Nanotechnology in medicines- Recent Developments and Future Prospects

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Abstract:

Much research today focuses on nanotechnology. This branch of science and technology usually deals with the study of matter at the atomic and molecular levels. The use of nanotechnology in modern medicine is overwhelming. Site-specific and targeted delivery of precise nanomedicine has made it possible to treat long-standing chronic human diseases. The synthesized nanoparticles can be used as diagnostic tools for biomolecular imaging, capture, and detection. Using nanoparticles as nano drugs can help deliver drugs to specific target tissues, called targeted drug delivery. Nanomedicine is also useful as a tissue regeneration tool. This chapter summarizes recent updates on nanotechnology in the medical field and describes how nanotechnology and nanomaterials are effective as drug delivery systems to treat various diseases. There is also debate about the future scope of nanotechnology as nanorobots play a significant role in the provision of healthcare. It also discusses the drawbacks of relying on man-made systems for internal care.

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Introduction

The word “nano” comes from a Greek term that means “dwarf”. When we consider one nanometer it means that 1-meter length divided by 1 billion, that is 10^{-9} m. Nanotechnology deals with studying and controlling matter on a molecular or atomic level. The material is changed to a size between 1-100 nanometers so that it gets smaller, stronger, and more durable.

Nanotechnology deals with the understanding, management, and control of matter at the individual atomic & molecular levels. The use of nanotechnology in medicine is known as nanomedicine and is characterized as the use of nanoparticles in disease detection, monitoring, prevention, control, and therapy. The first guidance on nanotechnology was published by C. Eric Drexler in his book. The US National Human Genome Research Institute has adopted a new environmentally friendly and socially acceptable approach to nanotechnology. This has been achieved by considering the social, legal, and ethical implications of nano products before they are placed on the market.

History

- The European Science Foundation at the beginning of 2003 started its first foresight study on “Forward look on nanomedicine”. The significance of this research was that it was focused mainly on the medical uses of nanotechnology and nano-sciences. Experts from around 100 European countries participated in the Forward Look and tried to assess the present status of the field.

- In 2005, a policy briefing document was published that summarized Forward Look’s recommendations.

- The UK Government asked the “Royal Academy of Engineering” and the UK National 23 February Academy of Science to conduct an independent analysis in June 2003 to evaluate whether nanotechnology can give rise to new social, ethical, or health and safety concerns that aren't already addressed by existing legislation.

- A final report with twenty-one suggestions for a sure, secure, and responsible growth of

nanotechnology was published in July 2004. Also, the European Communities Commission published its guidelines for the European Nanotechnology Strategy.

- Release of the Vision Paper and foundation for a "Strategic Research Agenda" for Nanomedicine in September 2005.

- The European Foundation for Clinical Nanomedicine was formed in Basel (Switzerland) in 2007.

- NIH ("National Institutes of Health") the Atlantic Ocean, published its first roadmap on nanomedicine in 2004.

- a national network of eight Nanomedicine Development Centers, NIH Nanomedicine Roadmap Initiative was developed in 2005-06.

- In 2004, the NCI ("National Cancer Institute"), a component of NIH, introduced the Cancer Nanotechnology Initiative, a strategic project designed to change clinical oncology and fundamental research via the directed use of nanotechnology.

Branches of Nanotechnology

There are three primary fields of nanotechnology–

I) Nanomaterials

Includes nano-scale products that have gained wide acceptance as biocompatible materials and analytic approaches. They are also utilized in dental and surgical practice, in the analysis of nerve cells & biomolecular studies.

II) Molecular nanotechnology

These include mechanical systems that are designed and manufactured at the molecular level and can play a significant role in medicine.

III) Biotechnology

The basic concept of using biological systems in technological and industrial processes includes genetic engineering and the creation of artificial images of organic life.

NANOTECHNOLOGY IN MEDICINES – NANOMEDICINES

Nanomedicine is actually nanotechnology in medicine. Even though the word "nanomedicine" is frequently used, it is more correct to speak of "nanotechnology-assisted medicine" in various sub-fields of medicine like monitoring, therapy, or diagnostics.

Definition Nanomedicine - Controversy

The description of nanomedicine on both sides of the Atlantic varies slightly. The U.S. National Nanotech Plan uses the term nanoscale, while the “European Science Foundation”, as well as “European Technology Platform” on Nanomedicine, disagree.

Different definitions

• United States National Nanotech Initiative

Nanotechnology is the study and control of matter at scales between 1 & 100 nanometers, where distinctive phenomena enable new applications. Modeling, measuring, imaging, and manipulating materials at this site are all part of nanotechnology. Nanomedicine is the term for the use of nanotechnology in medicine.

• The European Science Foundation

Nanomedicine is the field of science & technology using molecular tools and knowledge of the human body to identify, prevent, and treat illness and traumatic damage, reduce pain, maintain, and enhance human health.

• **The European Technology Platform on Nanomedicine**

Nanomedicine is the field of science & technology using molecular tools as well as knowledge of the human body to identify, prevent, and treat illness and traumatic damage, reduce pain, maintain, and enhance human health.

Principles and Properties of Nanomedicines/nanomaterials

The properties of nanomedicines should be understood in order to study their behavior in the human body. The following properties of nanomedicines can be defined based on their dustiness, dissolution rate/kinetics, water solubility, zeta potential, photocatalytic activity, charge, surface chemistry, chemical composition, porosity, particular surface area, crystal structure, aggregation and agglomeration state, size and shape distribution, and particle size.

Nanomaterials may be categorized as amorphous, crystalline, inorganic, or organic particles depending on their chemical composition. They may be single particles, aggregates, agglomerated powders, or distributed in a matrix, resulting in suspensions, emulsions, nanosheets, or films. A significant property in the expansion of drug delivery systems is their biocompatibility. A biocompatible surface is one that could not cause an undesirable reaction from the organism. Biocompatibility may be defined as “the ability of a material to exhibit an appropriate response in a particular application”.

Nanoparticles in medicines

Definition

Nanomaterials that are "zero-dimensional" are another name for nanoparticles. This description is based on the fact that all of its sizes are inside the nanoscale, in contrast to 1D nanomaterials, which have only 1 dimension greater than the nanoscale, and 2D nanomaterials, which have 2 dimensions greater than the nanoscale.

Nanoparticles are organic or inorganic structures that range in size from 1 to 100 nm, similar to DNA plasmids and antibodies. These materials have overall dimensions at the nanoscale, i.e., less than 100nm. Nanoparticles play an important role in contemporary medicine, with uses that range from contrast agents in “medical imaging” to gene delivery carriers.

According to FDA guidelines, there are 3 basic aspects to determine the existence of a nanomaterial. These include surface area, particle size distribution (PSD), and size. The most significant aspect to consider is size, as it applies to a variety of materials. The usual size varies between 1 and 100 nm. Particle size distribution is a parameter often used to identify the type of nanomaterial. It provides information about the range of size variations. Since the nanomaterial is usually polydisperse, it is important to determine the PSD, which means that it consists of particles of different sizes. Due to additional legislation, it is important to determine the volume-related surface area since it is a relational characteristic. If the volumetric surface area is greater than $60 m^2/cm^3$, the material may fall under the definition.

Types of nanoparticles

Nanoparticles can be divided into i) organic and ii) inorganic iii) Nanocrystals iv) Protein and polysaccharides

Organic Nanoparticles	**Inorganic Nanoparticles**	**Nanocrystals**	**Protein and polysaccharides**
Chitosan, Alginate, Cellulose, Dendrimers, Micelles, Liposomes.	Silica, Iron oxide, gold, and silver nanoparticles	Pure solid drug particles within a range of 1000 nm.	Natural biopolymers extracted from biological sources like marine sources, microorganisms, animals, and plants
	Metal nanoparticles like gold and silver have SPR ("Surface Plasmon Resonance") properties that dendrimers, micelles, and liposomes lack.	These are 100 percent drugs with no carrier molecule connected to them and are normally stabilized by utilizing surfactants or polymeric steric stabilizers.	Decomposable and metabolizable.

Chitosan: It has mucoadhesive properties and is, therefore, suitable to act on the tight junctions of epithelial. Nanomaterials based on chitosan are commonly utilized for continuous and sustained

drug release systems for different epithelial forms, such as oral, nasal, intestinal, ocular, and pulmonary epithelium.

Alginate: It is a mucoadhesive biopolymeric material that can be used in medicine as a drug carrier. Due to the presence of carboxyl end groups, it has been categorized as an anionic mucoadhesive polymer, which has stronger mucoadhesive strength than cationic & neutral polymers.

Cellulose: Various forms of cellulose can be used as BC (Bacterial Cellulose), CNF (Cellulose Nanofibrils), and CNC (Cellulose Nanocrystals). They have all been studied as drug delivery vehicles, and CNF and CNC were found to bind and release certain water-soluble medicines by ionic interactions, while BC releases drugs from flexible membranes. The reason for using nanocellulose is that the large material's surface area to volume ratio increases the capability to bind medicines to the surface.

Dendrimers: These are functional groups in the form of anionic, cationic, or neutral ions that can be used to change the overall molecular structure, resulting in improved properties. Dendrimers are macromolecules with branching repeating units and exterior functional groups that spread out from a central core. The interior of dendrimers can be used for the uptake of therapeutic agents or bound to the surface groups, making them highly biodegradable and bioavailable. When conjugated with peptides or saccharides, e.g., polyamidoamine-dendrimer-DNA complexes (so-called dendriplexes), they showed a significant improvement in their properties. Dendriplexes were studied as vectors for gene delivery and showed improvement in successive gene expression, targeted drug efficacy, and drug delivery.

Liposomes: Liposomes are lipid bilayers composed of "spherical vesicles" with particle sizes varying from 30nm to several micrometers. Hydrophilic therapeutic agents may be contained in the aqueous phase, while the liposomal membrane layer can accommodate hydrophobic agents. The surface properties may be altered with antibodies, proteins, and polymers so that macromolecular drugs such as crystalline metals and nucleic acids can be incorporated into

liposomes. Polyethylene glycol (PEG) ylated liposomal doxorubicin (Doxil) is the 1st FDA-approved nanomedicine for breast cancer treatment.

Micelles: The diameter of micelles is between 10 and 100 nm. They are surface-active substances consisting of lipids and amphiphilic molecules. Under aqueous conditions, micelle molecules spontaneously aggregate & self-assemble into spherical vesicles. Due to the hydrophilic nature of the outer hydrophobic and monolayer core, these molecules may be utilized to integrate hydrophobic therapeutic agents. This increases the solubility of hydrophobic active ingredients and improves bioavailability. Micelles can be used as therapeutic agents, drug delivery agents, imaging agents, and contrast agents.

Carbon nanotubes: Carbon nanotubes consist of cylindrical molecules with coiled layers of a single layer of "carbon" atoms (graphene). They are classified as multi-walled, single-walled, or consisting of multiple concentrically connected nanotubes. Carbon nanotubes have a high capacity to contain drugs owing to their large external surface area. Their unique optical, mechanical, and electronic properties also make them suitable for imaging contrast agents as well as biological sensors.

Metallic nanoparticles: Research on metallic nanoparticles has increased in various medical and dental uses, like biosensors, bioimaging, targeted/sustainable drug delivery, photoablation therapy, and hyperthermia. The ability to modify and functionalize these nanoparticles with certain functional groups allows them to bind to drugs, antibodies, as well as other ligands. The most intensively examined metallic nanoparticles are copper, iron, silver, and gold.

Quantum dots: QDs are "fluorescent semiconductor" nanocrystals with a size of 1-100nm) and have exhibited promise for various biomedical uses, like targeted drug delivery & cellular imaging. QDs consist of a shell-core structure, with the core structure consisting of II, VI, or III elements from group V of the periodic table.

Applications of nanoparticles in medicines

Nanoparticles play a major role in nanomedicine because of their application in 3 different fields:

I) Diagnosis (nano diagnosis); II) Controlled drug delivery (nano therapy); and III) Regenerative medicine

A new field known as Theranostic is emerging which combines diagnostics and therapeutics and is a promising method that holds the diagnosis/imaging agent and the medicine in the same system.

I) Diagnosis (nano diagnosis)

Diagnosis is among the most important steps in the medical field. All diagnoses should be rapid, specific, and accurate to avoid "false negative" cases. Molecular imaging along with image-guided therapy are now fundamental tools for disease monitoring and for the development of almost all applications of in vivo nanomedicine. Biological markers serve as fundamental tools for disease or symptom detection.

The use of nanotechnology has helped us develop highly accurate molecular imaging techniques. In addition to diagnosis, imaging also plays an important role in identifying potential toxic reactions, controlling the release of drugs, assessing the drug's distribution within the body, and closely monitoring the course of treatment. The most commonly used procedures in medicine include ultrasound, nuclear medicine, MRI (“Magnetic Resonance Imaging”), computed tomography, and X-ray. The use of targeting and contrast agents on the basis of nanotechnologies has improved specificity and resolution by improving the diseased location at the tissue level. Presently employed medical contrast agents are rapidly degraded and nonspecifically distributed, leading to undesirable toxic side effects. Because nanomaterials have lower toxicity, better permeability, and longer tissue residence time, the use of nanotechnologies has contributed to the development of more potent contrast agents for almost all imaging modalities.

II) Controlled drug delivery (nano therapy)

An ideal drug delivery system consists of two parts: a) controlled drug release and b) the ability to selectively kill harmful or carcinogenic cells, resulting in a significant reduction in side effects and ensuring greater drug efficacy. In addition, controlled release reduces the side effects of the drug. Because of their intravenous, small size, as well as other routes of administration are easier, resulting in less irritation and better penetration into tissues. Nanosized radioactive antibodies that are complementary to the antigens on cancer cells are attached to nanoparticle drug delivery devices to improve their specificity. This leads to desirable outcomes that enhance (a) uptake of poorly soluble drugs (b) specific drug delivery to the target site, and (c) drug bioavailability.

III) Regenerative medicine.

It is the process of developing life, functioning tissue to replace or restore tissue or organ function lost wing to aging, injury, illness, or congenital abnormalities. Tissue regeneration may be achieved by combining living cells and bioactive compounds at their target sites to treat various diseases. Various drug delivery systems have been tested, but several challenges remain, including the development of advanced technologies for successful drug delivery to target sites. Nano-based drug delivery systems are being investigated in depth to develop an innovative drug delivery system.

They were originally developed as carriers for anticancer drugs and vaccines. Nanoscale size can significantly improve drug delivery by altering drug bio-distribution and toxico dynamics. Many types of toxic drugs can be relatively easily delivered in vivo with nanomaterials.

NANO-BASED DRUG DELIVERY SYSTEM

Recently, there have been dramatic developments in drug delivery systems to provide therapeutic agents or drugs that can be efficiently taken up by cells. One of the recent advances in pharmacotherapy is the development of nano-sized colloidal drug carriers.

They serve as potential carriers for different types of drugs like anticancer drugs, antihypertensive agents, hormones, and so on. Submicron colloidal particles were utilized as nanoparticles and drug carriers for disease diagnosis.

Nanoparticles have expanded the pharmacokinetics field for insoluble drugs. For instance, the trans-retinoic acid nanoparticle system coated with CaCO3 was created as a novel drug delivery method that leads to the formation of aggregates during spray drying. The aggregates thus formed and then disperse in water, stimulating pancreatic islet cells to release insulin.

Applications for Nano based drug delivery systems

I) Cancer - A nanoparticle-based drug delivery system was created by Sengupta and colleagues (2005) and consists of 2 layers: a core made of PLGA: "poly (lactic-co-glycolic acid)" coupled with doxorubicin as well as a liposome made of phospholipids coupled with combretastatin and PEG. In this system, the chemotherapeutic drug is doxorubicin, while the antiangiogenic drug is combretastatin. These multilayer nanoparticles had a size of 80 to120nm.

The goal was to get the particles to the specific tumor location and then slowly release the medication via degrading the PLGA core. The particles were quickly absorbed by the tumor cells after intravenous administration to mice having tumors produced by melanoma or carcinoma cells. Administration of the nanoparticles significantly inhibited the development of a tumor and increased the animal's lifespan.

II) Neurodegenerative diseases - Researchers have found that nanoparticles synthesized from PHDCA ("Poly Hexadecyl Cyanoacrylate") and related compounds improve the movement of drugs across the BBB ("Blood-Brain Barrier"). Kreuter et al. (2003) adsorbed dalargine (an analgesic) onto PBCA ("Polybutylcyanoacrylate") nanoparticles and showed that the nanoparticle-loaded drug crossed the BBB in rats. In addition, Siegemund et al., (2006) demonstrated that thioflavin-loaded PBCA nanoparticles might target fibrillar amyloid β in an Alzheimer's disease mouse model. Calvo et al., (2002, 2001) produced a nanoparticle system from a copolymer of PEG & PHDCA.

Since PHDCA is hydrophobic and PEG is hydrophilic, the copolymer molecules can arrange in an aqueous environment to form particles with a PEG surface layer and an insoluble PHDCA core. PEG is often used in drug delivery systems because macrophages in the blood do not see it as a foreign substance, extending the half-life of drug carriers inside the blood (Chess and Harris 2003).

III) HIV/AIDS – De Jaeghere et al., (2000) produced pH-sensitive nanoparticles from an ethyl acrylate and copolymer of methacrylic acid and studied the delivery of an "HIV-1 protease" inhibitor, CGP 70726. A major problem with the delivery of CGP 70726 is its poor solubility in water. To synthesize the nanoparticles, De Jaeghere and his team emulsified a copolymer solution with a combination of benzyl alcohol and CGP 70726. The nanoparticles were given orally to dogs, and examination of their blood samples revealed the successful release of the drug.

IV) Ocular diseases - The main reason for the use of nanoparticle-based drug delivery methods in ophthalmology is the capacity to prolong the release of drug molecules by entrapping the drug inside the layer of ocular mucus.

Most ophthalmic drugs are given as eye drops. These are highly concentrated solutions that must be applied frequently, but rapid loss occurs in front of the eye due to the flow of mucus in blinking. This problem may be effectively resolved by employing nanoparticles as a "drug delivery" system. Combinations of polymer and drug were mixed in ethanol and then emulsified (using surfactant and water) to form nanoparticles embedded in the drug with a size of 100 nm. These nanoparticles were then introduced into the conjunctival sac of rabbit eyes. The nanoparticles loaded with ibuprofen and flurbiprofen efficiently inhibited the responses of inflammation caused by surgical trauma. These results were similar to those of traditional eye drops. The importance of the present study was that the nanoparticle method was used with a lower drug content than the control of eye drops. In addition, higher medication concentrations might be produced using the nanoparticle technique.

IV) **Respiratory diseases –** The applications of nanoparticles in respiratory diseases are rather limited. John and colleagues (2003) investigated the use of a liposome-based nanoparticle system to inhibit inflammation in a mouse model caused by allergic asthma. The method used was to inhibit P-selectin receptors on activated endothelial cells in the bloodstream. This in turn attenuates the development of peribronchial inflammation. The nanoparticles were designed to mimic the physiological P-selectin superligand (PSGL-1). Pneumonia and airway hyperreactivity were induced in mice by lipopolysaccharide (LPS) and cockroach antigen. In both cases, the liposomal nanoparticles were found to bind preferentially to selectins on activated endothelial cells. Histological examination showed that peribronchial inflammation and airway hyperreactivity decreased significantly in mice treated with the nanoparticles compared with controls.

NANOFIBER

The world of nanomaterials encompasses a wide range of interesting materials with excellent physical and chemical properties and characteristics. These materials include zero-dimensional nanoparticles such as quantum dots, one-dimensional nanowires, nanorods, nanofibers, nanotubes, or two-dimensional nanosheets. Among all these nanomaterials, nanofibers stand out from the rest of the nanomaterials. One of the most salient features of nanofibers is their exceptionally high surface-to-volume ratio and high porosity, which makes them an ideal candidate for many advanced applications. Nanofibers are one-dimensional (1D) nanostructures, meaning that two of their dimensions are at the nanoscale, which gives them optimal properties for biomedical, technological, and environmental applications.

Nanofiber synthesis

There are several methods to produce nanofibers, including melt spinning, air spinning, template synthesis, drawing, electrospinning, self-assembly, centrifugal spinning, and phase separation. Among all these methods, electrospinning is a simple

and cost-efficient approach that can create a broad variety of polymers in the form of nanometer as well as micrometer-scale fibers. An electric field is employed in electrospinning to transform a polymer solution or melt it into a fiber form. Electrospun nanofibers have distinctive properties such as a) a large “surface-to-volume” ratio, b) excellent surface adhesion, and c) increased pore density. The morphology of an electrospun nanofiber is influenced by the material used and the processing parameters.

Electrospinning technology

Electrospinning is among the most well-known and often utilized processes among the currently available methods for making 1D nanofibers. The electrospinning machine comprises a syringe with an electric field source, a nozzle, a grounded target or a counter electrode, and a pump. Electrospinning uses electrostatic forces to create continuous fibers with a diameter range from a few micrometers to a few nanometers. In a conventional electrospinning process, a syringe is filled with a solution of polymer and this solution is then forced to the tip of the syringe by external pumping with mechanical pistons. When the droplet of the solution has been created at the end of the metal needle, an electrical bias voltage is applied between the metal needle and a collector placed in front of it. Surface tension is overcome by electrical forces as the applied voltage is gradually increased, resulting in the formation of a jet. Eventually, the droplet elongates into a Taylor cone, from which polymer nanofibers are formed and deposited on the collector.

Non-electrospinning

In the non-electrospinning method, the nanofibers are produced by centrifugal force or compressed gasses rather than by an electric field. These methods use less solvent, raise output, and reduce production costs. The three most common non-electrospinning techniques used to produce nanofibers are fiber drawing, centrifugal spinning, and bubble spinning (gas jet spinning). In centrifugal spinning, the quantity or production output of nanofibers is higher, but the quality is lower.

Application of nanofibers in the medical field

Nanofibers have unique physical properties similar to those of extracellular matrix (ECM). These properties include surface area, diameter, and porosity. Various biomedical applications of nanofibers include medical implants, drug delivery vehicles, antimicrobial agents, wound dressings, scaffolds for enzyme immobilization, dental materials, and biomimetic actuators. Nanofiber scaffolds seeded with cells are used for tissue engineering. The fiber's porous structure facilitates the diffusion of drug particles from the matrix. The rate of drug release could be controlled by manipulating the thickness of the produced nanofiber mat. The drug component was placed onto the nanofiber membranes for drug delivery systems in order to deliver the medication to the target site.

Nanofibers as a drug delivery system.

Single nanofibers or nanofiber scaffolds, which can act as effective vehicles, can be used to deliver therapeutic agents in a localized and targeted manner. Active biomolecules, including drugs and growth factors, can be encapsulated or incorporated into various nanofibers to alter cellular functions. Nanofibers are more efficient as delivery systems for drugs and therapeutic agents because of their huge surface area and porous nature.

The creation of a drug-loaded nanofiber for the transport of therapeutic peptides across the BBB is among the most significant instances of the use of nanofibers as drug carriers. The peptide nanofibers were synthesized such that the active "peptide epitope" tightly encloses the nanofiber core.

APPLICATIONS OF NANOMEDICINES IN DIFFERENT DISEASES

I) Treatment of atherosclerosis with nanoparticles with annexin.

Atherosclerosis is one of the main causes of cardiovascular disease. It is a slowly progressive pathology that decreases the arteries' lumen, which can lead to critically reduced blood flow to key organs, resulting in their failure. Three pathomechanisms play an important role in atherosclerosis: damage to the arterial wall, an inflammatory

the response that does not resolve, and the release of procoagulant material into the bloodstream. Normally, AA1 ("Annexin A1"), a glucocorticoid-regulated protein that functions as a natural inflammatory inhibitor, mediates the resolution of the inflammatory response. To affect the development of atherosclerosis, Fredman et al. synthesized nanoparticles loaded with AA1 molecules and inserted them into the bloodstream of mice. This experimental study proved that nanoparticles containing dissolution mediators can activate receptors in myeloid cells to treat "atherosclerotic" lesions.

II) Cancer therapy –

Nanomedicine has made it possible to focus on alternative approaches to drug delivery and increase their efficacy. Current approaches to treating cancer include surgery, radiation therapy, and chemotherapy. While these methods are usually effective, they frequently result in serious systemic harm and destroy a significant amount of adjacent healthy tissue.

Recently, several treatment options have been explored to preserve surrounding healthy tissue during treatment. One of the techniques, known as the nanoshell approach, is currently undergoing clinical trials. Nanoshells are very tiny gold-coated nanoparticles that may particularly target cancer cells by penetrating deeply into tissues and could also be configured to absorb NIR ("Near-Infrared") range. These nanoshells can be implanted by injection into neoplastic tissue when expose to a NIR laser, which can cause ablation of tumor cells. Irradiation with the NIR laser can be delivered either through the skin or via an optical fiber, such as the lung. Nanoparticles bound with antibodies through polyethylene glycol can also be used in breast cancer therapy.

Clinical trials of albumin-bound paclitaxel formulations have shown that they are better tolerated by patients than conventional placitaxel therapy. In metastatic lung cancer therapy, CBSA ("Cationic Bovine Serum Albumin") was investigated as an effective approach for siRNA delivery. SiRNA may be combined with CBSA to create stable nanoparticles that are resistant to deterioration and improve the likelihood of lung delivery.

III) Treatment of inoperable neoplasms with nano knife –

Recently, a nano knife has been shown to be able to efficiently destroy cancer cells. Nanoknife works on the principle of irreversible electroporation (IEP), which means that the cancer cells are exposed to altered electric fields with a voltage of up to 3000V for milliseconds or microseconds. An electric current flow between electrodes located at the edges, causing a unique form of biological effect in the center of the tumor called IRE ("Irreversible Electroporation").

IRE is a new, non-thermal kind of ablation based on the creation of irreversible holes (pores) at the cell membrane level. The advantages of the nanometer over conventional ablation methods include less time required for the surgical operation and no harmful thermal effects on healthy tissue. The most striking feature of the nanometer compared to other methods is that living structures with collagen fibers like bile ducts blood vessels, or pancreatic ducts are preserved.

IV) Regeneration of damaged nerves by nano grafts or carbon nanotubes –

The unique properties of carbon nanotubes (CNTs) have made it possible to use CNTs as a means of tissue repair, especially for damaged tissue that requires electrical stimuli. Researchers have studied the effect of CNTs in combination with glass fibers ("CNT-PGFs") on sciatic nerves in rats. It has been found that CNTs have the ability to induce sciatic nerve regeneration. Therefore, CNT-PGFs scaffolds can be used at the interface between peripheral nerve tissues and nerve conduction. CNTs also have the ability to transport proteins across the cell membrane, which helps to exert their naturally mediated effects. Functionalization of CNTs with appropriate molecules may be one of the most promising strategies for selective nerve regeneration.

V) Tissue regeneration with bioactive nano molecules –

The use of bioactive nano molecules serves the following purposes: 1. identification of signaling systems that can influence the endogenous adult stem cell's capacity for self-healing. 2. formulation of effective targeting methods for adult stem cell treatments.

Following is the list of clinically approved nano drugs approved by the FDA –

Trade name	**Active ingredient**	**Indication**	**Nanotechnology**
AmBisome	Amphotericin B	Fungal infections	Liposome
Rapamune	Rapamycin	Immunosuppressant	Nanocrystal Elan
Abraxane	Paclitaxel	Metastatic breast cancer	Albumin bound nanoparticles
DepoCyte	Cytarabine	Lymphomatous meningitis	Liposome
Taxotere		Anti-neoplastic	Micelle

NANODENTISTRY

Maintaining comprehensive oral health care can be effectively accomplished through the application of nanomaterials, biotechnology, such as tissue engineering, and finally dental nanorobotics. Applications of nanoscience in dentistry have the potential to revolutionize it in many areas, including dentition renaturation, local anesthesia, hypersensitivity permanent treatment, full orthodontic adjustments during a single office visit, covalently bonded diamond-enhanced enamel, and ongoing oral health care with mechanical dental robots.

Applications of Nanoscience in Dentistry Prosthodontics

In 2017, a 3D-printed poly-methyl methacrylate (PMMA) denture base to which 0.4% titanium oxide (TiO2) nanoparticles were added to improve its antibacterial properties and mechanical properties were examined. FTIR (“Fourier Transform Infrared Spectroscopy”), antimicrobial efficacy, and scanning electron microscopy test results against Candida species showed improvements in the chemical, antimicrobial, and structural properties of the denture base.

Nano in immunoprophylaxis

The ability of nanomaterials to deliver sustained and controlled release profiles suggests that they can be an efficient antigen delivery system. In addition, nanomaterials have immunomodulatory impacts that can be utilized to enhance and shape the response of the humoral immune. Nanotechnology-based adjuvants may significantly improve vaccination outcomes.

The following nanostructures can be considered adjuvants: polymeric nanoparticles, liposomes, virus-like particles, immunostimulatory complements (ISCOMs), and nano-emulsions. The most important property of nanoparticles is that some of them can penetrate antigen-receiving cells and thus regulate the immune response. This triggers a Th1 response against intracellular pathogens, making them a viable option for delivery on the surface of the oral mucosa and by intradermal application.

FUTURISTIC NANOROBOTS

The current state of nanotechnology in medicine is overwhelming, and if the pace of progress continues at this rate, we can expect to see significant changes in healthcare in the future. Nanotechnology is composed of two main strands. The first is a Drexler's molecule-sized machine, capable of building and manipulating its surrounding at the atomic level. The 2nd is "biological" nanotechnology, which incorporates DNA and the life machinery to produce distinct structures from proteins and DNA.

DNA-based origami robots.

DNA-based nanorobots are considered one of the most advanced experiments in the field of nanorobots. These nanorobots were inserted into a living cockroach that can perform a specific task, such as releasing molecules stored inside it after receiving a command. These nanorobots are also known as origami robots because they may unfold and release drugs. These nanorobots can also be capable of executing complex programs such as diagnoses or treatments.

Shell-like microbots and nano swimmers

These are exceptionally microscopic, shell-like robots less than a millimeter in size that literally swims via our bodily fluids. They can be utilized to deliver drugs or other medical assistance in a very targeted way.

Ant-like robots

These nanorobots are very fast, can locate and use tools, and are controlled by magnets. They are able to construct three-dimensional structures at a rapid pace.

MagnetoSperm microrobots

Scientists at the College of Twente (Netherlands) and the German College of Cairo have established a microrobot termed MagnetoSperm that may be controlled with weak oscillating magnetic fields. An external magnetic field source is used to control its motion. Research is currently underway to develop a magnetic nanofiber that may be utilized as a “flagellum”.

Bacteria-powered robots

Robots are powered by bacteria. These bacteria-powered robots depend on electric fields and can navigate. They can be programmed to follow a specific path or change their route. These robots will play an important role in delivering drugs exactly where they are required, manipulating stem cells to control their building microstructure or growth.

Clottocyte nanorobots

These nanorobots, also known as artificial mechanical platelets, have a similar function to platelets in that they stick together to create a blood clot that prevents bleeding. They are able to store fibers, and when they encounter a wound, they deposit fibers to immediately assist in clot formation.

Respirocyte nanorobots

These are nano-beings that can act like red blood cells but are capable of carrying a greater amount of oxygen than natural red blood cells. This will be helpful in patients suffering from anemia.

Nanoindustries and Commercialization

The Nanomedicine market is markedly widespread and has the presence of several important members. Following is the list of manufacturers who are most active in nanomedicine:

- Wyeth Pharmaceuticals Inc.,
- Par Pharmaceutical Companies Inc.,
- Oxonica Plc,
- Nanosphere Inc.,
- Nano BioTix,
- MagForce GmbH,
- Life Technologies Corporation,
- Flamel Technologies S.A.,
- Elan Corporation PLC,
- Arrowhead Research Corporation
- AMAG Pharmaceutical Inc.,
- Abraxis BioScience Inc. (now Cel Gene),

FUTURE PROSPECTS

In the last two decades, numerous clinical trials and patents have been conducted in the field of nanotechnology and nanoscience. The best area where nanomedicine has made tremendous progress in cancer therapy. The use of nano-drug delivery and nanomedicine systems is one of the most promising research areas in the coming decades. The application of metal-based nanoparticles, such as silver and gold, in both diagnosis and treatment, is a research area that might potentially lead to the broader usage of nanomedicine in the future. The use of gold nanoparticles to treat soft tissue tumors due to the susceptibility of tumor cells to radiation-based heat therapy is also an area to focus on in the future. Despite the broad comprehension of the prospects of nanomedicine and nanomedicine delivery, its actual effect on the healthcare system and cancer treatment/diagnosis is very limited. This is due to the fact that the field of nanoscience.

There has been a lot of keenness on the growth of nanorobots (nanodevices) which can aid in tissue detection and repair with the complete external control system. This was not yet a reality and remains a future challenge that might be achieved by mankind shortly.

Issues and Controversies with Nanomedicines

Apart from their advantages, the potential risks of nanomedicines to humans & environment must also be studied in the long term. Therefore, all new biomaterials must be evaluated for acute or chronic toxicity impacts on humans and the environment. Biocompatibility is another important property in the development of drug delivery systems. A comprehensive biocompatibility testing program that includes in vivo research is necessary for the preclinical evaluation of nanomaterials. If the biocompatibility of nanomaterials cannot be assured, various types of nanosystems could raise toxicological issues.

Appropriate and precise standards for risk evaluation of nanomaterials are needed. This could be achieved through collaboration with various pharmaceutical industries, regulatory agencies, govt, and academics. Despite all the measures taken to assess the safety of nanomaterials, most of them are still treated as traditional chemicals, thus lacking clear, certain guidelines for safety. This could be accomplished with various pharmaceutical industries, regulatory agencies, govt, and academicians. In spite of all the measures taken for the safety of nanoscale materials, most of them are still treated as traditional chemicals, thus lacking clear certain guidelines for safety.

Different scientific organizations and international regulatory bodies have disagreed on the definition of a nanomaterial. However, attempts were made to come up with a consensual definition. The nanoscale properties greatly boost a set of options for drug development; although, the nano formulation’s physicochemical properties may change the pharmacokinetics, i.e., the metabolism, elimination, distribution, and absorption. Some of the problems with the use of nanomaterials include their propensity to more readily pass biological barriers, hazardous properties, and their persistence inside the environment and the human body.

CONCLUSION

The discovery of novel drugs or the reformulation of current ones has been made possible by increased research in nanomedicine. Modification in bioavailability, solubility, and toxicity profile are some of the changes that nanotechnology produces in medicines. We have seen the introduction of several nanomedicine applications in clinical practice, ranging from medical devices to nano pharmaceuticals, during the last decades. The establishment of methods for the characterization, assessment, and process control of nanomedicines, as well as the creation of a common definition, must all be done before there is full regulation of nanomedicines.

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