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Nanopharmaceuticals

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ABSTRACT

Nano-sized objects can be transformed in many ways to alter their characteristics. Drug molecules sized in nanometer provide some unique features which can lead to improved drug localization, prolonged circulation, 5 and enhanced drug efficacy of the drug. Nanotechnology improves the performance come through a variety of dosage forms. Various pharmaceutical nanotechnology based systems which can be termed as Nanopharmaceuticals like liposomes, carbon Nanotubes, quantum dots, dendrimers, and polymeric nanoparticles. This review summarizes the most important applications of nanotechnology.The purpose of that review paper is to look into the present aspects of "Nanotechnology". This paper gives a brief description of what Nanotechnology is? And its application in various fields like computing, medicine, food technology, Robotics, Solar cells etc. Nanotechnology also deals with the future perspectives of Nanotechnology, risks in advanced nanotechnology.

Keywords: Nanotechnology, Liposomes, , Dendrimers, Carbon Nanotubes, Quantum Dots, Nanopharmaceuticals,

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INTRODUCTION

Nanotechnology and Nanomedicines

Nanotechnology and Nanomedicines, the high risk, high pay off global phenomenon is in full swing. Advances of nanotechnology are being driven by collaborative research, patenting, commercialization, business development and technology transfer within diverse areas such as chemical engineering, biotechnology, the medical sciences, physical sciences and information technology [1-3].

The confusion and ambiguity surrounding the definition of nanotechnology continues to be one of the most significant problems shared by regulators, policymakers, researchers and legal professionals alike. Different definitions of nanotechnology have sprung up over the years. Nanotechnology has been described as the manipulation, precision placement, measurement, modeling or manufacture of matter in the sub-100 nm range [4], or in the 1 to 200 nm range.

Size reduction is important applications in pharmacy. Size reduction improving solubility and bioavailability, reducing toxicity, enhancing release. It providing better formulation opportunities for drugs. In some of the cases, size reduction is limited to micron size range, for example, various pharmaceutical dosage forms like powder, emulsion, suspension etc. Drugs in the nanometer size range improve performance in a variety of dosage forms. Major advantages of nanosizing include:

(i) increased surface area,

(ii) enhanced solubility,

(iii) increased rate of dissolution,

(iv) increased oral bioavailability,

(v) more rapid onset of therapeutic action,

(vi) less amount of dose required,

(vii) decreased fed/fasted variability, and

(viii) decreased patient-to-patient variability

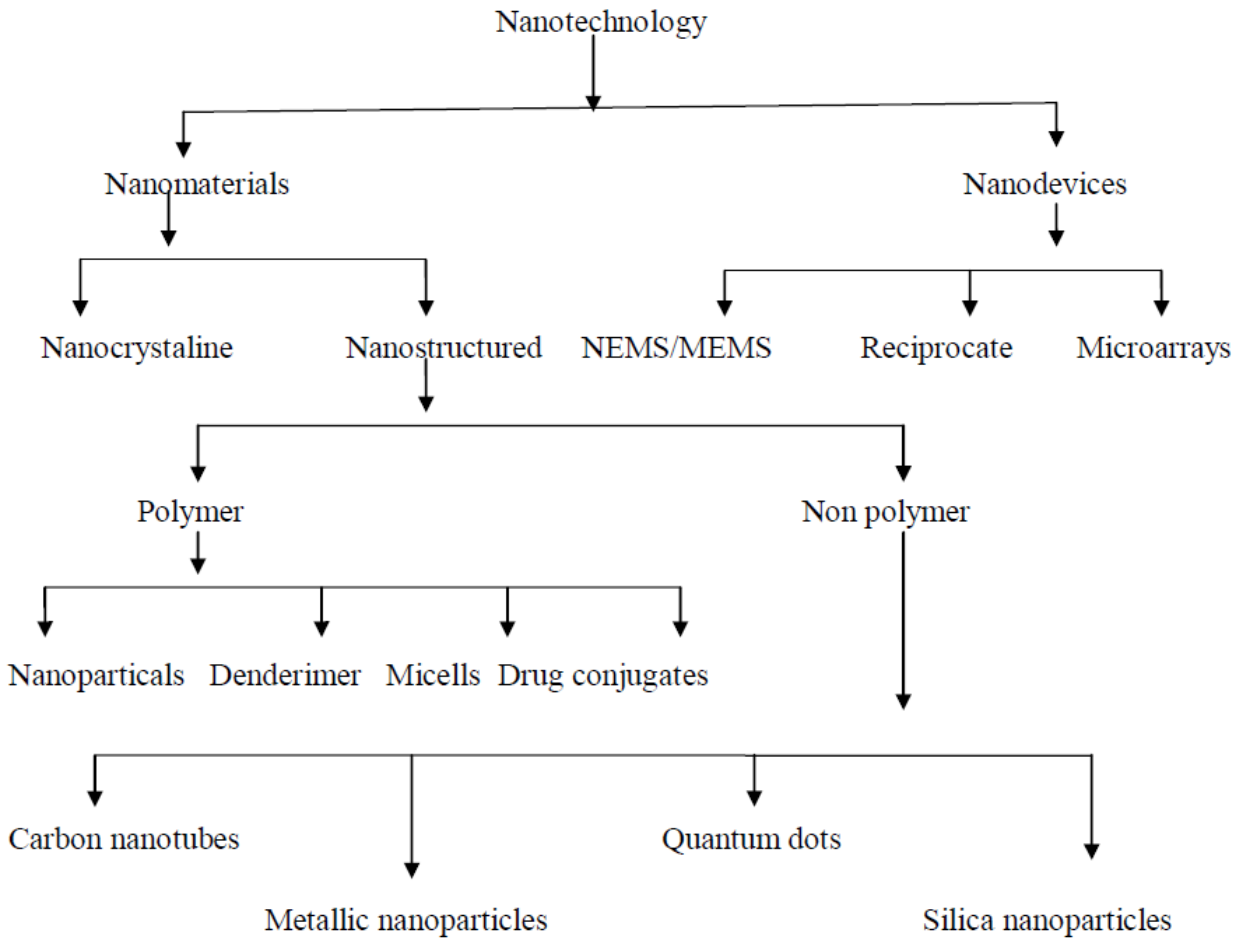

Table 1 :-Definitions of general nanotechnology:relatedterms

Term	Defination
1 Nanomaterial	Material with one or more external dimensions, or an internal structure, on the nanoscale, which could exhibit novel characteristics compared to the same material without nanoscale features NOTE Novel characteristics might include increased strength, chemical reactivity or conductivity.
2 Nanoparticle	Particle with one or more dimensions at the nanoscale NOTE 1 Also referred to as nanoparticulate, although this term is more often used adjectivally. NOTE 2 Novel properties that differentiate nanoparticles from the bulk material are typically developed at a critical length scale of under 100 nm.
3 Nanoscale	Having one or more dimensions of the order of 100 nm or less. NOTE Also referred to as nanosize.
4 Nanoscience	Study of phenomena and manipulation of materials at atomic, molecular and macromolecular scales, where properties differ significantly from those at a larger scale
5 Nanostructured	Having a structure at the nanoscale NOTE Agglomerates and aggregates of nanoparticles are examples of nanostructured particles.
6 Nanotechnology	Design, characterization, production and application of structures, devices and systems by controlling shape and size at the nanoscale

Table 2:- problematic soial trads and ways nanotechnology could contribute to solution, according to Roco and Bainbridge

Social problems	Nanotechnology contribution to solution
Health care and working capacity of aging polution	Convergence of nanotechnology with bitechnology, information technology and neurotechnology would adress chronic illness,losing senserial property, capacity, and maintainng work capacity.
Collapse of birth rate in most advanced nations, below level required for population stability.	Convergance of nanotechnology with biotechnology to overcome infertility.
Poverty and inequality, most urgently in under developed nations	Economic progress,fueled by technological development requiring systemic control of nanoscale processes and materils.
Loss of jobs in advanced nations, as work goes to nations with lower wages, weaker workers benefits, andworse workplace safety.	Progress in nanosence will allow industrial nations to maintain quality of life, generating new domestic industries with high quality jobs, even as poor nations benefits from globalization.
Threanted exhusion of natural resources.	Non-enalbed technologiesfor improved efficancy in use of non-renewable resources, inclouding energy production, water filteration, and invention of many high quality nano-fabricated substitute materials.
Environmental degradation, including global warming.	Reduced pollution from more efficient use of materials: specific new pollution remedition nanotechnoloies: improved environmental monitoring by means nano-enabled sensor nets.
World political instability theatens the gains achieved by newly denocratic nations.	Stability will require technology that can offer abundance to a majority of people in all socities with existing natural resourecs.
Security issues within industrial nations.	Numerous specific nanotechnalogy-based solutions; such as;sensors to detect bioterrorism substances: inexpensive “smart labels” to deter theft of valuable goods; armor and vehical components from nano-structed materials.
Cultural chaos in post-industrial, post-modern,pluralist society.	Nantechnology will permit rapid process in technologies of compulation, communication and creativity to sustain a culture of connectively, equal access to information and a myriad subcultures simultaneously.
Medical;currently incurable illness including cancer and AIDS	Molucular and nanobiosystems solutions for detection and treatment and the subcellular level.
Medical: diminishing returns from research; rising costs of health care	Fresh approaches to disease diagnosis and treatment from nanotechnology;prevension of disease from better nutrition and from quick detection and treatment of condition predisposing to disease.

CLASSIFICATION OF NANOPHARMACEUTICALS:-

CANRBON NANOTUBES:-

Carbon Nanotubes (CNTs) are hollow, well ordered, carbon nanomaterial.CNTs have variety of properties. These have high aspect ratio and surface area, and ultra-light weight.CNTs are classified as single-walled (SW) or multi-walled (MW) carbon Nanotubes. In that MWCNTs are made from a number of cylindrical carbon layers and have diameter 2-100 nm, and SWCMTs consists only one cylindrical layer and have diameter ranges from 0.4–2 nm. [5] CNTs provide a greater targeting ability to the formulations. following examples are presented inTable-3

Table3:- Drugs those can be delivered via Carbon Nanotubes

Drug	Type of disease	Type of CNTs
Daunorubicin	Leukemia	SWCNTs
Doxorubicin	Lymphoma	SWCNTs
	Breast cancer	MWCNTs
Methotrexate	Breast cancer	MWCNTs
Paclitaxel	Breast cancer	SWCNTs
Gemcitabine	Ovarian cancer	SWCNTs
Amphotericin B	Leishmania donovani	Not specified
Carboplastin	Bladder cancer	Not specified

QUANTUM DOTS:-

Quantum dots (QDs) have semiconductor core andcoated by a shell which improved optical properties. These have a cap which provides higher solubility in aqueous buffers. Functionalized QDs, conjugating them with targeting ligands, and used to target specific tissues. Various colloidal core/shell usually synthesized by are CdSe/ZnS, CdTe/CdSe, InP/ZnS and CdSe/CdS/ZnS [6].QDs have a potential for improved treatment of cancer.Before that, while preparing QD-drug formulations, some guidelines must be followed

(a)Surface of nanoparticles must be functionalized

(b)Nanoparticle size is to be minimized

(c)To avoid detrimental effects of the drug,drug molecules should be kept within the nanoparticle

(d)To avoid collapse, a biocompatible polymer must be attached to QD surface.

Some of drugs successfully delivered by QDs are listed in Table-4

Table4:- Drugs those can be delivered via Quantum Dose

Drugs/therapeutics	Target cells/Diseases	Types of QDs	Efficiency
Saquinavir	HIV-1	Carboxyl-terminated QDs	High site-specificity andcross BBB
Doxorubicin	Ovarian cancer	Mucin1-aptamer QD	Targeting and controlled drug delivery to cancer cells.
5-flurourasil	Breast cancer	ZnS QDs	Enhance drug uptake
Daunorubicin	Leukaemia	CdTe QDs	Inhibit multidrug resistance.
Daunorubicin	Leukaemia	CdS QDs	High accumulation on target

DENDRIMERS:-

Dendrimers are highly branched Nano-scale structure with several surface-active groups.These have smaller size (<100 nm),and due to that narrower molecular weight distribution, greater functionality, higher quantity of surface groups and relatively easier incorporation of targeting ligands.They are very good candidates for drug delivery. The main characteristics which make it special are three different topological sites A

(a) Polyfunctional core

(b) Interior layers and

(c) multivalent surface[7]

Table5:- drugs those delivered via Dendrimers

Drugs / therapeutics	Types of Dendrimers /Conjugates	Target cells / Indications / Functions.	Advantages / features
Efavirrenz	Tuftsin-conjugated PPE dendrimers	HIV	Targeted delivery to macrophages
Lamivudine	Mannose-capped PPE dendrimers	HIV	Increase the cellular uptake, reduced cytotoxicity.
SiRAN	Amino terminated carbosilane dendrimers	Lymphocytes	Reduced HIV infection, in-vitro
Sulphated Oligosaccharides	Polylysine dendrimers	HIV	Higher activity due to dendrimers product.
Galatosaccharide Analogues	Multivalent phosphorus containing catanionic dendrimers	HIV-1	Higher stability and anti-viral property, lower toxicity.
Doxorubicin	2,2bis(hydroxylmethyl) propanoic dendrimers	Colon carcinoma cells of rat	In vitro and in vivo, dendrimers product was ten times less toxic.
SN38	G3.5 PAMAM dendrimers.	Hepatic colorectal cancer cells	Increase oral bioavailability and decrease gastrointestinal toxicity
Boron	EGF-carrying PAMAM dendrimers.	Neuron capture technology	Intratumoral injection or CED
EGFR siRNA	Dendriworms	Knockdown EGFR expression	IV or CED
Plasmid pEGFP-N2	Angiopep-carrying PGEgylated PAMAM dendrimers G5.0	Encode green fluorescence protein	IV

LIPOSOMES:-

Liposomes are lipid vesicular systems. These are composed of an aqueous core enclosed by natural or synthetic phospholipid bilayers.Theaqueous core used to encapsulate hydrophilic drugs, as well as and amphiphilic drugs can be solubilized within the phospholipid bilayers. Depending on the structure of the lipid bilayers liposomes can be classified as

(a) Small unilamellar vesicles (SUV)

(b) Large unilamellar vesicles and (LUV)

(c) multilamellar vesicles (MLVs).

Liposomes were first introduced for drug delivery in 1965. [8] And in recent studies, these are the more widely used Nano-pharmaceutical carriers. Liposomes are rapidly cleared from blood by phagocytic cells and they possess a low transport rate. But these disadvantages can be overcome by coating the surface with a biocompatible and inert polymer such as PEG or by incorporating targeting ligands. [9]Liposomal formulations are well used for delivering chemotherapeutic and anticancer agents. Successful delivery of Placitaxel can be done by conjugating liposome with poly (d, l-lactic acid) - polyethylene glycol [PLA-PEG] [52]

Table6:-Drugs those delivered via Liposomes

Therapeutics	Typeof liposome	Indications
Tppotecan+Vincristin	PEG-Liposome	Brain Cancer
Lrinotecan+Cisplastin	Mixture of two Liposome	Small-Cell lung cancer
siRNA+Doxorubicin	PEG-Liposome	MDR-Breastcancer
Doxorubacin+verapamil	Transferrin-(TF)Conjugated PEG-Liposome	MDR-Leukemai
Budesonide	Small molucular Liposome	Asthma
Ketotifan	Small molucular Liposome	Asthma
VEGF gene	Gene liposome	Pulmonary Hypertension
Amiloride hydrochloride	Small molucular Liposome	Cystic Fibrosis
Tobramycin	Small molucular Liposome	Pulmonary Infection
Interlukin-2	Protein Liposome	Lung Cancer
Insulin	Protein Liposome	Diabetes

VEGF= Vascular endothelial growth factor

Table 7:- opthalmic drugs those can be delivered via Liposome.

Drug	Types of liposome	Effects
Diclofenac	Coated with low molucular weight chitosan	High cornal permeation, better sustained release
Ciprofloxacin	Liposomal Hydrogel	Fivefold higher transcorneal permeation
Demeclocycline	Not available	Effect of drug lasts for longer peroid of time
Plasmid DNA	Cationic Liposome	Increased transfection efficacy of pDNA

POLYMERIC NANOPARTICLES:-

Synthetic and semi synthetic polymers are a very potential media for Nano-technology based drug delivery.They have advantages like increased efficacy, lower toxicity, controlled release rates, sustained bioactivity, manufacturing reproducibility, higher stability, lesser administration frequency and capability of co delivering drugs resulting in synergistic effects.[10] Some polymers used for manufacturing nanoparticles are poly (lactic acid) [PLA], poly (lactic-co-glycolic acid) [PLGA], poly (ethylene glycol- co(lactic-glycolic acid)), poly (methyl) methacrylate, poly caprolactone) and poly (alkyl) cyanoacrylates. PNPs are produced by pairing with PEG to provide prolonged systemic circulation time. [11]

Table 8:- Drugs those can be delivered via polymeric Nanoparticles

Therapeutics	Type of polymer / Fictionalization on	Indication /Activity	Effect
Paclitaxel	Aptamer-PEG-PLGA	Golimas	Enhanced delivery
Cisplatin	Aptamer-PEG-PLGA	Prostate cancer	Higher efficiency
Vincristine+Verapamil	PLGA	Hepatocellular carcinoma	Reduced multidrug resistance
Doxarubasin+Cyclosporine A	PLGA	Various cancers	Synergistic effect
Zidovudine	Poly(isohexyl cyante)	Targeting lymphoid tissue	Drug level is four times higher
Zidovudine	Polyhexylcyanoacrylate	Targeting lymphoid tissue	Higher Zidovudine levels in the body
Stavudine	Polybeutilcyanoacrylate(PBCA)	HIV/AIDS	8-20 times higher permeation
Lamivudine	Methylmethacrylatesulfopropylmethacrylate	HIV/AIDS	100% increased BBB permeation
Nerve growth factor (NGF)	Polysorbate 80 coated PBCA	Parkinsonism	Improved transport across the BBB
Amphotericin B	PLA-b-PEG	Neurodegenerative diseases	Improved transport across the BBB.

PACA=polyalkylcyanoacrylate, **PLGA**= poly ((lactide-co-glycolide), **PLA-b-PEG** =Polysorbate 80 coated poly (lactic acid)-b-poly (ethylene glycol)

FDA APPROLVED, MARKETED NANOPHARMACEUTICALS:-

There are a number of FDAapproved, marketed nanopharma ceuticals [12] for the intravenous administration route (Tabl e 2) as well as the nonintravenous route (Table 9 and Table 4).However, numerous nanopharmaceuticals are still at the de velopmentor clinical trial phase due to the extremely comple x nature of human medicinal applications. This chapterwill di scuss approved nanopharmaceuticals for nanomedicine deliv ery (from a design and development perspective) by various administration routes including parenteral, oral, transdermal and pulmonary. In this chapter, the following terms are use d interchangeably: nanodrugs, nanomedicines and nanophar maceuticals.

Table 9:- select list of FDA-approved and marketed Nanopharmaceuticals products foe Intravenous (I.V) route of administration.

Drug	Nanotechnology	Brand name	Company	Therapeutic Area
Doxorubicin	PEGlyated lipoomes	Doxil Caelyx	othroBiotech Scherimg-plough	Metastatic ovarian cancer and AIDS related Kaposi`s sarcoma
Doxorubicin	Liposomes	Myocet	Zeneous pharma	Metastatic cancer
Paclitaxel	Albumin-bound-nanoparticals	Abraxane	Abraxis Bioscience	Various cancers
Paclitaxel	Polymeric micelles	Genesol-PM	Samyang	Various cancers
Amphotericin B	Liposomes	Ambisone	NeXstsr pharmaceuticals	Fungal infection
Amphotericin B	Phospholipid complex	Abelcet	Enzon	Invasive fungal infection
Propofol	Lipid emulsion	Diprivan	AstraZeneca	Anesthesia
Cytarabine	Liposomes	Depocyt	Skyepharma Enzon	Lymphomatous meningitis
Daunorubicin Citrate	Liposomes	Daunoxome	Gilead science	Advanced HIV related Kaposi`s sarcoma
Adenosine deaminase	PEGylation	Adagen	Enzon	Enzyme replacement therapy in immunodeficiency diseases.
Iron oxide	Super paramagnetic iron oxide nanoparticals coated with carboxydextran	Resovist	Bayer-schering pharma AG	Organ-specific MRI contrast agent
Iron oxide	Iron oxide nanoparticals	Feridix I.V	AMAG pharmaceuticals	MRI constrast agent

Table 10:- select list of FDA approved and marketed Nanopharmaceuticals products for oral and pulmonary route of administration

Route	Drug	Nanotechnology	Brand Name	Company	Therapeutic Area
Oral	Sirolimus	Nanocrystal	Rapamune	Wyeth, Elan	Transplants
	Fenofibrate	Nanocrystal	TriCor	Abbott	Primary Hypercholestremia
	Fenofibrate	Nanocrystal	Triglide	Skyepharma	Lipid Disorders
	Aprepitant	Nanocrystal	Emend	Merck, Elan	Nausea in Chemotherapy
	Megestrol Acetate	Nanocrystal	Megace ES	Per pharma, Elan	Antianorexic
	Morphine sulphate	Nanocrystal	Avinza	King pharma, Elan	Psycho-stimulant
	Dexmethylphenidate HCL	Nanocrystal	Folacin XR	Novartis, Elan	Attention deficit disorder
	Methylphenidate HCL	Nanocrystal	Ritalin LA	Novartis, Elan	Attention deficit disorder
	Tizanide HCL	Nanocrystal	Zanaflex Capsule	Acorda Inc	Muscle relaxant
	Cyclosporine A	SMEDDS	Neoral	Novartis	Transplant
	Saquinavir	SMEDDS	Forovase	Roche	Antiviral
	Ritonavir	SMEDDS	Norvir	Abbott Laboratories	Antiretroviral
Pulmonary	Artificial lung surfactant Replacement	Synthetic recombinant polypeptide liposomal lung surfactant	Surfaxin	Drug Delivery Labs	Respiratory distress syndrome
	Artificial lung surfactant Replacement	Natural bovine lung extract	Survanta	Abbott Labs	Respiratory distress syndrome
	Artificial lung surfactant	Synthetic lung	Exsurf	GlaxoAbbottLabsSm	Respiratory distress

	Replacement	surfactant (protein free)		ithKline	syndrome
	Artificial lung surfactant Replacement	Natural porcine lung extract	Curosurf	Dey	Respiratory distress syndrome
	Artificial lung surfactant Replacement	Natural bovine lung extract	Alveofact	Boehringer Ingelheim	Respiratory distress syndrome

Table11:- select list of FDA approved and marketed nanopharmaceuticals products for subcutaneous, Intramuscular, Transdermal/Dermal, ophthalmic, Intravitral route of administration.

Route	Drug	Nanotechnology	Brand Name	Company	Therapeutic Area
Subcutaneous	Interferon alfa-2a	PEGylation	Pegasys	Nekter Hoffmann-La Roche	Hepatitis C infection
	hGH(Human Growth Hormones	PEGylation	Somavert	Netker Pfizer	Acromegaly
	Recombinant methionly human G-CSF	PEGylation	Neulasta	Amgen	Neutropenia
	Glatiramer acetate	Copolymer of L-glutamic acid, L-analine, L-tyrosine,L-lycine	Copaxone	Teva	Multiple sclerosis
	Amphotericin B	Lipid colloidal dispersion	Amphotec	Sequus	Invasive aspergillosis
	Interferon alfa-2b	PEGylation	PEGIntro	Enzon Schering plough	Hepatitis C infection
	Asparginase	PEGylation	Oncaspar	Enzon	Leukemia
Intramuscular	Hepatitis A vaccine	IRIV(immunopotentiating reconstituted influenza virosome)	Epaxel	Berna Biotech	Hepatitis A immunization
Transdermal /Dermal	Estradiol	Micellar nanoparticals	Estrasorb	BioSante	Menopause
	Estradiol	Estradialgel incorporating calciumphosphate nanoparticals	Elestrin	Novavax	Menopause
	Lidocain	Liposomes	LMX-4	Ferndale Laboraterie s	Topical anesthenia
Ophthalmic	Cyclosporine A	Lipid emulsion	Restasis	Allergan	Dry eye
	Difluprednate	Lipid emulsion	Durezol	Siron therapeutic s	Corticosteroid
Intravitreal	Anti-VEGF	PEGylation	Macugen	OSI pharmaceut icals	Masculardegeneratio n

APPROVED NANOPHARMACEUTICAL PRODUCTS: PARENTERAL DRUG DELIVERY:-

The parenteral administration route can directly access syste mic circulation with a rapid onset of drug action, achieving an advanced molecular targeting to specific organs and tissue sites [13]. However, there are certain classic disadvantages with this approach, namely, insufficient drug accumulation at target sites while large amounts are dissipated and/or undesirable drug localization at normal tissue sites [14]. Given these drawbacks, there is extensive re search ocussed on increasing efficiency and bioavailability of nanomedicine delivered parenterally. Cur-rent strategies under investigation include the following:

- Creating a protective barrier around the nanomedicine s: This can be accomplished by creating satiric hindrance, hydrodynamic volume effects and/or charge repulsions around the nanomedicine. For example, polyethylene glycol (PEG)an FDA-approved polymeric excipient, provides both steric hindrance an d hydrodynamic volume effects for the protection of na nomedicines with an extended period of time resulting in enhanced circulation activity.
- Stimuli-triggered systems: Examples include ultrasonic, magnetic,electric and light from external-regulated sti muli as well as thermo-sensitive, pH-sensitive and enzy me-substrate reactions following as self-regulated stimuli [15].
- For the parenteral drug delivery of nanomedicines, intr avenous injection can be used for certain drugs having l ong half-lives. Additionally, long-acting parentral inject ions are also administered through intramuscular and s ubcutaneous routes [16].

APPROVED NANOPHARMACEUTICAL PRODUCTS: ORAL DRUG DELIVERY:-

Oral delivery is the most common administration route. This is mainly because of its high level of patient compliance due to its noninvasive nature, simplicity and convenience. Nano medicines based on oral drug delivery have been extensively

investigated and have resulted various approved, marketed products. However, the oral delivery of liposome's has been s omewhat limited
due totheir unpredictable absorption profiles and the rapid d egradation of liposomes in the GI tract via interaction with bi le salts [17, 18].

Some advantages of polymer
based nanomedicine include the following:

- increasing bioavailability with enhanced water solubilit y of hydrophobic
  drugs due to a large specific surface area;
- ability to protect biologically unstable drugs from the h ostile environment of the gastrointestinal tract;
- extending drug residence time through strong mucoadhesive properties;
- controlled drug release;
- facilitating transport of the drug through the epithelial membrane via endocytosis;
- bypassing or inhibiting efflux pumps such as glycoprotein; and
- Targeting specific carriers for receptor mediated transport.

APPROVED NANOPHARMACEUTICAL PRODUCTS: PULMONARY DRUG DELIVERY:-

The lung is an attractive target for drug delivery because it of fers a noninvasive means to provide not only local lung effect s but also possible high systemic bioavailability, avoidance of first-pass metabolism, faster onset of therapeutic action, and the availability of a large surface area [19, 20]. Nanomedicin es for pulmonary drug delivery have many advantages,such a s the ability to:

- achieve a relatively uniform drug distribution;
- enhance the solubility of the drug beyond its own aque ous solubility;
- achieve a sustained-release effect of the inhaled nondru g;
- deliver macromolecules;
- reduced toxic side effects;
- improve patient compliance; and
- Increase drug internalization by cells.

APPLICATIONS OF NANOBIOTECHNOLOGY IN MEDICAL AND CLINICAL FIELDS

a) Diagnostic applications

Current diagnostic methods for most of diseases.Depend on the manifestation of visible symptoms before medical professionals can recognize that the patient suffers from a specific illness. But by the time those symptoms have appeared, treatment may have a decreased chance of being effective. Therefore the earlier a disease can be detected, the better the chance for a cure is. Optimally, diseases should be diagnosed and cured before symptoms even manifest themselves. Nucleic acid diagnostics will play a crucial role in that process, as they allow the detection of pathogens and diseases/diseased cells at such an early symptomless stage of disease progression that effective treatment is more feasible. Current technology, such as- polymerase chain reaction (PCR) leads toward such tests and devices, but nanotechnology is expanding the options currently available, which will result in greater sensitivity as well as far better efficiency and economy.

1. Detection:-

Many currently used/conventional clinical tests reveal the presence of a molecule or a disease causing organism by detecting the binding of a specific antibody to the disease-related target. Traditionally, such tests are performed by conjugating the antibodies with inorganic/organic dyes and visualizing the signals within the samples through fluorescence microscopy or electronic microscopy. However, dyes often limit the specificity and practicality of the detection methods. Nanobiotechnology offers a\ solution by using semiconductor nanocrystals (also referred to as "quantum dots"). These minuscule probes can withstand significantly more cycles of excitations and light emissions than typical organic molecules, which more readily decompose [21].

2. Individual target probes

Despite the advantages of magnetic detections, optical and colorimetric detections will continue to be chosen by the medical community. Nanospheres(Northbrook, Illinois) is one of the companies that developed techniques that allow/allowing doctors to optically detect the genetic compositions of biological specimens. Nano gold particles studded with short segments of DNA form the basis of the easy-to-read test for the presence of any given genetic sequence. If the sequence of interest in the samples, it binds to complementary DNA tentacles on multiple Nanospheres and forms a dense web of visible\ gold balls. This technology allows/facilitates the detection of pathogenic organisms and has shown promising results in the detection of anthrax, giving much higher sensitivity than tests that are currently being used [22].

3. Protein chips

Proteins play the central role in establishing the biological phenotype of organisms in healthy and diseased states and are more indicative of functionality. Hence, proteomics is important in disease diagnostics and pharmaceutics, where drugs can be developed to alter signaling pathways. Protein chips can be treated with chemical groups, or small modular protein components, that can specifically bind to proteins containing a certain structural or biochemical motif [23]. Two companies currently operating in this application space are Agilent, Inc. and Nan oink, Inc. Agilent uses a non-contact ink-jet technology to produce microarrays by printing oligos and whole cDNAs onto glass slides at the Nanoscale. Nan oink uses dip-pen nanolithography (DPN) technology to assemble structure on a Nanoscale of measurement.

4. Sparse cell detection

Sparse cells are both rare and physiologically distinct from their surrounding cells in normal physiological conditions (e.g. cancer cells, lymphocytes, fetal cells and HIV-infected Tcells). They are significant in the detection and diagnosis of various genetic defects. However, it is a challenge to identify and subsequently isolate these sparse cells. Nanobiotechnology presents new opportunities for advancement in this area. Scientists developed nanosystems capable of effectively sorting sparse cells from blood and other tissues. This technology takes advantage of/exploits the unique properties of sparse cells manifested in differences in deformation, surface charges and affinity for specific receptors and/or ligands. For example, by inserting electrodes into microchannels, cells can be precisely sorted based on surface charge. They can also be sorted by using

biocompatible surfaces with precise nonporous. The nano-biotechnology center at Cornell University (NBTC) is currently using these technologies to develop powerful diagnostic tools for the isolation and diagnosis of various diseases [24].

5. Nanotechnology as a tool in imaging

Intracellular imaging can be made possible through labelling of target molecules with quantum dots (QDs) or synthetic chomophores, such as fluorescent proteins that will facilitate direct investigation of intracellular signaling complex by optical techniques, i. e. confocal Fluorescence microscopy or correlation imaging [25]

(b)Therapeutic applications:

Nanotechnology can provide new formulations of drugs with less side effects and routes for Drug delivery.

1. Drug Delivery:

Nanoparticles as therapeutics can be delivered to targeted sites, including locations that cannot be easily reached by standard drugs. For instance, if a therapeutic can be chemically attached to a nanoparticle, it can then be guided to the site of the disease or infection by radio or magnetic signals. These nanodrugs can also be designed to "release" only at times when specific molecules are present or when external triggers (such as infrared heat) are provided. At the same time, harmful side effects from potent medications can be avoided by reducing the effective dosage needed to treat the patient. By encapsulating drugs in nanosized materials (such as organic dendrimers, hollow polymer capsules, and nanoshells), release can be controlled much more precisely than ever before. Drugs are designed to carry a therapeutic payload (radiation, chemotherapy or gene therapy) as well as for imaging applications [26].

2. Gene delivery

Current gene therapy systems suffer from the inherent difficulties of effective pharmaceutical processing and development, and the chance of reversion of an engineered mutant to the wild type. Potential immunogenicity of viral vectors involved in gene delivery is also problematic [2and nanoparticle-based nonviral vectors (usully50-500 nm in size) in transportation of plasmid DNA described. Therefore, successful introduction of less immunogenic nanosize gene carriers as a substitution of the disputed viral vectors seems beneficial in repairing or replacing impaired genes in human [27].

3. Liposomes

A liposome being composed of a lipid bilayer can be used in gene therapy due to its ability to pass through lipid bilayers and cell membranes of the target. Recent use of several groups of liposomes in a local delivery has been found to be convincingly effective [28, 29]. Liposomes can also help achieve targeted therapy. Zhang et al demonstrated widespread reporter expression in the brains of rhesus monkeys by linkingnanoparticle (such as polyethylene glycol) treated liposomes to a monoclonal antibody for human insulin reporter. These successful trials reflect the future of targeted therapy and the importance of nanometer-sized constructs for the advancement of molecular medicine.

4. Surfaces

In nature, there are a multitude of examples of the complicated interactions between molecules and surfaces. For example, the interactions between blood cells and the brain or between fungal pathogens and infection sites rely on complex interplays between cells and surface characteristics. Nanofabrication unravels the complexity of these interactions by modifying surface characteristics with nanoscale resolutions, which can lead to hybrid biological systems. This hybrid material can be used to screen drugs, as sensors, or as medical devices and implants. Nanosystems, owned by the Irish drug company Elan, developed a polymer coating capable of changing the surface of drugs that have poor water solubility [30].

5. Bimolecular Engineering

The expense and time involved in traditional biomolecule designing limit the availability of bioactive molecules. Nanoscale assembly and synthesis techniques provide an alternative to traditional methods. Improvements can b achieved due to the ability to carry out chemical and biological reactions on solid substrates, rather than through the traditional solution based processes. The use of solid substrate usually means less waste and the ability tomanipulate the biomolecule far more precisely. EngeneOS (Waltham, Massachusetts) pioneered the field of biomolecular engineering. To address this issue, nanotechnological tools in human gene therapy have been tested company developed the engineered genomic operating systems that create programmable biomolecular machines employing natural and artificial building blocks. These biomolecules machines have broad range of commercial applications-as biosensors, in chemical synthesis and processing, as bioelectronic devices and materials, in nanotechnology, in functional genomics and in drug discovery.

6. Biopharmaceuticals

Nanobiotechnology can develop drugs for diseases that conventional pharmaceuticals cannot target. The pharmaceutical industry traditionally focuses on developing drugs to treat a defined universe of about five hundred confirmed disease targets. But approximately 70 to 80 percent of the new candidates for drug development fail, and these failures are often discovered late in the development process, with the loss of millions of dollars in R&D investments. Nanoscale techniques for drug development will be a boon to small companies, which cannot employ hundreds of organic chemists to synthesize and test thousands of compounds. Nanobiotechnology brings the ability to physically manipulate targets, molecules and atoms on solid substrates by tethering them to biomembranes and controlling where and when chemical reactions take place, in a fast process that requires few materials (reagents and solutions). This advance will reduce drug discovery costs, will provide a large diversity of compounds, and will facilitate the development of highly specific drugs. Potential Pharmaceuticals (Louisville, Kentucky) is an early-stage company that is attempting to streamline the drug development process with the use of nanotechnologies (Harvard Business School 2001).

7. Nanotechnology in cardiac therapy

Nanotechnology is currently offering promising tools for applications in modern cardiovascular science to explore existing frontiers at the cellular level and treat challenging cardiovascular diseases more effectively. These tools can be applied in diagnosis, imaging and tissue engineering [31]. Miniaturized Nanoscale sensors like quantum dots (QDs), nanocrystals, and nanobarcodes are capable of sensing and monitoring complex immune signals in response to cardiac or inflammatory events [32]. Nanotechnology can also help detect and describe clinically-significant specific mechanisms implicated in cardiac disorders. In addition, it is useful in

designing atomic-scale machines that can be incorporated into biological systems at the molecular level.

8. Nanotechnology in dental care

Nanotechnology will have future medical applications in the field of dentistry. The role of nanodentistry by means of the use of nanomaterials, biotechnology, and nanorobotics will ensure better oral health .Millions of people currently receiving poor dental care will benefit from such remarkable breakthrough in the science of dental health [33,34]. Moreover, nanodental techniques in major tooth repair may also evolve. Reconstructive dental nanorobots could be used in selective and precise occlusion of specific tubules within minutes, and this will facilitate quick and permanent recovery.

9. Nanotechnology in orthopedic applications

Nanomaterials sized between 1 and 100 nm have role to play as new and functional constituents of bones being also made up of nanosized organic and mineral phases [35,36]. Nanomaterials, nanopolymers, carbon nanofibers, nanotubes, and ceramic nanocomposites may help with more efficient deposition of calcium-containing minerals on implants. Based on these evidences and observations, nanostructure materials represent a unique realm of research and development that may improve the attachment of an implant to the surrounding bone matters by enhancing bone cell interactions, and this will indeed aid in improving orthopedic implant efficacy while drastically minimizing patient compliance problems.

OPPORTUNITIES AND CHALLENGES OF NANOTECHNOLOGY IN THE GREEN ECONOMY

The potential nanotechnology impact on green innovations:-

Green nanotechnology is expected to play a fundamental role in bringing a key functionality across the whole value chain of a product, both through the beneficial properties of NMs included as a small percentage in a final device, as well as through nano-enabled processes and applications without final products containing any NMs [36,37]. However, most of the potential green nano-solutions are still in the lab/start-up phase and very few products have reached the market to date. Further studies are necessary to assess the applicability, efficiency and sustainability of nanotechnologies under more realistic conditions, as well as to validate NM enabled systems in comparison to existing technologies. The following paragraphs will describe the potential fields of application for green nanotechnology innovations.

1. Nanomaterials for energy conversion

One of the most interesting and most flexible renewable energy technologies is the direct conversion of sunlight into electric power: the photovoltaic effect. Carbon NMs, including C_{60} fullerenes, carbon nanotubes (CNTs) and graphene have been studied as extremely efficient electron acceptors in polymer and quantum dot solar cells. Relatively new, dye sensitized solar cells are of great promise. In these devices, a nanocrystalline mesoporous titanium dioxide (TiO_2) film, with a monolayer of the charge transfer dye attached to its surface, is pasted on a transparent conductive substrate [38,39].

Another important future energy option is the hydrogen gas as an endless source of clean fuel for many applications [40]. Semiconductor NMs, e.g. TiO_2 and cadmium sulfide nanostructures, have been studied as efficient catalysts for water conversion into oxygen and hydrogen [40–43]. Moreover, nano-structured carbons, metal-organic frameworks and polymers as well as metal hydrides and related complex hydrides are examples of investigated NMs for hydrogen storage and transportation for high hydrogen capacity and minimal deterioration during hydrogenation.

2. Nanomaterials for energy storage

Nanotechnology may have a profound influence on electrical storage technologies, i.e. batteries and electrochemical super capacitors [44]. Redox-based supercapacitors with nano-structured electrode materials have shown the potential to combine the high energy density of conventional batteries with the high power capabilities of electrostatic capacitors at the lab scale. Mixed metal oxides, e.g. ruthenium oxide (RuO_2), manganese oxide (MnO_2), magnetite (Fe_3O_4, CNTs [48], grapheme and carbon-metal oxide composites have been investigated as electrode NMs aimed at a high specific capacity and rate capability Concerning rechargeable lithium batteries, the energy densities and the performances of these devices largely depend on the physical and chemical properties of the electrode material [45].

3. Nanomaterials for water clean-up technologies

Nanotechnology-enabled water and wastewater treatment promises not only to overcome major challenges faced by existing treatment technologies, but also to provide new treatment capabilities that could allow economic utilization of unconventional water sources to expand the water supply [46]. Interesting applications may include the incorporation of functional NMs, such as metal-oxide NPs (aluminum oxide, TiO_2 and zeolite), anti-microbial NMs (silver-NPs (Ag-NPs) and CNTs) and photo catalytic NMs (bimetallic-NPs, TiO_2) into membranes in order to improve their permeability, fouling resistance, biofilm control, mechanical and thermal stability, as well as to provide pollutant degradation and self-cleaning ability [47]

4. Nanomaterials for construction industry

Manufactured NMs and nanocomposites offer great opportunities in the construction and related infrastructure industries. Strength, durability, and lightness of various materials [48, 49], as well as heat-insulating, self-cleaning, fire-retardant, anti-fogging and sensing structural health properties may be improved or provided *de novo* by NMs.

Table 12:-Example relationships among guiding principles for a green economy and the opportunities and challenges for nano-applications

Guiding principles for a green economy	
P1	Is a means for achieving sustainable development.
P2	Creates decent work and green jobs
P3	Improves governance and the rule of law-by being inclusive, democratic, participatory, accountable, transparent and stable.
P4	Is equitable, fair and just between and within countries and between generations.
P5	Reduce poverty and increases well-being livelihoods, social protection and access to essential services.
P6	Protects biodiversity and ecosystem
P7	Is resource and energy efficient
P8	Respects planetary boundaries or ecological limits or scarcity.
P9	Uses integrated decision making
P10	Internalizes externalizes
P11	Measure beyond gross domestics product indicators and metrics.

Example opportunities for nano-applications in a green economy (and related principles)	
Energy conversion and storage	-Small energy nanotechnology can improve power delivery systems to be more efficient, reliable and safe (P1, P2, P5) -Nano-devices may trade on renewable energy produced through naturally replenished resources, i.e. sunlight and wind. this may reduce fossils as energy resources and the impact for the greenhouse gas emissions balance (P3 ,P4, P5,P6 ,P7 ,P9) -Energy different nanotechnology requires less energy to perform the same function. Created energy (P7, P8 ,P10)
Water cleanup technologies	**-**Design nano-enabled infrastructure necessary to manage water and keep it clean is linked to prospects for economic development and livelihood conditions (P1,P2) -Access to clean water and adequate sanitation is a basic human right and is critical to the alleviation of poverty (P3,P4,P5)
Construction industry	**-**nanotechnologyaims to increase the efficiency buildings use resources-energy, water, materials. -while reducing building impacts on environment and human health through better siting, construction, and removal (P1,P2,P6,P7,P8,P10)
other applications	-Nano-enabled applications may provide slow release and dosage of fertilizers and an efficient water resources for plants. This may contribute to a great agriculture productivity, especially in a countries with prolonged dry spells(P1, P2, P4, P5)

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