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Nanotechnology: Applications in Medicine and Drug Delivery- A Review

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Abstract: *The use of nanotechnology in medicine and more specifically drug delivery is set to spread rapidly. Currently many substances are under investigation for drug delivery and more specifically for cancer therapy. Interestingly pharmaceutical sciences are using nanoparticles to reduce toxicity and side effects of drugs and up to recently did not realize that carrier systems themselves may impose risks to the patient. Nano medicine is a comparatively new field of science and technology. Brief explanation of various types of pharmaceutical nano systems is discussed. Classification of nano materials based on their dimensions is also explained. Applications of Nanotechnology in diverse fields such as health and medicine, electronics, energy and environment, are discussed. Applications of various nano systems in cancer therapy such as carbon nano tubes, dendrimers, nano crystals, nano wires, nano shells, nanorods etc. are given. Nano pharmaceuticals can be applied to diagnose diseases at ample earlier stages. The applications of nanotechnology in the medical sector together are designated as Nanomedicine. Nanoparticles have prospected applications in the field of medical sciences such as new diagnostic tools, imaging agents and methods, targeted drug delivery, bio implants, pharmaceuticals and tissue engineering. High toxic potential drugs like cancer chemotherapeutic drugs can be provide with better safety profile with the profitability of nanotechnology. The object of the study of the nanotechnology in the medical sciences is to develop new materials and methods to diagnose and treat diseases in a targeted, precise, effective and lasting way, with the eventual goal of making medical practice impervious and less obtrusive.*

Keywords: *Nano devices; nano tubes, dendrimers, nano crystals, Nano material; Nano medicine; Nano pharmaceutics; Drug delivery.*

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I. Introduction

Nanotechnology is the field which is making an impact in all spheres of human life. Nanotechnology is a multidisciplinary as well as an interdisciplinary area of inquiry and application. The broad spectrum of applications that nanotechnology is and will be catering to speaks of its omnipresence.[1] Be it in agriculture, energy, electronics, medicine, healthcare, textiles, transport, construction, cosmetics, water treatment etc., nanotechnology finds a role to play or rather a 'defining role' to play, as suggested by many scholars worldwide.[2]

The ideas and concepts behind nanoscience and nanotechnology started with a talk entitled "There's Plenty of Room at the Bottom" by physicist Richard Feynman at an American Physical Society meeting at the California Institute of Technology on 29 December 1959 [3], long before the term nanotechnology was used. In his talk, Feynman described a process in which scientists would be able to manipulate and control individual atoms and molecules. Over a decade later, in his explorations of ultra precision machining, Prof. Norio Taniguchi coined the term nanotechnology[4]. It wasn't until 1981, with the development of the scanning tunneling microscope that could aid in viewing individual atoms that modern nanotechnology began. Eric Drexler expanded Taniguchi's definition and popularised nanotechnology in his book Engines of Creation: The Coming Era of Nanotechnology [5]**.**

Advancement in the field of nanotechnology and its applications to the field of medicines and pharmaceuticals has revolutionized the twentieth century. Nanotechnology is the study of extremely small structures. The prefix **"nano"** is a Greek word which means **"dwarf".** The word "nano" means very small or miniature size[6,7]. Nanotechnology is the treatment of individual atoms, molecules, or compounds into structures to produce materials and devices with special properties. Nanotechnology involve work from top down i.e. reducing the size of large structures to smallest structure e.g. photonics applications in nano electronics and nano engineering, top-down or the bottom up, which involves changing individual atoms and molecules into nanostructures and more closely resembles chemistry biology[8]**.** Nanotechnology deals with materials in the size of 0.1 to 100 nm; however it is also inherent that these materials should display different properties such as electrical conductance chemical reactivity, magnetism, optical effects and physical strength, from bulk materials as a result of their small size [9].

II. History of Nanotechnology

The development in the field of nanotechnology started in 1958 and the various developmental stages have been summarized in **Table 1** [10].

1.	1959	R. Feynman initiated thought process
2.	1974	The term nanotechnology was used by Taniguchi for the first time.
3.	1981	IBM Scanning Tunneling Microscope
4.	1985	“Bucky Ball”
5.	1986	First book on nanotechnology Engines of Creation published by K. Eric Drexler, Atomic Force Microscope
6.	1989	IBM logo was made with individual atoms
7.	1991	S. Iijima discovered Carbon Nano tube for the first time.
8.	1999	1st nano medicine book by R. Freitas “Nano medicine” was published
9.	2000	For the first time National Nanotechnology Initiative was launched
10.	2001	For developing theory of nanometer-scale electronic devices and for synthesis and characterization of carbon nanotubes and nano wires, Feynman Prize in Nanotechnology was awarded
11.	2002	Feynman Prize in Nanotechnology was awarded for using DNA to enable the self-assembly of new structures and for advancing our ability to model molecular machine systems.
12.	2003	Feynman Prize in Nanotechnology was awarded for modeling the molecular and electronic structures of new materials and for integrating single molecule biological motors with nano-scale silicon devices.
13.	2004	First policy conference on advanced nanotech was held. First center for nano mechanical systems was established, Feynman Prize in Nanotechnology was warded for designing stable protein structures and for constructing a novel enzyme with an altered function.
14.	2005-2010	3D Nano systems like robotics, 3D networking and active nano products that change their state during use were prepared.
15.	2011	Era of molecular nano technology started
16.	2012	The NNI launched two more Nanotechnology Signature Initiatives (NSIs)
17.	2013	The NNI starts the next round of Strategic Planning,
18.	2014	Review on the Coordinated Implementation of the NNI 2011 Environmental, Health, and Safety Research Strategy.

Table 1: Yearly Developments in nanotechnology

III. Evolution of Nanotechnology in India

The 9th Five-Year Plan (1998-2002): National facilities and core groups were set up to promote research in frontier areas of Science and Technology, which included superconductivity, robotics, neurosciences and carbon and nano materials. Planning Commission has initiated number of such R&D programmes under basic research [11].

In 2000 the Department of Science and Technology (DST) launched “Programme on Nanomaterials: Science and Devices” and these projects leading to tangible processes, products and technologies after realising the importance of nanomaterials and their far-reaching impact on technology.

In 2001-2002, the DST has set up an Expert Group on “Nanomaterials: Science and Devices”. In the 10th Five Year Plan (2002-07) the Government identified the need to initiate a Nanomaterials Science and Technology Mission (NSTM) for the developments in nanotechnology.

The Tenth Five Year Plan (2002-2007) has identified various important areas such as technology for bamboo products, drugs and pharmaceutical research, instrument development including development of machinery and equipment, seismology, and also nano science and technology[12].

The National Nanoscience and Nanotechnology Initiative (NSTI) was launched in October, 2001 under the aegis of the Department of Science and Technology (DST) of the Ministry of Science. The motive of launching NSTI in 2001 was to create research infrastructure and promote basic research in nanoscience and nanotechnology. It focused on infrastructure development, basic research and application oriented programmes in nanomaterials, such as drugs/drug delivery/gene targeting and DNA chips.

Overwhelmed by the promising prospects of nanotechnology applications and in order to further enhance the visibility of India in nano science and technology, a Nano Science and Technology Mission (NSTM) was anticipated to give thrust to research and technology development in this area [13].

The Eleventh Five-Year Plan (2007-2012) indicated projects to create high value and large impact on socio-economic delivery including nano material and nano devices in health and disease. The magnanimous Eleventh Five Year Plan Budget allocation of Rs. 1000 crore was attributed for the Nano Mission which was launched in 2007 [14].

On 3 May 2007, a Mission on Nano Science and Technology, Nano Mission was launched by the DST to foster, promote and develop all aspects of nanoscience and nanotechnology which have the potential to benefit the country. The Mission is steered by a Nano Mission Council (NMC) under the Chairmanship of Prof. CNR Rao.

The primary objectives of the Nano-Mission are:

- Infrastructure Development for Nano Science and Technology Research
- Public Private Partnerships and Nano Applications and Technology Development Centres Human Resource Development
- International Collaborations
- Academia-Industry partnerships to be nurtured under these programmes[15].

In the Twelfth Five Year Plan (2012-2017) the government gave its approval for continuation of the Mission on Nano Science and Technology (Nano Mission) in its Phase-II at a total cost of Rs. 650 crore. The Nano Mission, in this new phase, would make greater effort to promote application-oriented R&D so that some useful products, processes and technologies also emerge. It will continue to be anchored in the Department of Science and Technology and steered by a Nano Mission Council chaired by an eminent scientist [16].

IV. Classification of Nano Materials

Nano materials can be classified dimension wise into following categories:
Classification Examples

- Nano rods, nano wires have dimension less than 100 nm.
- Tubes, fibers, platelets have dimensions less than 100 nm.
- Particles, quantum dots, hollow spheres have 0 or 3 Dimensions < 100 nm.

On the basis of phase composition, nano materials in different phases can be classified as:

- The nano material is called single phase solids. Crystalline, amorphous particles and layers are included in this class.
- Matrix composites, coated particles are included in multi-phase solids.
- Multi-phase systems of nano material include colloids, aero gels, Ferro fluids, etc.

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. Different characters of tools and methods for nanoparticles are summarised in **Table 2.**

S.No	Activity of Nanoparticles	Characterization and method
1.	Carrier-drug interaction	Diffential scanning calorimetry
2.	Charge determination	Laser Doppler Anemometry Zeta potentiometer
3.	Chemical analysis of surface	Static secondary ion mass spectrometry Sorptometer
4.	Drug stability	Bioassay of drug extacted from Nanoparticles Chemical analysis of drug
5.	Nanoparticle dispersion stability Particle size and distribution	Critical fl occulation temperature (CFT) Atomic force microscopy
		Laser defractometry Photon correlation spectroscopy (PCS)
		Scanning electron microscopy Transmission electron microscopy
6.	Release profile	In vitro release characteristics under physiologic and sink conditions
7.	Surface hydrophobicity	Rose Bengal(dye) binding Water contact angle measurement X-ray photoelectron spectroscopy

Table - 2: Various characterization tools and methods for nanoparticles [17].

Nanoclusters

Nanoscaled materials are usually categorized as materials having structured components with at least one dimension less than 100 nm. Smaller nanoparticles containing 104 or less atoms are refered to as nanoclusters. These clusters can explain the transition from atomic properties to bulk material properties [18].

A Few Types of Nanoclusters

a) Van der Waals nanoclusters

Inert gas atoms make nanoclusters that are weakly bound by the Van der Waals force. The long-range atomic attraction is due to the induced dipole force. The short range revulsion is due to quantum closed shell electronic interactions and the binding energy per atom is less than 0.3 eV. Echt, et al. [19] have shown practically that rare gases form Van der Waals clusters with icosahedral shapes as shown in **Figure 1.**

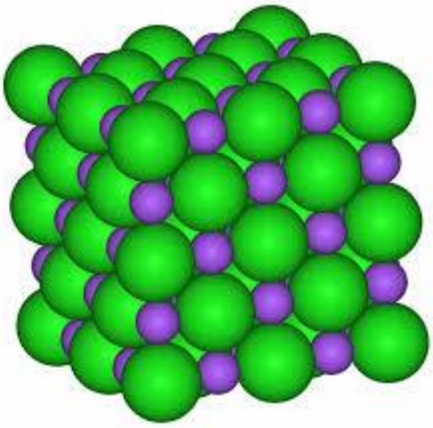

Figure - 1: Van der Waals clusters with icosahedral shapes

b) Ionic nanocluster

Ionic clusters are formed from ions allured by the electrostatic force. NaCl is a critical example of an ionic cluster. The electrostatic bonds in ionic clusters are formed around 2-4 eV per atom. It is ten times more strong as the bond of a Van der Waals nanocluster. **Figure-2.** Shows the crystal structure of NaCl.

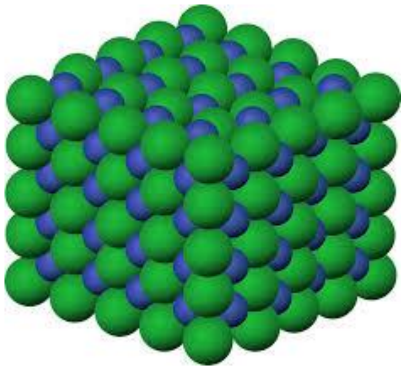

Figure-2: Crystal structure of NaCl

c) Metal nanoclusters

Metal nanoclusters, are more intricated in their bonding. Some metals make bond primarily by the outer valence '**sp'** electrons. Others make bond with the '**d orbitals'** below the valence orbitals. Due to the variation in bonds of metal clusters, the valence can vary from about 0.5 to 3 eV per atom. Metal nanocluster of certain number of atoms having extraordinary stability originating from either atomic or electronic shell closing are known as magic clusters. Many of the metal clusters show following series of magic numbers: 2, 8, 18, 20, 34, 40, 58 etc. It is important to understand the crystal structure of metal nanoparticles to describe the chemistry on their surfaces. Most of the metals having the crystal structure remains intact even in nano scale. Conventionally the metals possess cubic lattices. Typical elements are crystallize in the face centred cubic (FCC) structure include: Cu, Ag, Au, Ni, Pd, Pt, and Al. The typical elements crystallize in the body centred cubic (BCC) structure include: Fe, Cr, V, Nb, Ta, W and Mo [20].

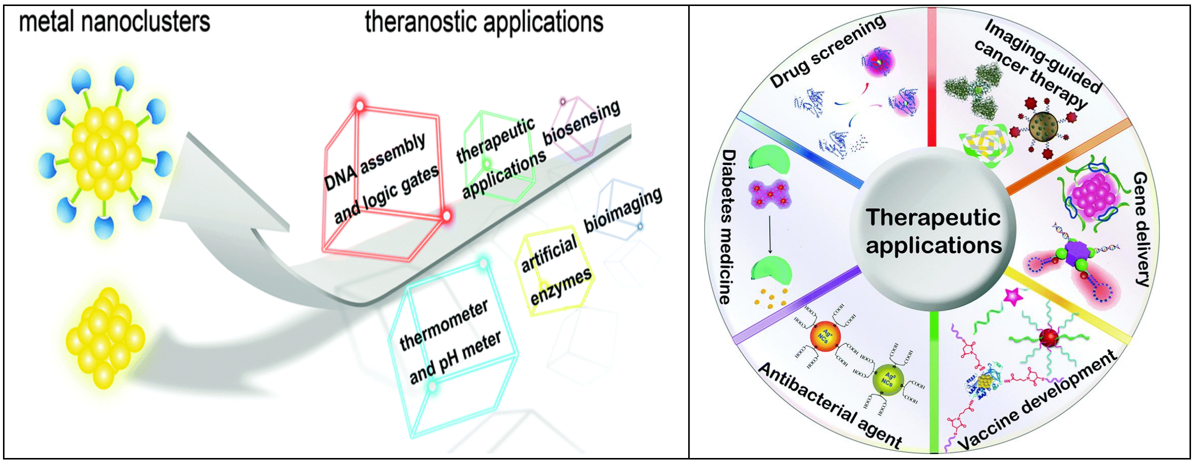

Figure-3: Metal Nanoclusters

Applications of Nanotechnology

The different fields that find potential applications of nanotechnology are as follows:

a. Health and Medicine
b. Electronics
c. Transportation
d. Energy and Environment
e. Space exploration

Nano scale and Nanostructures

The nano scale is the place where the properties of most common things are determined just above the scale of an atom. Nano scale objects have at least one dimension (height, length, depth) that measures between 1 and 999 nanometers (1-999 nm) (Figure-4).

The brief explanation of pharmaceutical nano system is as follows: As shown in the schematic diagram (Figure **5**), pharmaceutical nanotechnology is divided in two basic types of nano tools viz. nano materials and nano devices. These materials can be sub classified into nano crystalline and nano structured materials. Nano structure consists of nano particles, dendrimers, micelles, drug conjugates, metallic nano particles etc.

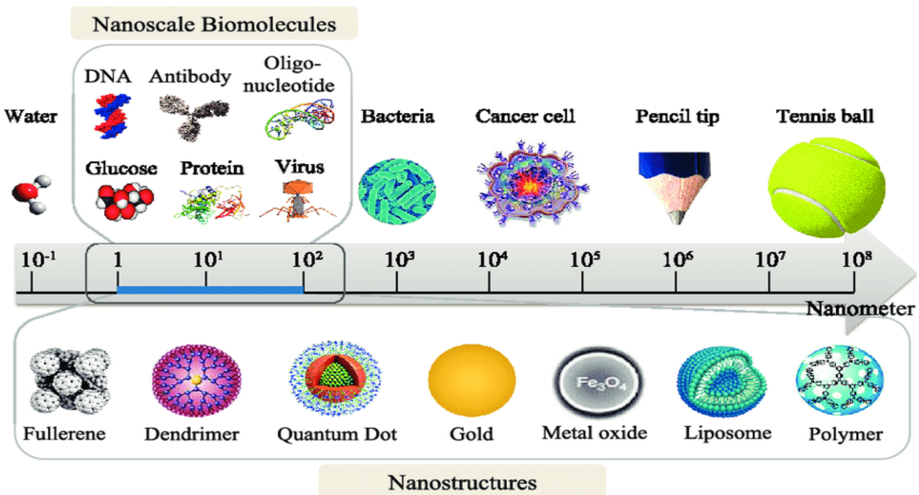

Figure-4: Nanoscale and Nanostructures

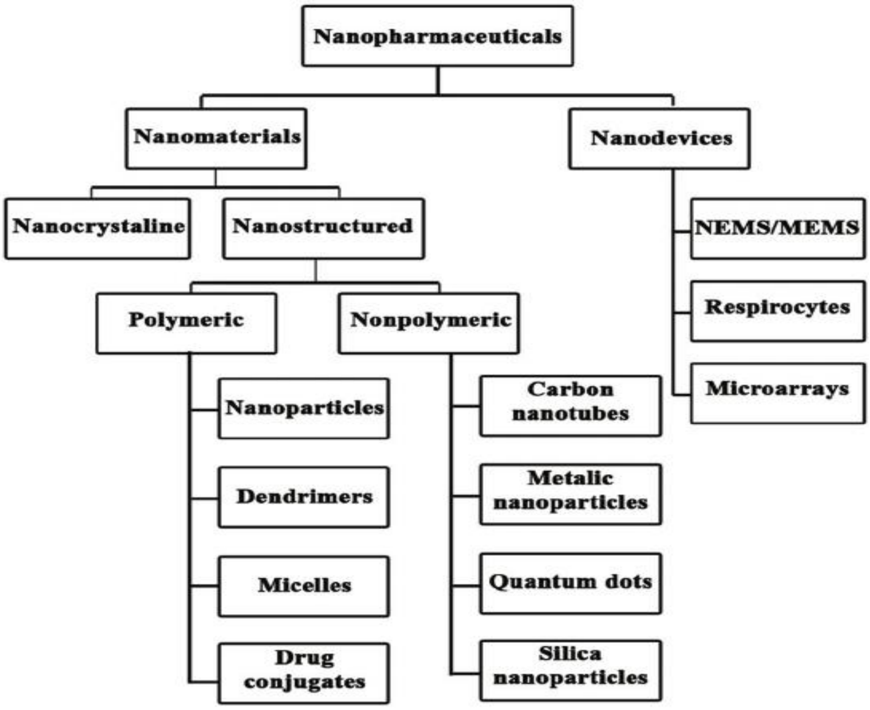

Figure -5: Illustrations demonstrating various types of pharmaceutical nanosystems

Nanoparticles contained specific drug targeting and delivery platforms reduce toxicity and other side effects and also develop the therapeutic index of the targeted drug. In the primary objective of nanotechnology especially in cancer therapy is the development of suitable targeting delivery systems which has been taking the lead in what concerns overcoming the MDR problem. Such targeted delivery systems that are based 'Nanosizing' of drugs:

- Decrease drug resistance
- Decrease toxicity [21]
- Enhance oral bioavailability [22]
- Enhance rate of dissolution
- Enhance solubility [23]
- Enhance the stability of drug and formulation [24]
- Improve drug targeting ability [26, 27]
- Increase patient compliance [25]
- Increase surface area[28]
- Reduce the dose needed [29]

Pharmaceutical Nanotechnology based systems representing two basic types of nano tools such nanomaterials and nanodevices, which play a vital role in realm of pharmaceutical nanotechnology and associated fields. Nanomaterials are biomaterials used, for example, in orthopedic or dental implants or as scaffolds for tissue-engineered products. Their surface modifi cations or coatings might greatly enhance the biocompatibility by favouring the interaction of living cells with the biomaterial. These materials are sub classified into nanocrystalline and nanostructured materials. Nanocrystalline materials are voluntirily manufactured and can depute the less performing bulk materials. Raw nanomaterials can be used in drug encapsulation, bone replacements, prostheses, and implants. Nanostructured materials are processed structured of raw nanomaterials that provide special shapes or functionality, for example quantum dots, dendrimers, fullerenes and carbon nanotubes. Nanodevices are tiny devices in the nanoscale and some of them which are included nano- and microelectro mechanical systems, microfluidics, 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 (Figs-4). Various prominent features and applications of nanosystems are mentioned in Table 3**.**

Types of Nanosystems	Size (nm)	Characteristics	Applications
Carbon nanotube	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 effi ciency, 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 fl uorescence, 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 specifi c 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 modifi ed nanoparticles can be used for active and passive delivery of bioactives

Table-3: Various prominent features and applications of nanosystems[30]

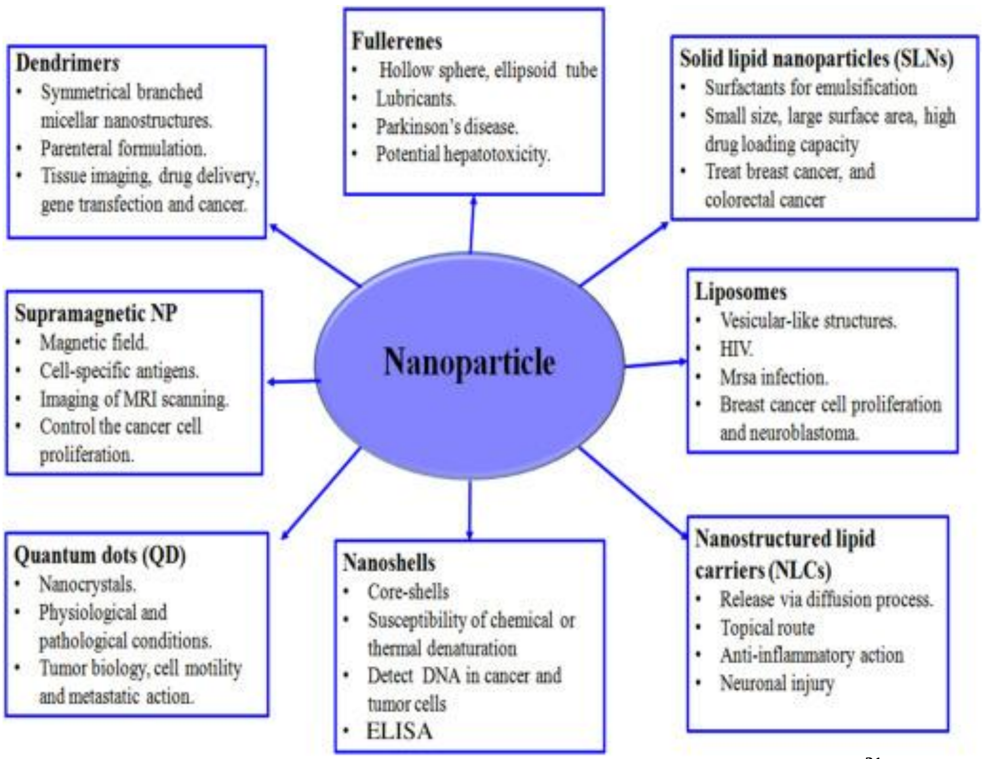

Figure-6: Applications of nanoparticles in diagnosis and treatment [31]

Metallic nano particles:

Metallic nano particles have used in drug delivery, especially in treatment of cancer and also in biosensors. Amongst various metals, silver and gold nano particles are of prime importance for biomedical use (Figure 3) [32]**.**

Advantages of Metallic Nanoparticles

a. Enhance Rayleigh scattering
b. Surface enhanced Raman scattering
c. Strong plasma absorption
d. Biological system imaging
e. Determine chemical knowledge on metallic nanoscale substrate [33]

Disadvantages of Metallic Nanoparticles [34]

- **a. Particles instability**: Nanomaterials will undergo transformation, as they are thermodynamically precarious and lie in the region of high energy local minima. This leads to degeneration of quality, poor corrosion resistance, and main related is retaining the structure becomes strenuous.
- **b. Impurity:** During synthesising of nanoparticles, nitrides, oxides, formation can aggravated from the impure environment. As nanoparticles are highly reactive, there can also be high chances of impurity as well. In solution form, nanoparticles will be synthesized in the form of encapsulation. So, it becomes a challenge to vanquish impurity in nanoparticles.
- **c. Biologically harmful:** Nanobased materials have been reported as toxic, carcinogenic and cause irritation as they become transparent to the cell dermis.
- **d. Explosion:** Exothermic (heat releasing) agitation will lead to detonation, as fine metal particles would act as strong explosives.
- **e. Difficulty in synthesis:** During synthesizing nanoparticles, they should be encapsulated, because they are extremely challenging to retain the nanoparticles size in solution form [35].

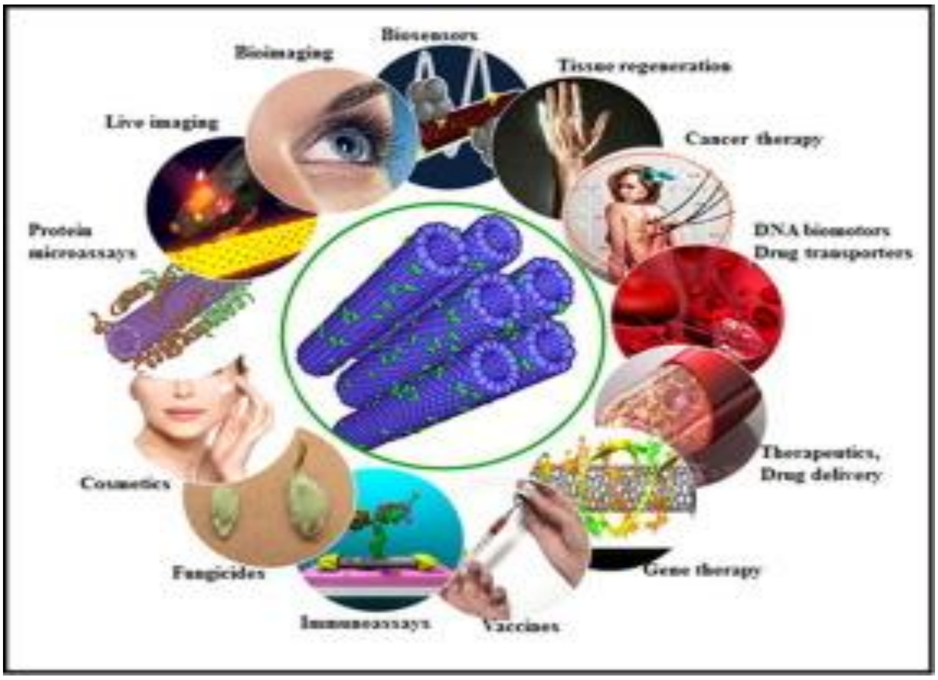

Figure-7: Functionalized carbon nanotubes: Applications, limitations and future directions

V. Characteristics of Metallic Nanoparticles

a. Large surface energies
b. As compared to bulk they have large surface area to volume ratio
c. Quantum confinement
d. Plasmon excitation
e. Increased number of kinks [36].

Characterization of Metallic Nanoparticles

- **a) Absorbance Spectroscopy:** Spectroscopy is useful to characterize metal nanoparticles, because they possess bright colour which is visible by naked eye.

b) Infrared Spectroscopy: This method can provide information on organic layers surrounding metallic nanoparticles. It also gives valuable information to understand the surface structure of the metal nanoparticles.
c) TEM (Transmission electron microscope): It is also widely used to characterize nanomaterials to gain information about particle size, shape, crystallinity and interparticle interaction.
d) SEM: (Scanning Electron Microscopy): It is a powerful technique for imaging any material surface with a resolution down to about 1nm.
e) AFM: It is a better choice for nonconductive nanomaterials.
f) XRD: It is useful and widely used technique for determining the crystal structures of crystalline materials.
g) FTIR: It is widely adopted techniques compared to IR spectroscopy.
h) EXAFS: (Extended X-ray Absorption Fine Structure): this is one of the most reliable and powerful characterization technique to evaluate the structure of metallic nanoparticles; especially it is useful to determine bimetallic nanoparticles.
i) XPS: (X-ray Photoelectron Spectroscopy): it is used to provide information on metal state.

Carbon nano tubes:

These are small macromolecules that are unique importance for biomedical use (**Figure 3**). Carbon Nanotubes composed of excellent mechanical strength, electrical and thermal conductivities makes them a suitable substance toward developing medical devices. In addition, high surface area-to-volume ratio enable them to use in an intense real time applications such as detection and treatment of cancerous cells, nervous disorders, tissue repair and so on. But, most of the biomedical applications of CNTs must be applied after successful functionalization[37]**.**

Carbon nanotubes and their applications are emphasized and some of well known examples of carbon nantubes and their respective applications are arranged in **Table-4.**

S.No	Drug	Type of Disease
a.	Amphotericin B	Breast Cancer Leishmania donovani (Parasite)
b.	Carboplatin	Bladder Cancer
c.	Daunorubicin	Leukemia
d.	Doxorubicin	Lymphoma
e.	Gemcitabine	Ovarian Cancer
f.	Methotrexate	Breast Cancer
g.	Paclitaxel	Breast Cancer

Table-4: Carbon nanotubes and their applications[38].

Liposomes:

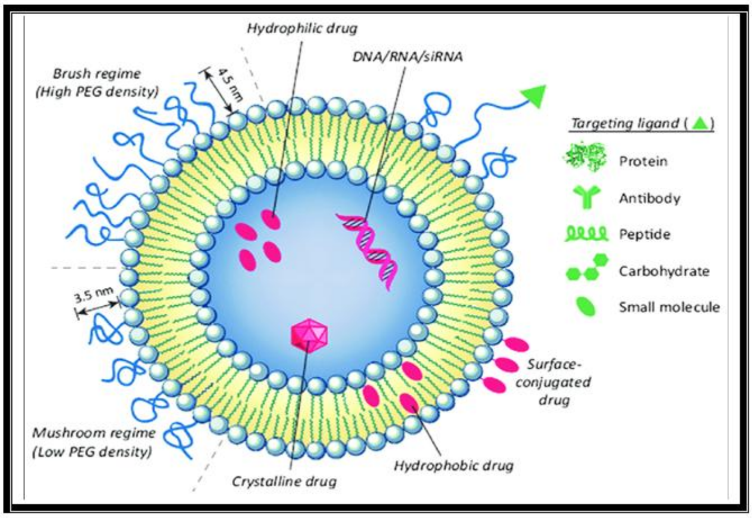

Figure- 8: Structural Features of Lyposomes.

Liposomes have been extensively explored and most developed nano carriers for novel and targeted drug delivery due to their small size, these are 50-200 nm in size (**Figure 4**). Their applications are as long as circulatory and in passive and active delivery of gene, protein and peptide. Liposomes were first engineered nanoparticles used for drug delivery. Cancer chemotherapeutic drugs and other toxic drugs like amphotericin and hamycin, when used as liposomal drugs produce much better efficacy and safety as compared to conventional preparations. These liposomes are crammed with drugs either in the aqueous chamber or in the lipid membrane. Liposomes can transport hydrophilic drugs (water soluble) inside the core (aqueous compartment) and hydrophobic drugs (water insoluble but soluble in lipid) between the two layers [39].

Dendrimers:

The dendrimers are highly branched, well-defined molecular architectural polymers. Firstly in 1978 by Vogtle has provided a novel and one of the efficient nanotechnology platforms for drug delivery. Dendrimers are hyper branched, tree-like structures. It contains three different regions: core moiety, branching units, and closely packed surface (**Figure 9 and 10**). It has globular structure and encloses internal cavities. Its size is less than 10 nm. These are long in their size, shape, and have unique physical properties. Nano tubes are having special advantages over the drug delivery and diagnostic systems (**Figure-8**) because of their unique physical properties. They are used in medical sciences for intended drug delivery and contrast agent in MRI. The cavities of dendrimers can be used as binding sites for smaller molecules - effectively then the dendrite becomes a nanosized "container" for various molecules [40].

Advantages of dendrimers over conventional anti-cancer agents

- High drug loading capacity
- Dendrimers having appropriate nanosize ranging 1-100 nm for pre detectable release profile, favorable pharmacokinetics and targeting potentials
- Dendrimer improve the solubility of poorly soluble anti-neoplastic drugs.
- Clearance is reduced through Reticuloendothelial system due to small size.
- Heterogenous functional groups are occupied on outer surface of dendrimers, which can be used to attach vector devices for targeting to distinct site in the body.
- Presence of numerous peripheral functional groups on dendrimers is responsible for tumor cell-specific delivery [41, 42].

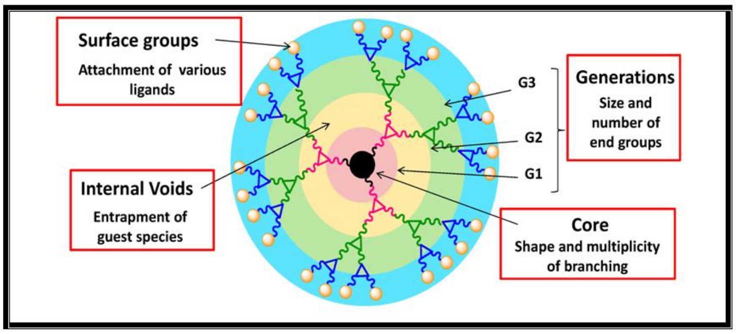

Figure-9: General representation of the model structure of a dendrimers

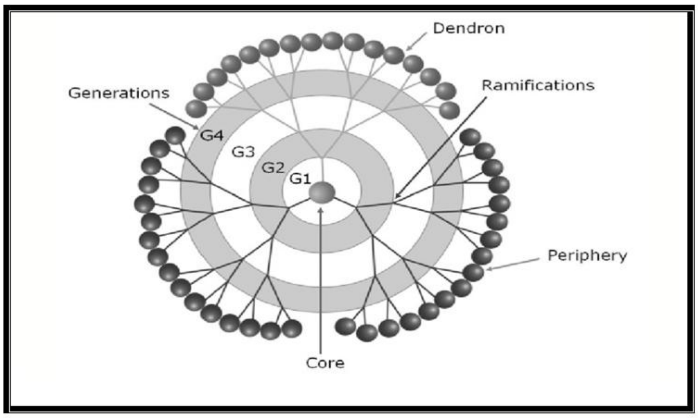

Figure-10: Schematic representation of the Dendrimer

Nanoshells

Nanoshell comprises a spherical core of a compound surrounded by a shell or outer coating of thin layer of another material of 1–20 nm thick. Nanoshell materials can be synthesized from semiconductors, metals, or insulators. The property of nanoshells is determined by the materials used and core-to-shell ratio.

Metal nanoshell comprise dielectric core enclosed by metallic shell, especially gold (AuNSs). In these cases, drug is encapsulated or adsorbed onto the shell surface via specific functional groups or by electrostatic stabilization. AuNS are employed to deliver antitumor drugs (e.g., doxorubicin, paclitaxel, small interfering RNA, and single-stranded DNA) into cancer cells, which enhance the efficacy of treatment. AuNSs can also be functionalized with active targeting ligands, such as antibodies, aptamers, and peptides to increase the particles' specific binding to the desired targets [43, 44].

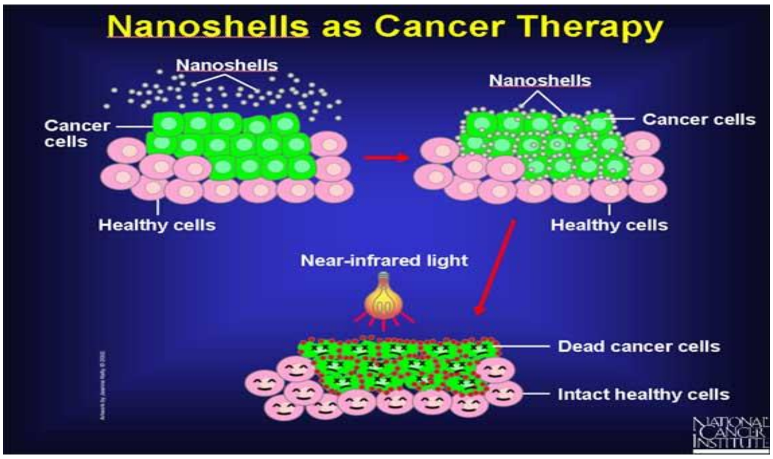

Figure-11: Nanoshells in Cancer Therapy

Nanorods

In nanotechnology, nanorods morphologically are of nanoscale objects. Each of their dimension ranges from 1–100 nm. Nanorods are synthesized from metals or semiconducting materials with ratios are 3-5. Snthesis of nanorods is produced by direct chemical synthesis is one of the ways. (**Figure-12**) The different combinations of ligands are acting as shape control agents and bond to different facets of the nanorod with different strengths. It permits different faces of the nanorod to grow at disperate rates, producing an elongated object. Gold nanorods are regarded eminent candidates for biological sensing applications due to the absorbance band changes with the refractive index of local material [45], allowing for immensely accurate sensing. In addition to that nanorods with near-infrared absorption peaks can be excited by a laser at the absorbance band wavelength to produce heat, potentially accepting for the selective thermal destruction of cancerous tissues [46]. Nanoscale materials such as fullerenes, quantum dots and metallic nanoparticles are having unique properties, because of their high surface area to volume ratio [47]. Gold nanospheres and nanorods are also having unique optical properties, due to presence of quantum size effect [48]. Gold nanorods are cylindrical which range from less than ten to over forty nm in width and up to several hundred nm in length. These particles are commonly characterized by their aspect ratio (length divided by width) [49, 50].

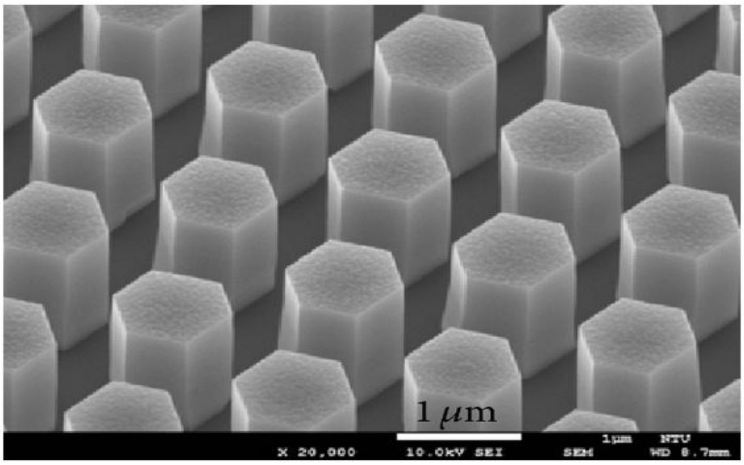

Figure-12: Nanorods

VI. Research And Development In Medical Field

Nanotechnology has hailed as the next big thing for decades, but it is only one now is truly becoming a reality in the medical device space.

Research and Development (R&D) of newer drug delivery systems based on nanotechnology methods is being tried for conditions like cancer, diabetes, fungal infections, viral infections and in gene therapy. The main advantages of this auditory modality of treatment are targeting of the drug and intensify safety profile. Nanotechnology has also find out its employ in diagnostic medicine as contrast agents, fluorescent dyes and magnetic nanoparticles.

Some of the applications of nanomaterials to biology or medicine are listed below:

- Fluorescent biological labels [51, 52]
- Drug and gene delivery [53, 54]
- Bio detection of pathogens [55]
- Detection of proteins [56]
- Probing of DNA structure [57]
- Tissue engineering [58, 59]
- Tumour destruction via heating (hyperthermia)[60]
- Separation, purification and identification of biological molecules and cells [61]
- MRI contrast enhancement [62]
- Phagokinetic studies [63]

VII. Importance For Developing Countries

As, nanotechnology has many wider applications, experts have computed a list of top ten nanotechnology application areas which are of related for developing countries such as India with respect to addressing UN Millennium Development Goals (MDGs) goals (**Table 5**).

Sl.No.	Applications	Examples
1.	**Energy storage, production, and conversion**	• Novel hydrogen storage systems based on carbon nanotubes and other lightweight nanomaterials • Photovoltaic cells and organic light emitting devices based on quantum dots • Carbon nanotubes in composite film coatings for solar cells • Nanocatalysts for hydrogen generation • Hybrid protein-polymer biomimetic membranes
2	**Water treatment and remediation**	• Nanomembranes for water purification, desalination, and detoxification • Nanosensors for the detection of contaminants and pathogens • Nanoporous zeolites, nanoporous polymers, and attapulgite clays for water purification • Magnetic nanoparticles for water treatment and remediation • TiO2 nanoparticles for the catalytic degradation of water pollutants
3	**Disease diagnosis and screening**	• Nanoliter systems (Lab-on-a-chip) • Nanosensor arrays based on carbon nanotubes • Quantum dots for disease diagnosis • Antibody-dendrimer conjugates for diagnosis of HIV-1 and cancer • Nanowire and nanobelt nanosensors for disease diagnosis • Nanoparticles as medical image enhancers
4	**Drug delivery Systems**	• Nanocapsules, liposomes, dendrimers, buckyballs, nanobiomagnets, and attapulgite clays for slow and sustained drug release systems
5	**Food processing and storage**	• Nanocomposites for plastic film coatings used in food packaging • Antimicrobial nanoemulsions for applications in decontamination of food equipment, packaging, or food • Nanotechnology-based antigen detecting biosensors for identification of pathogen contamination
6	**Agricultural productivity Enhancement**	• Nanoporous zeolites for slow-release and efficient dosage of water and fertilisers for plants, and of nutrients and drugs for livestock • Nanosensors for soil quality and for plant health monitoring • Nanomagnets for removal of soil contaminants

Table-5: Applications of Nanotechnology with Examples (Contd...)

Sl.No.	Applications	Examples
7	**Air pollution and remediation**	• TiO_2 nanoparticle-based photocatalytic degradation of air pollutants in self-cleaning systems • Nanocatalysts for more efficient, cheaper, and better-controlled catalytic converters • Nanosensors for detection of toxic materials and leaks
8	**Construction**	• Nanomolecular structures to make asphalt and concrete more robust to water seepage • Heat-resistant nanomaterials to block ultraviolet and infrared radiation • Nanomaterials for cheaper and durable housing, surfaces, coatings, glues, concrete, and heat and light exclusion • Self-cleaning surfaces (e.g., windows, mirrors, toilets) with bioactive coatings
9	**Vector and pest detection and control**	• Nanosensors for pest detection • Nanoparticles for new pesticides, insecticides, and insect repellents
10	**Health monitoring**	• Nanotubes and nanoparticles for glucose, CO_2, and cholesterol sensors and for *in-situ* monitoring of homeostasis.

Table-5: Applications of Nanotechnology with Examples.

The new emerging nanotechnology can have several impacts on health. The positive and negative impacts can be seen. While the use of new technology that will promote animal and human good health, the undesirable adverse effects of the modern nanotechnology are also observed. At present, the interrelationship between nanotechnology and health becomes the attentive issue in global public health. Various observations are stated for the need to related on nanotechnology and its health [64, 65, 66].

Nanotechnology in health and medicine

It is well known that various diseases such as diabetes, cancer, Alzheimer's disease, Parkinson's disease, cardiovascular diseases and multiple sclerosis as well as different kinds of inflammatory or infectious diseases (e.g. HIV) constitute more number of serious and complex illnesses which are posing a major problem for the mankind. Nano-medicine is an application of nanotechnology which works in the field of health and medicine. Nano-medicine makes use of nano materials, and nano electronic biosensors. In the future, nano medicine will benefit molecular nanotechnology. The medical area of nano science applications have many projected benefits and are potentially valuable for all human races [67].

With the help of nano medicine early stage of detection and prevention, improved diagnosis, proper treatment and follow-up of diseases is feasible. Some of nano scale particles are used as tags and labels, biologically can be performed quickly, the testing has become more sensitive and more flexible. Gene sequencing is becoming more efficient with the invention of nano devices like gold nano particles. The gold particles when tagged with short segments of DNA can be used for detection of genetic sequence in a particular sample.

Nanotechnology facilitated to damaged tissue can be reproduced or repaired. In this process artificially stimulated cells are used in tissue engineering, which might revolutionize the transplantation of organs or artificial implants.

The applications of nanotechnology could be seen in various fields including medicine. In medical field, the applied nanotechnology is the new applied medical technology. Nanomedicine is the distinct medicine subject that covering the principle of nanomedical science and nanomedical technology. It can be applied in many ways of medicine from disease diagnosis to treatment. First, the nanomedicine can deal with diagnosis. Many new diagnostic tools are found based on the new nanotechnology. For treatment of all knowing diseases, there are many new drugs developed based on the nanotechnology. In addition, the nanotechnology can also be applied for preventing the disease in medicine. Many new vaccines are well developed based on new approaches in nanotechnology[68].

Diagnosis and nanomedicine

The application of nanotechnology might be useful for the development of new generation diagnostic system in medicine. It is fact that, the measurement of substance at nanolevel (such as vitamin and hormone) is a big challenge. At present, with the use of new technology such as electrochemiluminescence, the measurement of the substance at nanolevel is possible[69]. In addition, the applied nanotechnology for imaging purpose is also possible. The cellular imaging by nanoprobe is possible for medical diagnostic purpose [70]. At present, the examples of available nanoprobes are quantum dots, plasmonic nanoparticles, magnetic nanoparticles, nanotubes, nanowires, and multifunctional nanomaterials [71, 72]. The advantage in the diagnosis of nanoprobes is due to high volume/surface ratio, surface tailorability, multifunctionality, and intrinsic properties. It is no doubt that nanoprobes can be applied for diagnosis of several infectious diseases and cancers [73]. The use of nanomaterials are integrated with other advanced technology such as surface plasmon spectroscopy, amperometry, and magnetic relaxation become the actual development in diagnostic medicine [74].

Nanotechnology in Medicine-Application: Drug Delivery

The application of nanotechnology in medicine currently is being developed involve employing nanoparticles to deliver drugs, heat, light or other substances to specific types of cells (such as cancer cells). Particles are engineered so that they are attracted to diseased cells, which allow direct treatment of infected cells. This technique reduces the damage of neighbour healthy cells in the body **(**Figures- 13 & 14**).**

Nanoparticles that deliver chemotherapy drugs directly attack on cancer cells. Research is in advance for targeted delivery of chemotherapy drugs and their final approval for their use with cancer patients are under progress. Cytoimmune has published the results of a Phase 1 Clinical Trial of their first targeted chemotherapy drug. Another company, BIND Biosciences, has also published preliminary results of a Phase 1 Clinical Trial for their first targeted chemotherapy drug and proceed with a Phase 2 Clinical Trial.

By using nanoparticles in a influenza vaccine that targets a portion of the virus that is present in all influenza viruses. The intent is to develop a vaccine that will work on all influenza viruses [75].

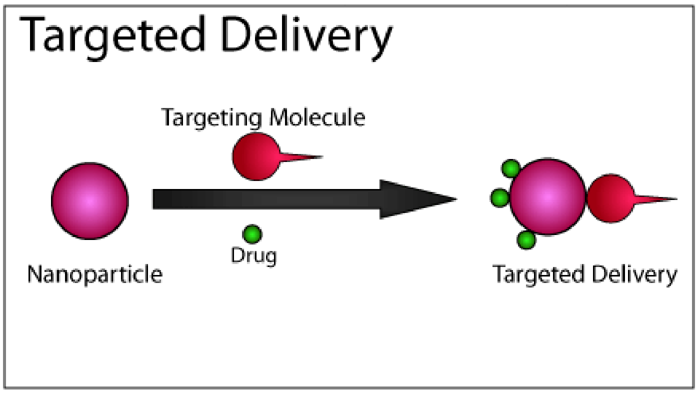

Figure- 13: Schematic representation of the targeted drug delivery.

The Wyss Institute has been testing nanoparticles that release drugs when subjected to sheer force, such as occurs when passing through a section of artery that is mostly blocked by a clot. Lab tests on animals have shown that this method is highly effective in delivering drugs which might be used to dissolve blood clots. The Houston Methodist Research Institute scientists have demonstrated a targeted drug delivery method in mice using silicon nanoparticles that degrade inside a tumour, releasing polymer strands that form a nanoparticle containing the drug to be delivered. This polymer nanoparticle can be dissolved inside and delivering the drug to the cancer cell [76, 77]. The University of Illinois have demonstrated that gelatin nanoparticles can be used to deliver drugs to damaged brain tissue more accurately than standard methods. This was demonstrated successfully in the lab, so the scientists hope that this method will more effectively deliver the drug for brain injuries.

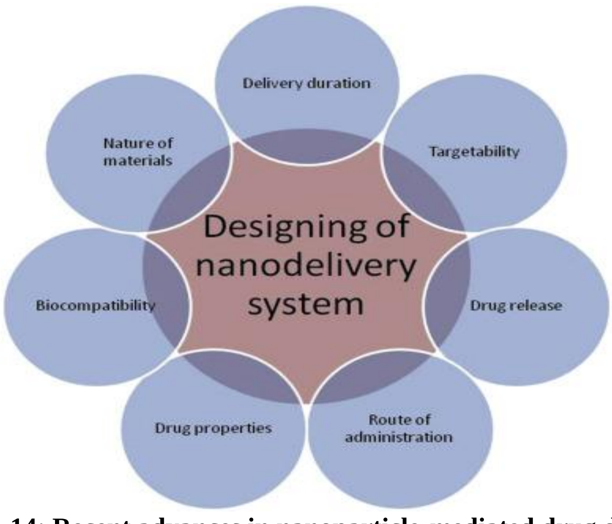

Figure - 14: Recent advances in nanoparticle-mediated drug delivery.

VIII. Nanotechnology in Medicine Application: Therapy Techniques

In recent years developed "nanosponges" that absorb toxins and remove them from the bloodstream. The nanosponges are polymer nanoparticles coated with a red blood cell membrane. The red blood cell membrane allows the nanosponges to travel freely in the bloodstream and attract the toxins [78].

A method is developed to generate sound waves that are powerful, but also tightly focused, that may eventually be used for noninvasive surgery. They use the lens coated with carbon nanotubes to convert light from a laser to emitted sound waves. The purpose is to develop a method that could blast tumours or other infected areas without damaging healthy tissue. Some investigations are demonstrated that the use of bismuth nanoparticles to concentrate radiation used in radiation therapy to treat cancer tumours.

Nanoparticles composed of polyethylene glycol-hydrophilic carbon clusters (PEG-HCC) have shown to absorb free radicals at a abundant higher rate than the proteins out body uses for this function. This ability to absorb free radicals may reduce the harm, caused by the release of free radicals after a brain injury.

Targeted heat therapy is being developed to destroy tumors of breast cancer. In this method antibodies are strongly attracted to proteins which are produced in one type of breast cancer cells attached to nanotubes, causing the nanotubes to accumulate at the tumor. Infrared light from a laser is absorbed by the nanotubes and generates heat that incinerates the tumour [79].

Benefits of Nano Carriers in Drug Delivery Systems [80]

- Exhibit higher intracellular uptake
- Nano carriers can penetrate the submucosal layers while the microcarriers are predominantly localized on the epithelial lining.
- Nano carriers can be administered into systemic circulation without the problems of particle aggregation or blockage of fine blood capillaries[81].
- The development of targeted delivery is strenuously built on extensive experience in pharmaco-chemistry, pharmacology, toxicology, and nowadays it is being pursued as a multi-and interdisciplinary effort.

IX. Conclusion

Nanotechnology is very much predominant almost every facet of life. Nanotechnology is a new useful technology that can be the solution for many activities. Its application in medicine is warranted and becomes the new hop in diagnosis, treatment, and prevention. The applications of nanotechnology can be seen in several fields of medicine and become the new things that practitioner has to recognize and use.The change in behaviour of material at nanoscale is dominated in the first place by quantum mechanics and is additionally attributable to material confinement in small space, and the increase in surface area per volume. At the nanoscale, biology, chemistry, physics, material science, and engineering intersect toward the same principles and tools. Resulting the development in nanoscience has very far-reaching impact. Nanoparticles have prospective applications in the field of medical sciences including new diagnostic tools, imaging agents and methods, targeted drug delivery, pharmaceuticals, bio implants and tissue engineering. Drugs with more toxic possible like cancer chemotherapeutic drugs can be given with better safety portrait with the profitability of nanotechnology. A molecule of drug can be supported to reach the proper site in order to reduce the side effects of the dose and its quantity. Quantum dots with MRI scan can produce excellent images of a tumour. Gold nanoshells can be used to detect, find, accumulate, and potentially liquidate the tumor by heating the Nanoparticles. In the forthcoming days, we can envision a new world with medical nanodevices, implanted or even inserted into the body. An intercontinental perspective and collaboration might be required in the field of research and development to give such fruitful results to humankind society.

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