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NANOTECHNOLOGY BASED APPROACH TO FIGHT AGAINST NEUROLOGICAL DISORDERS

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ABSTRACT

Nanotechnology is the study of particularly small structures in the range of nanometers i.e. 10^{-9} m.The nanoparticles have physical, chemical,electrical and optical properties that are different from bulk material properties.Various types of nanomaterials like liposomes,dendrimers, quantum dots, metallic nanoparticles,carbon nanotubes can be used for targeted drug delivery and for the treatment of various diseases. These nanoparticles are synthesized either by top down approach or by bottom up approach.This article discusses about the various applications of nanotechnology in the field of medicine,food, for diagnosing diseases, for drug delivery and for the treatment of neurodegenerative diseases and also for the treatment of tuberculosis.

Keywords: Alzheimer's disease, Nanoparticles, Nanomaterials, Parkinson's disease, Tuberculosis.

I. INTRODUCTION

Nanotechnology is one of the important, advanced and promising technology tool in the present scenario for curing the disease. The term "Nanotechnology" is coined by Norio Taniguchi,Professor of Tokyo University of Science in 1974. It is the science that deals with manipulating materials, devices or structures at nanoscales ranging from 1 to 100 nm.[1] There is a combination of three words: 'Nano' means tiny, 'Bio' means living things and 'technology' means Science of crafts. Royal Society and Royal Academy of Engineering of London defines that "Nanoscience" is the branch of science that develops materials at atomic, molecular and macromolecular scales though Nanotechnology is the designing and characterization of devices by controlling their shape and size at nano level.[2]

The properties of nanoparticles are different from bulk compositions of molecules and nanomaterials have novel characteristics like greater strength, high chemical reactivity and conductivity.[3] This review emphasize on the properties of nanomaterials and their application in the field of critical disease cure.

II. NANOPARTICLES

Nanoparticles have various properties that are discussed below:

2.1. Physical properties

2.2. Electrical properties

2.3. Optical properties

2.4. Chemical properties

2.1. Physical properties

2.1.1 Color

2.1.2. Melting Point

2.1.3 Hardness

2.1.1 Color

Nanosize particles show different color such as gold material appears yellowish in color but on reducing its size at nanoscale level, it turns into red in color. This happens due to Surface Plasmon Resonance phenomenon.In this phenomenon, particles have high surface electron densities which are known as surface plasmons. These plasmons undergo oscillations when they get excited by light at specific wavelength. These oscillations are known as Surface Plasmon Resonance (SPR). For small (~30nm) monodispersed gold nanoparticles the surface plasmon resonance phenomona is responsible for an assimilation of the blue-green spectrum (~450 nm) while red light (~700 nm) is reflected, producing a rich red color.(Fig.5).[3,4]

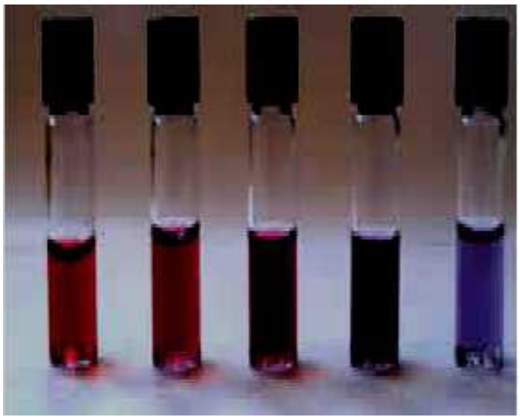


Fig.1. Suspensions of gold nanoparticles of different sizes

2.1.2. Melting Point

Melting point decreases at the nanoscale level. It happens due to larger surface to volume ratio than bulk materials and also due to alteration in their thermodynamic and thermal properties.[3,4]

2.1.3 Hardness

Hardness of particles is inversely proportional to size of particle. It happens because of reduction in crystal defects on reducing size. In bulk materials there is presence of crystal defects in the form of atomic vacancies but on reducing size crystal defects get reduced. So, hardness of nanoparticles increases linearly with decreasing size of the particle.[3,4]

2.2 Electrical properties

At nanoscale level, there would be two different striking effects on electrical conductivity. On reducing material's dimensions, crystal perfection occurs and thus, electron scattering phenomenon gets reduced. As a result reduction in resistivity is observed. While on the other hand, resistivity increases due to increase in surface scattering phenomenon at nanoscale level. Additionaly, reduction in material's dimensions below a critical dimension, i.e. (electron de Broglie wavelength), would result in a customized electronic structure with broad and distinct band gap. This would result in an increased electrical resistivity.[3,4]

2.3. Chemical properties

Nanoparticles are highly reactive and have high absorption rate because surface area increases due to which particles show high chemical reactivity.[3,4]

3. Biological properties

Nanoparticles have same dimensions as biological molecules like proteins. The ability of nanoparticles to stick on the surface of target cell is utilized for drug delivery. It is possible to deliver a drug directly to a specific cell in the body by functionalizing the surface of nanoparticle so that it adsorb specifically on the surface of target cell and also they have the capability to cross the barriers present inside the body due to their small size. But these properties of nanoparticles may enhance the intrinsic toxicity and cause damage to tissues.

4. Nanovehicles

Nanomaterials are named according to their shapes and dimensions like particles, tubes, wires, films, flakes, pores or shells which have one or more nanometer in dimension. Nanocarrier systems are designed so that it can interact with target cells and tissues and respond to stimuli which induces desired physiological responses.[5]

4.1. Liposomes

Liposomes work as microscopic carrier which is composed of concentric lipid bilayers and it is separated by aqueous medium. Lipophiles are inserted into the membrane and hydrophilic substances are encapsulated in the compartment containing aqueous medium. These carriers consists of phospholipids (synthetic or natural), an antioxidant and sterols.[6,7]

Liposomes are classified on the basis of their size (small, large, or giant), surface charge (anionic, cationic, or neutral) and number of lamellae (oligo-, uni- or multilamellar). Unilamellar liposomes (ULs) have single bilayer and with size ranges: small unilamellar liposomes (SUVs), having diameters of approximately 25–100 nm; large unilamellar liposomes, having diameters of 100 nm -1 μm; and giant unilamellar liposome, having diameters greater than 1 μm. Multilamellar liposomes (MLVs) consists of multiple lamellae having onion-like structure. ULs are present in dilute solutions of surfactants, while MLVs are present in concentrated solutions.[6,7]

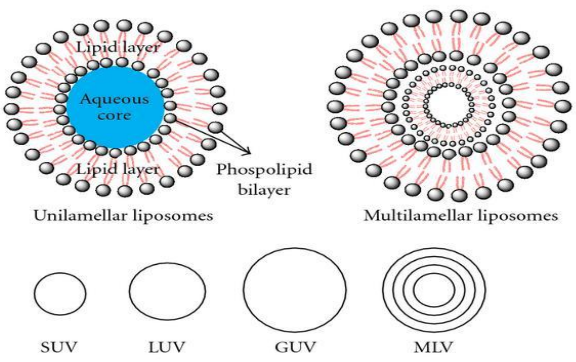


Fig 2: Structure of liposome

4.2. Dendrimers

Dendrimers are highly branched synthetic polymer having monomer unit attached core and called as "Polymers of the 21st century" and it leads to monodisperse, star-shaped, tree-like or generational structure with diameter in the range of 2 to 10 nm size. They have unique properties like, high degree of branching, multivalency, globular structure, high solubility, biocompatible and less toxic. Dendrimers acquire three well-known architectural components, i.e. a central core (single atom or an atomic group). This central core have branches which are emanating from it and composed of repeating units in radial position and terminal functional groups are present at the exterior of the macromolecule.[8,9]

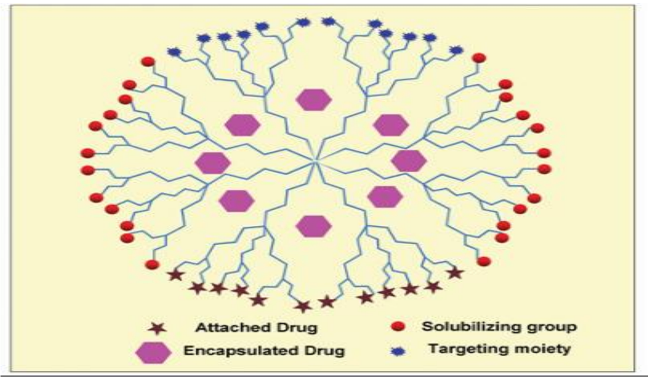


Fig 3: Structure of dendrimer

4.3. Quantum dots (Qdot)

Qdot means zero dimensional nanomaterial[10,11] and also known as artificial atoms as they exhibit narrow line spectra.[12] Qdots consists of many atoms between atomic-molecular level and bulk material having band-gap which depends on important factors such as bond type and strength. I current scenario, Qdots are highly used in various electronic devices as light emitting devices(LED), biological markers and photovoltaic cells. On changing the size of Qdot, it exhibit different color of emission.[13]

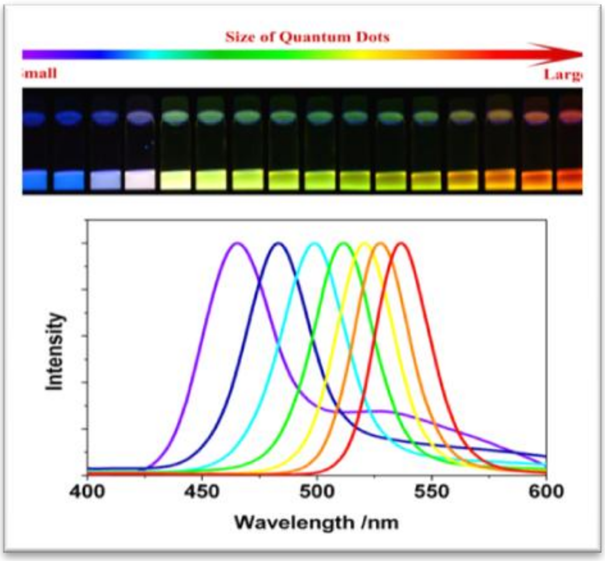


Fig 4. Top: CdSe Qdots excited by a near-ultraviolet lamp exhibiting sixteen emission colors from small (blue) to large (red); size of Qdots ranges from ~1 nm to ~10 nm. Bottom: CdSe Qdots Photoluminescence spectra.

4.4.Metallic nanoparticles

Gold and iron nanoparticles are charged metallic nanoparticles that absorb light in the visible region strongly due to the presence of surface plasmons.[14] They are used in bio-molecular detection.[15]Metallic nanoparticles are biocompatible, noncytotoxic, favorable carrier for drug delivery, approved by FDA.[16]

4.5. Carbon Nanotubes

Carbon Nanotubes (CNTs) are cylindrical molecules having hexagonal arrangement of sp^2-hybridization of carbon atoms (C-C distance of 1.4 Å).CNTs are hollow cylinders fashioned by rolling the single or multiple layers of graphene sheets into flawless cylinders. These cylindrical structures can be of two forms; firstly, Single walled carbon nanotubes (SWNTs) that are made up of a single cylindrical graphene layer with capping at both ends in a hemispherical arrangement of carbon networks and secondly, Multi walled carbon nanotubes (MWNTs) that consists of many concentric cylinders of graphitic shells with an interlayer separation of about 0.3nm and have a larger outer diameter (2.5–100 nm) than SWNTs (0.6–2.4 nm). MWNTs have less stable nanostructure due to more structural defects but SWNTs have more defined diameter.[17]

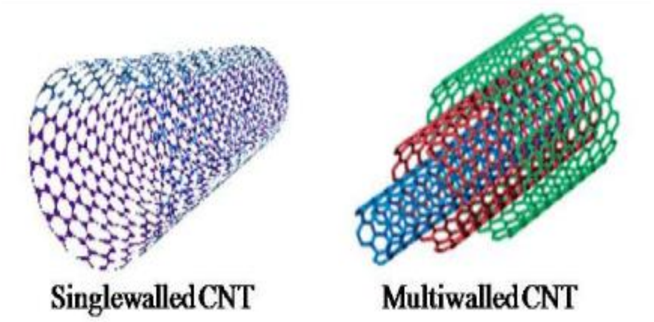


Fig 5: Single walled CNT and Multiwalled CNT

V. SYNTHESIS OF NANOPARTICLES

Synthesis of nanoparticles can be done by two approaches: **1. Top-down approach 2. Bottom up approach**

5.1. Top-down approach

In this approach,bulk material is broken down/dissociates into nanosized nanoparticles by applying various lithographic techniques e.g.: grinding, milling etc.

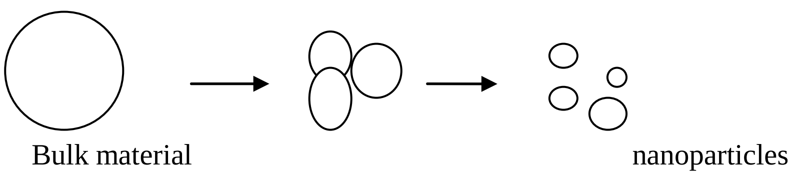
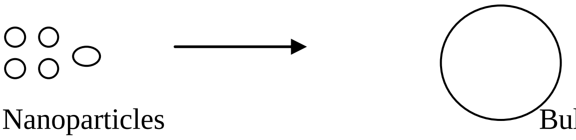


Fig 6: Top down approach

5.2.Bottom up approach

In this approach, atoms are combined and developed to form new nuclei which grow at nanoscale by using different methods like physical, chemical and biological methods. Among the all, biological method is most commonly used method for synthesis of nanoparticles due to its eco-friendly nature, low cost, easily available, non- hazardous.



Nanoparticles Bulk material

Fig 7:Bottom up approach

VI. APPLICATIONS OF NANOTECHNOLOGY

Nanotechnology is extensively used for many products which are available in market like cosmetics and sunscreens, filteration of water, stain-resistant and dust proof clothing , more lightweight tennis rackets, more durable tennis balls but nowadays, researchers are more paying attention towards biomedical applications of nanoparticle in terms of disease cure[18]

6.1. Biomedical applications

Nanobiotechnology have clinical applications like,disease diagnosis, targeted drug delivery, and molecular imaging.[20]

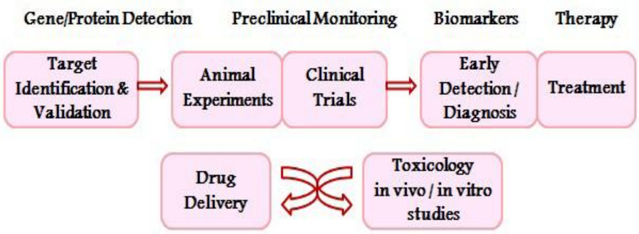


Fig.8: Biomedical application of nanotechnology.[19]

6.1.1. Diagnostics

Nanomolecular diagnostics, also known as nanodiagnostics which includes concepts of nanotechnology in molecular diagnostics.[21] The diagnostic regimen aims to develop procedure that involves non-invasiveness and precise diagnosis with greater sensitivity and cost effectiveness. enables simultaneous real-time detection of a wide spectrum of diseases with high accuracy and greater cost-effectiveness.[22] To provoke greater functionality and bioavailability, nanoparticles are immobilized on amorphous or nanocrystalline materials.[23] Molecular imaging strategies like Infrared (IR) or Magnetic Resonance Imaging (MRI) are the approaches for early detection of diseases. For instance, phosphorothioate-modified oligo DNA sequences (PS-ODNs) complementary to c-fos Mrna with superparamagnetic iron oxide nanoparticles (SPION) are used in magnetic resonance imaging (MRI) to diagnose neurodegenerative diseases.[23,24] Further, functionalized nanoparticles are used for detecting deadly disease like cancer by identifying complementary functional groups that are present on outer layer of cell surface.[23]

6.1.2. Nanoarrays

Microarray technique is novel and potential novel platform for high-throughput diagnosis of multiplexed DNA, proteins but it has certain drawbacks like requirement of large sample volumes, longer incubation time, bulky instrumentation, robust amplification and labeling, analysis is quite laborious and expensive while Nanoarray is high accuracy level of an array of molecules scattered in range of micron or sub-micron. Nanoarray is used in various analysis of Biological samples like protein, DNA, RNA and viruses and non biological samples like solutions, colloids, and particle suspension. Nanoarrays have distinctive advantage i.e. economized reagent costs, expedited analysis and greater sensitivity and specificity.[25] Nanoarrays are also used for biomolecular analysis. Nanoarray are capable of detecting pathogens even at trace quantities and also have higher sensitivity and selectivity.[26]

Nanoarrays are used to differentiate healthier cells from diseased cells at a single-cell resolution scale. Thus, nanoarrays are more efficient in analyzing cell mixtures. Nanoarray also includes measuring of atomic vibrational frequency, the targeted species are detected without labeling.

6.1.3. Micro-electromechanical systems (MEMS)

Micro-electromechanical (MEM) systems consist of Microfluidic and microcantilever devices that are fabricated using nanotechnology for in vitro diagnostics.

6.1.3.1. Microfluidics (lab-on-a chip)

Microfluidics involves manipulation of fluids, particles like protein, DNA, cells, viruses, etc and controlling them at micrometer and sub micrometer dimensions based on the particle's electro kinetic properties (size, density, charge, light scattering and antigenic properties).The procedure of DNA analysis is integrated into a single chip that comprises of a glass and silicon substrate due to which these chips are easy to use. The chip consists of heating systems, micro fabricated fluidic chambers, temperature sensors and fluorescence monitors that examines nanolitre sized DNA specimens.[27] The applications of microfluidics is to monitor allergic response. At the time of allergic response, cells are cultured in the chamber of a chip and dyes with fluorescently labelled tags, are released upon allergic stimulation and then they were detected by photomultiplier tube (PMT) which is connected with microscope.[28] Microfluidic systems could be used to analyze the composition of cells.[29] These devices are capable in capturing considerable amount of cancer cells from cell mixture. Microfluidic chips offer probable resolution to surmount the drawbacks. Further, they are also playing essential part in monitoring allergic responses.[30]

6.1.3.2. Microcantilevers

Micro cantilevers sensors measure variations when cantilever bends. These sensors have more advantages like minimum amount of sample requirement, high sensitivity, low cost, accurate testing procedure and rapid response. They can also be used to detect disease markers, blood glucose level, biological and chemical warfare agents.[31] In this approach, microcantilever's surface are coated with PSA specific anitbodies. Due to antigen-antibody interaction, cantilever bends and detected optically by photo detector. Another approach is to measureby immobilizing the enzymecalled glucose oxidase on microcantilever's surface.[32] Microcantilever are useful in detecting lowdensity lipoprotein (LDL) and oxidized LDL (oxLDL) because of its efficiency in

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measuring surface stress. This is of great importance as oxLDL is interconnected to deposition of cholesterol in aorta, a crucial step in coronary heart disease.

6.1.4. Nanocantilevers:

Nanocantilevers are the next generation tools in the progression of cantilevers. Harold Craighead and co-workers verified the probability of employing 90 nm thick, silicon nitride nanocantilevers to discriminate DNA strand of 1578 base pairs. These nanocantilevers remove the amplification step as it could correctly detect 0.23 attograms (1 atto gram =10-18 gram) of molecules.[33]

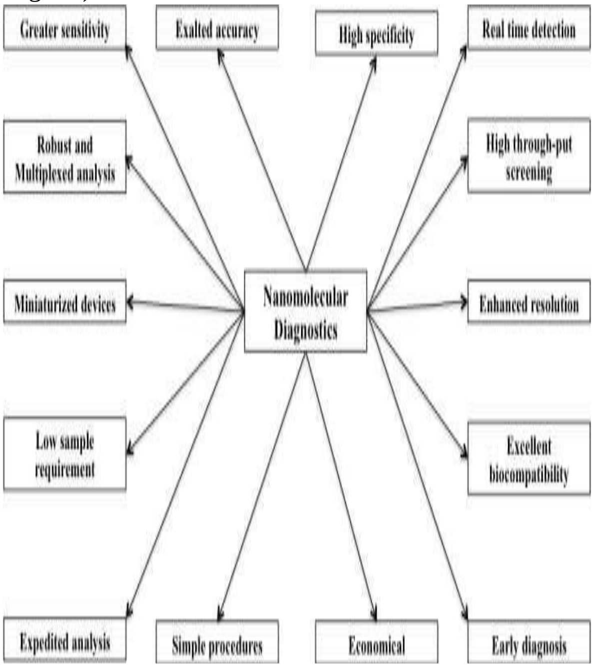

Fig 9: Nanomolecular diagnostics having salient features that make them superior to conventional molecular diagnostics

6.1.5. Drug Delivery

Nanoparticles are used for targeted drug delivery. In this technique the required amount of drug dose is delivered and protected from side-effects including reduces the cost and pain to the patients.. Micelles work as nanovehicle can be used for drug encapsulation. They transfer small drug molecules to the desired location. Similarly, nano electromechanical systems are used for the release of drugs actively. Iron nano particles have important application in the cancer treatment. Nanomedicines are made up of nano scale particles or molecules which can develop drug bioavailability.[34] With the advancement of nanotechnology, self-assembled biocompatible nanodevices detects the cancerous cells and estimate the disease. Proper designing of drug delivery systems by use of lipid and polymer based systems can be used for improving the pharmacological and therapeutic properties of drugs.[35] The effectiveness of drug delivery systems is their ability to amend the pharmacokinetics and biodistribution of the drug. Nanoparticles are designed to keep away from the body's defense mechanisms.[36] Complex drug delivery mechanisms are being developed, in which drugs permeates through cell membranes and into cell cytoplasm, thus increasing efficiency. Drugs in the body can be activated on receiving a particular signal. A drug having poor solubility will be replaced by a drug delivery system that have improved solubility due to occurrence of both hydrophilic and hydrophobic environments.[37] In the study of excretory system of mice, dendrimers are encapsulated for drug delivery of positively-charged gold nanoparticles that enters into the kidneys and negatively-charged gold nanoparticles remained in the organs like spleen and liver. The positive charge on the surface of the nanoparticle decreases opsonization rate of nanoparticles in the liver and effects the excretory pathway. Due to small size of 5 nm, nanoparticles can get stored in the peripheral tissues, and therefore accumulated in the body long time. Thus nanoparticles can be used efficiently for targeting and distribution, further researches are going on nano toxicity so that its medical uses can be improved.[38]

6.1.6. Treatment of neurodegenerative disorders

Neurodegenerative disorders are major challenging issue in medical science. In curing of neurodegenerative diseases, nanotechnology play a determining role in the diagnosis as well as treatment by various ways like delivery of Central Nervous System(CNS) therapeutics, various nano carriers such as, nano gels, dendrimers, nanoemulsions, liposomes, polymeric nano particles.[39] The transportation of nano medicines has been effected across Blood Brain Barrier(BBB) models by endocytosis and early preclinical success for the management of CNS conditions hasbecome possible. The nanomedicine can be highly developed further by improving permeability to BBB and reducing their neurotoxicity (Fig. 10).

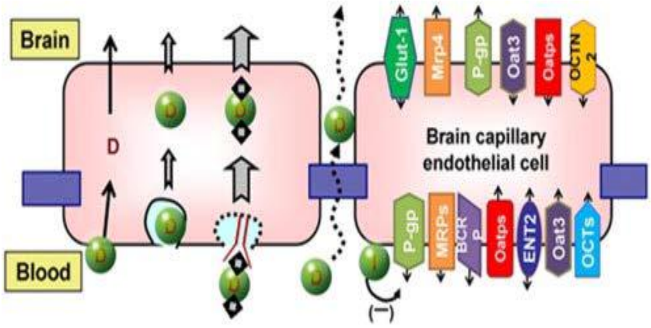

Fig 10: Delivery of nano medicine to CNS through BBB

6.1.6.1. Parkinson's disease

Parkinson's disease (PD) is another fatal neurodegenerative disease followed by Alzheimer's disease and affects above the age of 65 years. It is a disease of the central nervous system and it involves neuro inflammatory responses that results into difficulty in body motions. The present day therapies cannot improve the progression of the neurodegenerative process and aim to improve the functional capacity of the patient for as long as possible.

Regeneration and neuro protection of the central nervous system (CNS) is the aim of applied nanotechnology. In order to minimize the peripheral side-effects of usual forms of Parkinson's disease therapy, research focus on designing and optimizing of nano scaffold device for the targeted delivery of dopamine to the brain, as a strategy. Peptides and peptidic nano particles are recent tools for various CNS diseases.

6.1.6.2. Alzheimer's disease

More than 35 million people are affected by Alzheimer's disease (AD), which is the most general type dementia. Nano technology finds important applications in neurology. Nanoparticles (NPs) have affinity for the circulating amyloid-β (Aβ) forms and consequently may provoke "sink effect" and develop the AD condition.

Ultrasensitive NP-based immune sensors, as well as scanning tunneling microscopy can be used for diagnosing AD because these techniques are capable of detecting Aβ1−40 and Aβ1−42. Figure showing recent research on use of nanoparticles in the treatment of Alzheimer's disease.[40]

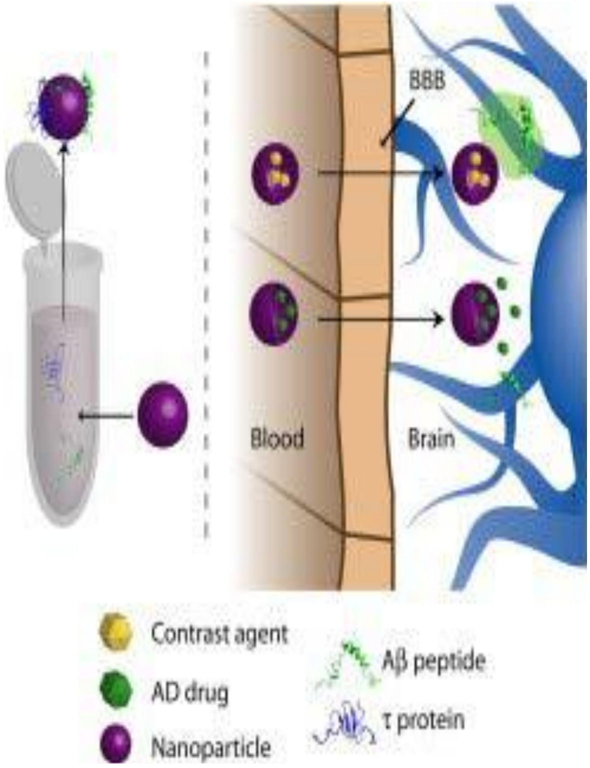

Fig 11: Use of nanoparticles in Alzheimer's disease

6.1.7. Tuberculosis

Tuberculosis (TB) is an infectious disease that kills millions of people every year. Due to long duration of the treatment, the pill burden can hamper patient lifestyle and may causes the development of multi-drug resistant (MDR) strains. To overcome this drug resistance, novel antibiotics are designed. Nanotechnology is one of the approaches for the improvement of more effective and acquiescent medicines. The advancements of drug delivery systems for encapsulation and for releasing anti-TB drugs can results into the development of a more effective and reasonable TB pharmacotherapy.

6.2. Tissue engineering

Tissue Engineering is the study of the growth of tissues, or organs, from cells and a collagenous scaffold to produce a functional organ for implantation back into the donor host. Magnetic force-based tissue engineering (Mag-TE), offers a major advancement in tissue engineering by using magnetite nanoparticles.[41] For ex: gold nanoparticles are used for rapid cardiac tissue growth.

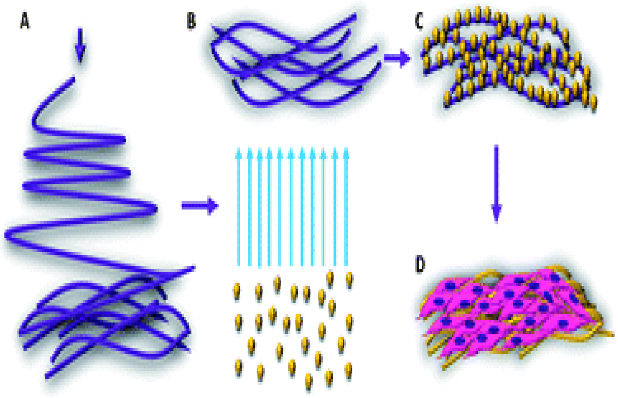

Fig.12 showing engineering cardiac tissues within gold NP's.[42]

6.3. Bioinformatics contribution to Nanotechnology

Today lifescience researches has entered in a nanoscale period, where the continuous attempt is in trying to achieve insight into living systems through their molecular function and coordinated activity. Bioinformatics application in the field of nanotechnology has opened up new ways for the development of nanomaterials. These computational approaches will help achieving the goal of pathogen detection on the basis of their nucleic acid sequences. Nanotechnology convergence holds promise for molecular diagnosis and cancer therapy and other human diseases.

It also helped for blocking cancer channels(blood vessels) to stop their nutrition so that cancer cells die due to starvation. Similarly, nanodevice can be made for cancer destruction by studying about human genomes and using computational skills. Combining bioinformatics and nanotechnology leads to rapid, portable, highly sensitive, specific, inexpensive detection technology that overcome challenges we encounter today in pathogen detection.

6.4. Nanotechnology in food industry

The applications of nanotechnology in the field of food are only new emergent, but predicted to grow rapidly in the coming years. Applications of nanotechnology in the field of food , already extent development of improved tastes, color, flavor, texture, and constancy of foodstuffs, increased absorption and bioavailability of nutrients and health supplements, novel food packaging materials with developed mechanical, antimicrobial properties, and nano-sensors for traceability and evaluating the food condition during transport and storage.

The properties of nanomaterials offer many new opportunities for the food industry.[43] Different forms of functional nanostructures are behaves as building blocks to create new structures and assign new functionalities into foods for e.g. nanoliposomes, nanoemulsions, nanoparticles and nanofibers. Engineered nanomaterials (ENMs) used in food applications comprises inorganic compounds, organic substances and surface functionalized materials.[44]

Inorganic nanomaterials for application in food, food additives, food storage or packaging include (ENMs) transition metals like silver and iron; alkaline earth metals like calcium,magnesium; and non-metals like selenium and silicates. Metal (oxide) ENMs can be used for food packaging. Nanosilver is finding a budding use in a number of consumer products, including food and health food, water, and food contact surfaces and packaging materials.

Surface functionalized nanomaterials add functionality to the matrix like antimicrobial activity or a preservative action through absorption of oxygen. For food packaging materials, functionalized ENMs are used to bind with the polymer matrix that offers mechanical strength or a barrier against the movement of gases, volatile components (like flavors) or moisture. They are more likely to react with different food components, and bound to food matrices, thus, they are not available for migration from packaging materials to other organs outside the GI tract.

Organic nanomaterials are used in food products for their increased uptake and absorption, and bioavailability of vitamins, antioxidants in the body as compared with conventional bulk equivalents. A wide range of materials are available, for example food additives (eg, citric acid, benzoic acid, ascorbic acid) and supplements (eg, vitamins A and E, beta-carotene, omega-3 fatty acids, and coenzyme-Q10). Another example of an organic nanomaterial is the tomato carotenoid lycopene. A synthetic nanosized form of lycopene has been formed and found as corresponding sources of lycopene compared to natural lycopene.[45]

The food industry is also searching for new technologies to improve and inhance the nutritional value, shelf-life, improved tastes, reduce the amount of salt, sugar, fat and preservatives, address food-related illnesses (e.g. obesity and diabetes), develop targeted nutrition for different lifestyles and aging population, and uphold sustainability of food production, processing, and food safety. It is therefore not surprising that one of the best ever moving sectors to hold new technologies, such as nanotechnology, to realize the prospective benefits is the food industry.

VIII. CONCLUSION

The multidisciplinary field of nanobiotechnology is bringing the science of the almost incomprehensibly small device closer to reality. The effects of these improvements will at some point be so huge that they will probably affect nearly all fields of science and technology. Nanobiotechnology offers a wide range of application in medicine. Drug delivery systems are only the beginnings of something new. Many diseases that cannot be cured today may be cured by nanotechnology in the future. Although the expectations from nanobiotechnology in medicine are high and the advantages are endlessly enlisted, the safety of nanomedicine is still not defined. It is possible that nanomedicine play an important role in treatment of human diseases and also in improvement of normal human physiology. If everything goes on smoothly, nanobiotechnology will, one day, become an predictable part of our everyday life and will help save many lives.

Nanotechnology has the capability to improve foods, making them tastier, healthier, and more nutritious, to create new food products, new food packaging, and storage. However, many of the applications are aimed at high-value products, at least in the short term. Like any other new technology, public confidence, trust, and acceptance are possible key factors that will decide the success or failure of applications of nanotechnology in the field of food.

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