechnology”[97]. Nanotechnology will change dentistry, healthcare, and human life more profoundly than many developments of the past. As with all technologies, nanotechnology carries a significant potential for misuse and abuse on a scale and scope never seen before. However, they also have potential to bring about significant benefits, such as improved health, better use of natural resources, and reduced environmental pollution.

Current work is focused on the recent developments, particularly of nanoparticles and nanotubes for periodontal management, the materials developed from such as the hollow nanospheres, core shell structures, nanocomposites, nanoporous materials, and nanomembranes will play a growing role in materials development for the dental industry[101]. Nanomedicine needs to overcome the challenges for its application, to improve the understanding of pathophysiologic basis of disease, bring more sophisticated diagnostic opportunities, and yield more effective therapies and preventive properties[99]. Molecular technology is destined to become the core technology underlying all of 21st century medicine and dentistry.[100]

Summary

Nanotechnology is part of a predicted future in which dentistry and periodontal practice may become more high-tech and more effective looking to manage individual dental health on a microscopic level by enabling us to battle decay where it begins with bacteria. Construction of a comprehensive research facility is crucial to meet the rigorous requirements for the development of nanotechnologies.

Researchers are looking at ways to use microscopic entities to perform tasks that are now done by hand or with equipment. This concept is known as nanotechnology. Tiny machines, known as nanoassemblers, could be controlled by computer to perform specialized jobs. The nanoassemblers could be smaller than a cell nucleus so that they could fit into places that are hard to reach by hand or with other technology. Used to destroy bacteria in the mouth that cause dental caries or even repair spots on the teeth where decay has set in, by use of computer to direct these tiny workers in their tasks.

Nanotechnology has tremendous potential, but social issues of public acceptance, ethics, regulation, and human safety must be addressed before molecular nanotechnology can be seen as the possibility of providing high quality dental care to the 80% of the world's population that currently receives no significant dental care.

Role of periodontitis will continue to evolve along the lines of currently visible trends. For example, simple self-care neglect will become fewer, while cases involving cosmetic procedures, acute trauma, or rare disease conditions will become relatively more commonplace.

Trends in oral health and disease also may change the focus on specific diagnostic and treatment modalities. Increasingly preventive approaches will reduce the need for cure prevention a viable approach for the most of them.

Diagnosis and treatment will be customized to match the preferences and genetics of each patient. Treatment options will become more numerous and exciting. All this will demand, even more so than today, the best technical abilities, professional skills those are the hallmark of the contemporary dentist and periodontist.

Developments are expected to accelerate significantly. Nanometers and nanotubes, technologies could be used to administer drugs more precisely. Technology should be able to target specific cells in a patient suffering from cancer or other life-threatening conditions. Toxic drugs used to fight these illnesses would become much more direct and consequently less harmful to the body.

References

1. . Roshan Noor Mohamed,Sathyajith Naik,Poornima Parameswarappa ;Nanodentistry: The next big thing is small,Article · April 2014

2. S A P Rasheed1, Mathews Jude2, Kevin Suresh3, Suneethi Dey4, Shubhalakshmi Sunil5, Dan Varghese6; Nanotechnology and Its Applications in Dentistry; International Journal of Advanced Health Sciences • Vol 2 Issue 9 • January 2016 the Future! JIDA 2002;173:299-303

3. Binu NS, Varghese NO, nanodreams in dentistry .a step ahead the future. JIDA 2002;173:299.303

4. Pankaj Gupta, Heeresh Shetty; Nanotechnology: Its Role in Restorative Dentistry and Endodontics;2016

5. Priyanka parman ; Nanodentistry: Meaning, Advantages and Disadvantages;2018

6. A. Alagarasi ; INTRODUCTION TO NANOMATERIALS;2011

7. Freitas RA Jr. What is nanomedicine? Nanomed Nanotechnol Biol Med 2005;1:2-9.

8.. John G. Richard Feynman: A Life in Science. NY: Dutton; 1997. p. 170.

9. Taniguchi N. “On the Basic Concept of ‘Nano-Technology’,” Proc. Intl. Conf. Prod. Eng. Tokyo, Part II. Japan Society of Precision Engineering; 1974. p. 18-23.

10. Challa S.S.R. Kumar, Faruq Mohammad, Adv. Drug Delivery Reviews, 63 (2011) 789.

11. Martin CR. Welcome to nanomedicine. Nanomedicine. 2006;1(1):5.

12. Nahar M, Dutta T, Murugesan S, Asthana A, Mishra D, Rajkumar V, Tare M, Saraf S, Jain NK. Functional polymeric nanoparticles: an efficient and promising tool for active delivery of bioactives. Crit Rev Ther Drug Carrier Syst. 2006;23(4):259–318.

13. Hett A. Nanotechnology: small matters, many unknown. 2004.

14. Vyas SP, Khar RK. Targeted and controlled drug delivery.CBS publishers and distributers. New Delhi. 2002;1:331–43.

15.Redhead HM, Davis SS, Illum LJ. Control. Release. 2001;70:353.

16. Betancor L, Luckarift HR. Trends Biotechnol. 2008;26:566. Dunne M, Corrigan.

17. DeAssis DN, Mosqueira VC, Vilela JM, Andrade MS, Cardoso VN. Release profiles and morphological characterization by atomic force microscopy and photon correlation spectroscopy of 99m Technetium—fluconazole nanocapsules. Int J Pharm. 2008;349:152–60.

18. Jores K, Mehnert W, Drecusler M, Bunyes H, Johan C, MAder K. Investigation on the stricter of solid lipid nanopartuicles and oil-loaded solid nanoparticles by photon correlation spectroscopy, fi eldfl ow fractionasition and transmission electron microscopy. J Control Release. 2004;17:217–27.

19. Molpeceres J, Aberturas MR, Guzman M. Biodegradable nanoparticles as a delivery system for cyclosporine: preparation and characterization. J Microencapsul. 2000;17:599–614.

20. Dan Guo, Guoxin Xie and Jianbin Luo; Mechanical properties of nanoparticles: basics and applications; 9 November 2014

21. Muhlen AZ, Muhlen EZ, Niehus H, Mehnert W. Atomic force microscopy studies of solid lipid nanoparticles. Pharm Res. 1996;13:1411–6.

22. Shi HG, Farber L, Michaels JN, Dickey A, Thompson KC, Shelukar SD, Hurter PN, Reynolds SD, Kaufman MJ. Characterization of crystalline drug nanoparticles using atomic force microscopy and complementary techniques. Pharm Res. 2003;20:479–84.

23. Polakovic M, Gorner T, Gref R, Dellacherie E. Lidocaine loaded biodegradable nanospheres. II. Modelling of drug release. J Control Release. 1999;60:169–77.

24. Pangi Z, Beletsi A, Evangelatos K. PEG-ylated nanoparticles for biological and pharmaceutical application. Adv Drug Del Rev. 2003;24:403–19.

25. Scholes PD, Coombes AG, Illum L, Davis SS, Wats JF, Ustariz C, Vert M, Davies MC. Detection and determination of surface levels of poloxamer and PVA surfactant on biodegradable nanospheres using SSIMS and XPS. J Control Release. 1999;59:261–78.

26. Kreuter J. Physicochemical characterization of polyacrylic nanoparticles. Int J Pharm. 1983;14:43–58.

27. Kreuter J. Nanoparticles. In: Kreuter J, editor. Colloidal drug delivery systems. New York:n Marcel Dekker; 1994. p. 219–342.References 88

28. Reverchon E, Adami R. Nanomaterials and supercritical fl uids. J Supercrit Fluids. 2006;37:1–22.

29. Rolland JP, Maynor BW, Euliss LE, Exner AE, Denison GM, DeSimone JM. Direct fabrication and harvesting of monodisperse, shape-specifi c nanobiomaterials. J Am Chem Soc. 2005;127:10096–100.

30. Kompella UB, Bandi N, Ayalasomayajula SP. Poly (lactic acid) nanoparticles for sustained release of budesonide. Drug Deliv Technol. 2001;1:1–7.

31. Ravi MN, Bakowsky U, Lehr CM. Preparation and characterization of cationic PLGA nanospheres as DNA carriers. Biomaterials. 2004;25:1771–7.

32. Li YP, Pei YY, Zhou ZH, Zhang XY, Gu ZH, Ding J, Zhou JJ. Gao, XJ, PEGylated polycyanoacrylate nanoparticles as tumor necrosis factor-**[**alpha**]** carriers. J Control Release. 2001;71:287–96.

33. Kwon HY, Lee JY, Choi SW, Jang Y, Kim JH. Preparation of PLGA nanoparticles containing estrogen by emulsification-diffusion method. Colloids Surf A Physicochem Eng Aspects. 2001;182:123–30.

34. Zambaux M, Bonneaux F, Gref R, Maincent P, Dellacherie E, Alonso M, Labrude P, Vigneron C. Influence of experimental parameters on the characteristics of poly(lactic acid) nanoparticles prepared by double emulsion method. J Control Release. 1998;50:31–40.

35. Song CX, Labhasetwar V, Murphy H, Qu X, Humphrey WR, Shebuski RJ, Levy RJ. Formulation and characterization of biodegradables nanoparticles for intravascular local drug delivery. J Control Release. 1997;43:197–212.

36. Jaiswal J, Gupta SK, Kreuter J. Preparation of biodegradable cyclosporine nanoparticles by high-pressure emulsification solvent evaporation process. J Control Release. 2004;96:169–78.

37. Soppinath KS, Aminabhavi TM, Kulkurni AR, Rudzinski WE. Biodegradable polymeric nanoparticles as drug delivery devices. J Control Release. 2001;70:1–20.

38. Tice TR, Gilley RM. Preparation of injectable controlledrelease microcapsules by solventevaporation process. J Control Release. 1985;2:343–52.

39. Tabata J, Ikada Y. Protein pre-coating of polylactide microspheres containing a lipophilic immunopotentiator for enhancement of macrophage phagocytosis and activation. Pharm Res. 1989;6:296–301.

40. Ueda H, Kreuter J. Optimization of the preparation of loperamide- loaded poly (l-lactide) nanoparticles by high pressure emulsification solvent evaporation. J Microencapsul. 1997;14:593–605.

41. Allemann E, Gurny R, Doekler E. Drug-loaded nanoparticlespreparation methods and drug targeting issues. Eur J Pharm Biopharm. 1993;39:173–91.

42. Bodmeier R, Chen H. Indomethacin polymeric nanosuspensions prepared by micro- fluidization. J Control Release. 1990;12:223–33.

43. Koosha F, Muller RH, Davis SS, Davies MC. The surface chemical structure of poly (hydroxybutyrate) microparticles produced by solvent evaporation process. J Control Release. 1989;9:149–57.

44. Lemarchand C, Gref R, Passirani C, Garcion E, Petri B, Muller R. Influence of polysaccharide coating on the interactions of nanoparticles with biological systems. Biomaterials. 2006;27:108–18.

45. Niwa T, Takeuchi H, Hino T, Kunou N, Kawashima Y. Preparation of biodegradable nanoparticles of water-soluble and insoluble drugs with D, Llactide/glycolide copolymer by a novel spontaneous emulsifi cation solvent diffusion method, and the drug release behavior. J Control Release. 1993;25:89–98.

46. Vandervoort J, Ludwig A. Biodegradable stabilizers in the preparation of PLGA nano particles: a factorial design study. Int J Pharm. 2002;238:77–92.

47. Ubrich N, Bouillot P, Pellerin C, Hoffman M, Maincent P. Preparation and characterization of propanolol hydrochloride nano particles: a comparative study. J Control Release. 2004;19:291–300.

48. Couvreur P, Dubernet C, Puisieux F. Controlled drug delivery with Nano particles: current possibilities and future trends. Eur J Pharm Biopharm. 1995;41:2–13.2 Nanoparticles Types, Classifi cation, Characterization, Fabrication Methods… 89

49. Jung T, Kamm W, Breitenbach A, Kaiserling E, Xiao JK, Kissel T. Biodegradable nano particles for oral delivery of peptides: is there a role for polymer to affect mucosal uptake? Eur J Pharm Biopharm. 2000;50:147–60.

50. Quintanar-Guerrero D, Allemann E, Fessi H, Doelker E. Preparation techniques and mechanism of formation of biodegradable nanoparticles from preformed polymers. Drug Dev Ind Pharm. 1998;24:1113–28.

51. Lambert G, Fattal E, Couvreur P. Nanoparticulate system for the delivery of antisense oligonucleotides. Adv Drug Deliv Rev. 2001;47:99–112.

52. Takeuchi H, Yamamoto Y. Mucoadhesive nanoparticulate system for peptide drug delivery. Adv Drug Del Rev. 2001;47:39–54.

53. Vargas A, Pegaz B, Devefve E, Konan-Kouakou Y, Lange N, Ballini JP. Improved photodynamic activity of porphyrin loaded into nano particles: an in vivo evaluation using chick embryos. Int J Pharm. 2004;286:131–45.

54. El-shabouri MH. Positively charged nano particles for improving the oral bioavailability of cyclosporine-A. Int J Pharm. 2002;249:101–8.

55. Fessi H, Puisieux F, Devissaguet JP, Ammoury N, Benita S. Nano capsule formation by interfacial deposition following solvent displacement. Int J Pharm. 1989;55:R1–4.

56. Calvo P, Remunan-Lopez C, Vila-Jato JL, Alonso MJ. Novel hydrophilic chitosan-polyethylene oxide nanoprticles as protein carriers. J Appl Polym Sci. 1997;63:125–32.

57. Calvo P, Remunan-Lopez C, Vila-Jato JL, Alonso MJ. Chitosan and chitosan/ethylene oxidepropylene oxide block copolymer nanoparticles as novel carriers for proteins and vaccines. Pharm Res. 1997;14:1431–6.

58. Zhang Q, Shen Z, Nagai T. Prolonged hypoglycemic effect of insulin-loaded polybutylcyanoacrylate nanoparticles after pulmonary administration to normal rats. Int J Pharm. 2001;218:75–80.

59. Boudad H, Legrand P, Lebas G, Cheron M, Duchene D, Ponchel G. Combined hydroxypropyl-[beta]- cyclodextrin and poly(alkylcyanoacrylate) nanoparticles intended for oral administrationof saquinavir. Int J Pharm. 2001;218:113–24.

60. Puglisi G, Fresta M, Giammona G, Ventura CA. Influence of the preparation conditions on poly(ethylcyanoacrylate) nanocapsule formation. Int J Pharm. 1995;125:283–7.

61. Jung J, Perrut M. Particle design using supercritical fluids: literature and patent survey. J Supercrit Fluids. 2001;20:179–219.

62. Sun Y, Mezian M, Pathak P, Qu L. Polymeric nanoparticles from rapid expansion of supercritical fluid solution. Chemistry. 2005;11:1366–73.

63. J. Nayak et al., Physica E 24 (2004) 227–233

64. Dabbousi et al., J. Phys. Chem. B 1997, 101, 9463-9475

65. After: S. J. Oldenburg, R. D. Averitt, S. L. Westcott, N. J. Halas, Chem. Phys. Lett. 288, 243 (1998)

66. C. Buzea, I. Blandino, K. Robbie, Biointerphases, 2007, 4, 17-172.

67. R. Rikken, R. Nolte, J. Maan, D. Wilson, P. Christianen, Soft Matter, 2014, 10, 1295-1308.1.

68. E. Bull, S. Madani, R. Sheth, A. Seifalian, M. Green, A. M. Seifaliam, Int J Nanomedicine. 2014, 9, 1641-165

69. Abhilash M. Potential applications of Nanoparticles. International Journal of Pharma and Bio Sciences. 2010; 1(1): 1-10.

70. Wang J, Hartmann FK, Fedorov R. Can man-made nanomachines compete with nature biomotors. ACS Nano 2011; 3(1): 4-9.

71. R.B.Durairaj1, Shanker.J2, and Dr.M.Sivasankar; Nano Robots In Bio Medical Application;2012

72. Babel S, Mathur S. Nanorobotics: Headway Towards Dentistry. International Journal of Research in Science And Technology. 2011; 1(3): 1-9.

73.Joy B, why the future does not need us, 2000-8;804-810

74. SNEHA SUNDAR RAJAN , SHASHI RASHMI ACHARYA AND VIDYA SARASWATHI; NANODENTISTRY; Indian J.Sci.Res. 4(2) : 233-238, 2013

75.Freitas Jr RA. Nanodentistry. J Am Dent Assoc 2000; 131(11): 1559-66.

76. Estafan DJ. Invasive and non-invasive dental analgesia techniques. Gen Dent; 46(6); 600-601

77. Herzog A. Of Genomics, Cyborgs and Nanotechnology: A Look into the Future of Medicine.Connecticut Medicine.2002;66(1);53-54.

78. Mjör IA, Nordahl I. The density and branching of dentinal tubules in human teeth.Arch Oral Biol 1996; 41(5); 401–12.

79. Sumikawa D.A., Marshall G.W., Gee L., et al. Microstructure of primary tooth dentin Paediatric Dentistry 1999; 21(7);439 – 44.

80. Freitas R.A. Jr. Exploratory design in medical nanotechnology: A mechanical artificial red cell. Artificial Cells Blood Substitute Immobile Biotechnology 1998; 26(4): 30-32.

81. Li Y, Denny P, Ho CM. The Oral Fluid MEMS/NEMS Chip (OFMNC): Diagnostic and Translational Applications. Adv Dent Res 2005; 18(1): 3-5.

82. Gau V, Wong D. Oral fluid nanosensor test (OFNASET) with advanced electrochemical -based molecular analysis platform. Ann NY Acad Sci 2007; 1098: 401-10.

83. Song JM, Kasili PM, Griffin GD, Vo-Dinh T. Detection of cytochrome C in a single cell using an optical nanobiosensor. Anal Chem 2004; 76(9): 2591-4.

84. Tumor gets selective with nanoparticles: Nan Today. 2007;2(5):35.

85. Mubben and Singh A. Nanotechnology in the field of oral medicine and diagnosis- a review. Indian dentist research and review. 2010; 5: 41-43.

86. Saravana RK, Vijayalaksmi R . Nanotechnology in dentistry. Ind J Dent Res 2006; 17(2):

87. Vargas A, Pegaz B, Debefve E. Improved photodynamic activity of porphyrin loaded into nanoparticles: An in vivo evaluation using chick embryos. Int J Pharm 2004; 286(1-2): 131-45

88. Cavalcanti A. assembly automation with evolutionary nanorobots with censor based control applied to nano-medicine. IEEE transactions on nanotechnology. 2003; 2(2): 82-87

89. Freitas R.A. Nanodent. J. Am. Dent. Assoc. 2000;131(3):1559–1566.

90.Shetty NJ, Swati P. David K Nanorobots: Future in dentistry. The Saudi Dental Journal2013; 25: 49–52. 91.Nagpal Archana, Kaur Jasjit, Sharma Shuchita, Bansal Aarti, Sachdev Priyanka. Nanotechnology – the era of molecular dentistry. Indian J. Dent. Sci. December 2011;3(5). **[**13**]**Kumar S.R., Vijayalakshmi R. Nanotechnology in dentistry. Indian J. Dent. Res. 2006;17:62–69.

92. Muhlen AZ, Muhlen EZ, Niehus H, Mehnert W. Atomic force microscopy studies of solid lipid nanoparticles. Pharm Res. 1996;13:1411–6.

93.Zohaib Khurshid 1,†, Muhammad Zafar 2,†,*, Saad Qasim 3,†, Sana Shahab 4,†, Mustafa Naseem 5,† and Ammar AbuReqaiba; Advances in Nanotechnology for Restorative Dentistry; Materials 2015, 8, 717-731; doi:10.3390/ma8020717

94. Dr. Priyal N. Shah, Dr. Sonali Kapoor; Nano-Biomaterials and Their Biocompatibility in Restorative Dentistry: A Review; Volume 6 Issue 4 ‖ April 2017 ‖ PP. 01-06

95. Sheenam Markan, Gurvanit Lehl* and Shammi Kapoor;

Recent Advances of Nanotechnology in Endodontics, Conservative and Preventive Dentistry-A Review; 10 Aug, 2017

96. Shahin Shadlou, Babak Ahmadi-Moghadam and Farid Taheri Adhesion Adhesives, Vol. 2, No. 3, August DOI: 10.7569/RAA.2014.097307Nano-Enhanced Adhesives: A Critical Review

97.Bumb SS, Bhaskar DJ, Punia H. Nanorobots & challenges; faced by nanodentistry. General. Sept 2013

98. Bharath N, Gayathri G.V., D.S. Mehta. Nanorobotics in Dentistry- The Present Status And Future Perspective. Journal of Dental Practice and Research . 2013:1; (2); 41-47.

99.Freitas R.A. Nanodent. J. Am. Dent. Assoc. 2000;131(3):1559–1566.

100. Kukreja BJ, Dodwad V, Singh T. Robotic dentistry- the future is at the horizon. Jounal of Pharmaceutical and biomedical sciences. 2012;16(1):1-4.

101.P atil M, Mehta DS, Guvva S. Future impact of nanotechnology on medicine and dentistry. J Indian Soc Periodontol. 2008;12(2):34-40

102. SNEHA SUNDAR RAJAN , SHASHI RASHMI ACHARYA AND VIDYA SARASWATHI ; NANODENTISTRY; Indian J.Sci.Res. 4(2) : 233-238, 2013

103. Shreemoy Dash, Sowmya Kallepalli; influence of nanotechnology in operative dentistry and endodontics –think “BIG” act “SMALL”; Journal of Advanced Medical and Dental Sciences Research |Vol. 3|Issue 4| October- December 2015

104. Sachdeva S,Kapoor P, Tamrakar AK,Noor R; Nano-composite dental resins: an overview; Annals of Dental Specialty Vol. 3; Issue 2. Apr – June 2015 |

105.Dr. Mehra P, Dr. Nabhi K; A Nanorobotics - The Changing Face of Dentistry; Index Copernicus Value (2013): 6.14 | Impact Factor (2014): 5.611

106. Deepak Ranjan Dalai1, D. J. Bhaskar, Chandan Agali R., Nisha Singh, Devanand Gupta, Swapnil S. Bumb; Futuristic Application of Nano-Robots in Dentistry; International Journal of Advanced Health Sciences | July 2014 | Vol 1 | Issue 3

107.Rita Chandki , M. Kala , Kiran Kumar N. , Biji Brigit , Priyank Banthia , Ruchi Banthia; ‘NANODENTISTRY’: Exploring the beauty of miniature; J Clin Exp Dent. 2012;4(2):e119-24.

108. Rohit Kumar, Omprakash Baghel, Sanat Kumar Sidar; Applications of Nanorobotics; ISSN 2278 – 0882 Volume 3, Issue 8, November 2014

109. Sumit Mohan ,Anuraag Gurtu , Anurag Singhal and Ankita Mehrotra; Nanotechnology : Its Implications in Conservative Dentistry and Endodontics; Journal of Dental Sciences & Oral Rehabilitation 2013; July – September

110. Munish Goel, Neeraj Sharma, Sheenam Garg and Anish Garg;; Nanodentistry - “Unbounding The Future”; April 11, 2016

111. Ramandeep Singh Gambhir, G. M. Sogi, Ashutosh Nirola, Rajdeep Brar, Tegbir Sekhon,Heena Kakar Nanotechnology in dentistry:Current achievements and prospects; January 16, 2017, IP: 47.11.2.162**]**

112.Sivaramakrishnan SM and Neelakantan P; Nanotechnology in Dentistry - What does the Future Hold in Store?; Dentistry 2014, 4:2

113. Sivaramakrishnan SM and Neelakantan P; Nanotechnology in Dentistry - What does the Future Hold in Store?; Dentistry 2014, 4:2