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Application of Nanotechnology in Medicine

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Abstract

In contemporary times, the pursuit of minimalism has gained ascendancy, surpassing the trend table and permeating into various facets of life, such as architecture, interior design, economics, and notably, science. Within the realm of science, this inclination is recognized as nanoscience, wherein the focus is on the study of matter at the nanoscale. Nanotechnology, a branch of nanoscience, is concerned with the synthesis, manipulation, and application of nanomaterials and nanoparticles in technology.

This scholarly work aims to provide a comprehensive exploration of the multifarious uses of nanotechnology in the domain of medicine. The study delves into the vast applications of nanotechnology in medicine, with a view to understanding the strides that have been made in enhancing the quality of the medical field and improving the well-being of patients' post-treatment. The diverse aspects of medicine scrutinized in this research encompass but are not limited to dentistry, surgery, drug delivery methods, antibiotics, and regenerative medicine.

Despite the potential of nanotechnology to revolutionize the field of medicine by offering expedited treatment options for various ailments and even purportedly speeding up the healing of wounds and burns, it is essential to acknowledge that like any other scientific innovation, it also possesses its share of drawbacks and constraints. The application of nanotechnology in medicine may present certain limitations and disadvantages that must be taken into consideration when assessing its overall impact on patient care and treatment outcomes.

Keywords: Nanotechnology; nanoscience; medicine; nanoparticles; nanomaterials

Chapter 1. Introduction to Nanotechnology

The word "nano" in the English language is used to describe a unit that is extremely minute or small. To put this into context, it might be helpful to understand just how small a nanometer is when we realize that a human hair is approximately 80,000 - 100,000 nanometers wide. The application of a unit that minute in technology and its advancement constitutes the science of nanotechnology.

Nanotechnology is a multidisciplinary field of science and engineering that deals with the study and manipulation of matter at the nanoscale level. It involves the development and use of materials and devices with dimensions of less than 100 nanometers (nm), where the unique physical and chemical properties of materials at this scale are exploited.

Although the term nanotechnology was first used in 1974 by the late Norio Taniguchi (University of Tokyo) to refer to the ability to engineer materials precisely at the scale of nanometers [23], the implementation of nanoparticles in science has been since the inception of the field itself, focus on the term however increased drastically during the industrial revolution.

At its core, nanotechnology is centered on the utilization of single atoms and molecules to fabricate practical structures. This cutting-edge field finds widespread applications in various medical domains, such as drug discovery, clinical diagnosis, immune system augmentation, cryogenic preservation of biological tissues, protein detection, DNA structure investigation, tissue regeneration, hyperthermia-based cancer treatment, cell and molecule sorting, and enhancement of magnetic resonance imaging (MRI) contrast. Nanotechnology influences almost every facet of everyday life from security to medicine.

The concept of nanotechnology is that when one goes down to the bottom of things, one can discover unlimited possibilities and potential of the basic particle. In nanotechnology, analysis can be made to the level of manipulating atoms, molecules, and chemical bonds between them. The various nanoparticles include nanopores, nanotubes, quantum dots, nano shells, nanospheres, nanowires, nano capsules, dendrimers, nanorods, liposomes and so on. More recently, tiny machines called nano assemblers that could be controlled by computer to perform specialized jobs have been invented [1].

Why Nanotechnology?

Despite the numerous technological advancements made over the years, and how undeniably obvious the impact of technology is today. There are still numerous aspects of technology that necessitate improvement owing to various factors, such as size, capacity, and even feature control. The inability to control some of these factors is often a source of drawback, leading to constant upgrades, and change.

Nanotechnology is the manipulation or self-assembly of individual atoms, molecules, or molecular clusters into structures to create materials and devices with new or vastly different properties. Nanotechnology can work from the top down or the bottom up [32].

When the most important aspects of nanotechnology namely size, structure and novel properties are considered, it is easy to realize why nanotechnology quickly became a dominant force in science and technology. As the world tilts towards quantum science and minimalism, the importance of microscopic properties is now emphasized more than ever. Instead of dealing with materials in large quantities, scientists now focus on manipulating individual atoms and molecules.

Through an examination of the distinctive attributes of individual molecules, it is conceivable to arrange them in meticulous arrangements, leading to the creation of innovative materials possessing exceptional properties. The realm of nanotechnology holds immense potential in the production of a diverse array of pioneering materials and devices, which have the potential for deployment in various domains, such as the field of medicine.

The innovative materials and devices developed through nanotechnology may exhibit extraordinary characteristics, such as high tensile strength, enhanced thermal conductivity, or unique optical properties, among others. Such properties make them ideal for applications in numerous fields, including biomedicine, where they may be utilized to improve the efficacy of drug delivery, tissue engineering, or other therapeutic interventions.

Chapter 2. Application of Nanotechnology in Medicine

Nanotechnology has a wide-ranging and ever-expanding array of applications, particularly in the realm of medicine, or what is commonly referred to as nanomedicine, which is the science of preventing, diagnosing, and treating disease and preserving and improving human health, using nanosized particles. The multifaceted domains of medicine are increasingly being permeated by nanotechnology, which serves not only as a diagnostic tool but also as an agent for improved treatment, drug delivery, antibacterial therapy, and tissue regeneration. In fact, nanomedicine serves as a novel technique in genomic medicine as an advancement in precision medicine and functional genomics.

Application of Nanotechnology in Dentistry

Dentistry as a sub field of medicine is not a stranger to nanoparticles, as often, it is small sized bacterial build up those leads to dental plaques, toothaches, cavities and so on that form in the mouth. The introduction of nano dentistry is an innovative method to tackle such issues at the minimal level. It is theorized in fact, that nano dentistry might help maintain an almost perfect oral health through the involvement of nanomaterials. The several methods through which nanotechnology can be applied in nano dentistry include:

Local Anesthesia

Nano materials can be used as an anesthetic delivery tool before a dental procedure is carried out. The gingiva of the patients is instilled with a colloidal suspension containing millions of active, analgesic, micron-sized dental robots that respond to input supplied by the dentist. After contacting the surface of crown or mucosa, the ambulating nanorobots reach the pulp via the gingiva sulcus, lamina propia and dentinal tubules, guided by chemical gradient, temperature differentials controlled by the dentist. Once in the pulp, they shut down all sensation by establishing control over nerve-impulse traffic in any tooth that requires treatment. After completion of treatment, they restore sensation thereby providing patient with anxiety-free and needless comfort. The anesthesia is fast acting, and reversible, with no side effects or complications associated with its use [10, 25]. This method presents several benefits, including its ability to alleviate concerns, its rapid action, and its complete reversibility.

Nano diagnostics

Nano diagnosis in dentistry is an emerging field that leverages the principles of nanotechnology to diagnose oral health issues at an early stage. The nano diagnosis approach involves the use of nanoscale diagnostic tools and devices that can detect even the slightest changes in the oral tissues and biomolecules. This technology utilizes the unique physical and chemical properties of nanoscale materials to enhance the sensitivity, accuracy, and speed of diagnosis.

One promising application of nano diagnosis in dentistry is the early detection of dental caries (tooth decay). Currently, traditional diagnostic methods such as visual inspection and x-rays can only detect caries once they have caused significant damage to the tooth structure. Nano diagnosis, on the other hand, can detect caries at the molecular level, allowing for earlier intervention and treatment.

Another potential application of nano diagnosis in dentistry is the detection of oral cancer. By using nanoscale sensors and probes, oral cancer biomarkers can be identified in the saliva or other oral fluids, enabling earlier diagnosis and treatment of this potentially life-threatening condition. Overall, the use of nanotechnology in dental diagnosis has the potential to revolutionize the field of dentistry by enabling earlier, more accurate, and less invasive detection and treatment of oral health issues.

Nanorobotic dentifrice (Dentifrobots)

Toothpastes and mouthwashes have the potential to incorporate advanced nanorobots, known as Dentifrobots, which could be designed to perform regular surveys of all gingival surfaces in the mouth. In addition, these Dentifrobots could be programmed to break down harmful materials, such as plaque and bacteria, into harmless substances, and continually remove calculus buildup to prevent dental issues. The utilization of such nanotechnology-based solutions in oral care could revolutionize the way we maintain our oral health and reduce the risk of dental diseases.

Orthodontic Treatment

Orthodontic treatment using nanotechnology is an emerging field that aims to improve the effectiveness and efficiency of orthodontic procedures using nanomaterials and nanotechnology- based devices. One application of nanotechnology in orthodontics is the development of nanoscale wires and brackets for braces. These tiny components can be made from materials such as titanium or shape-memory alloys like nickel-titanium, which allow for greater flexibility, durability, and biocompatibility. This can lead to more comfortable and effective treatment for patients.

Another application is the use of nanomaterials in orthodontic adhesives. These adhesives can contain nanoparticles that improve bonding strength and reduce the risk of enamel damage during the bonding process. Additionally, nanomaterials can be used in clear aligners to improve their mechanical properties and durability. Nanotechnology-based devices such as nanorobots and nano sensors are also being developed for orthodontic applications. These devices can be used for tasks such as monitoring tooth movement and measuring forces during treatment, which can help to optimize treatment outcomes.

Application of Nanotechnology in Drug Delivery

Nanoparticles as a drug delivery technique is a brilliant notch in medicine as a treatment method, particularly for cells that take a while to break down large molecules. Nanotechnology has become crucial in drug delivery due to its ability to manipulate molecules and supramolecular structures, resulting in the creation of devices with programmed functions. The term “nano vehicles” is now used to refer to conventional liposomes, polymeric micelles, and nanoparticles, but this term is only correct in reference to their size scale. However, it’s important to note that these drug delivery systems would have still progressed to their current state without the impact of nanotechnology. To fully comprehend the significance of nanotechnology in drug delivery, it’s useful to categorize drug delivery systems based on the era before and after the emergence of nanotechnology. Nanoparticles used as drug delivery vehicles are generally less than 100 nm in at least one dimension and consist of different biodegradable materials such as natural or synthetic polymers, lipids, or metals. Nanoparticles are taken up by cells more efficiently than larger macromolecules and therefore, could be used as effective transport and delivery systems [29].

Clinical Nanomaterials

So far, various nanoparticles and nanomaterials have been researched and permitted for clinical purpose, some of these nanoparticles include:

1. *Micelles*: Micelles are minute spherical structures formed by the assembly of amphiphilic surfactant molecules in aqueous conditions. These structures have a hydrophilic outer layer and a hydrophobic inner core, which makes them an excellent candidate for incorporating hydrophobic therapeutic agents. The size of these micelles ranges from 10 to 100 nanometers, making them extremely tiny yet effective vehicles for drug delivery. The unique characteristics of micelles provide an advantage in improving the solubility of hydrophobic drugs, which ultimately enhances their bioavailability.
   This property is particularly significant in drug development, where the efficient delivery of drugs to target sites is crucial. Apart from their use in drug delivery, micelles also have numerous other applications. They can serve as imaging agents in medical diagnostics, as contrast agents in MRI scans, and as therapeutic agents in the treatment of various diseases. Micelles’ versatility and ability to modify their properties make them an attractive option for a wide range of applications. Their design and development continue to evolve, and researchers are exploring new ways to enhance their efficiency and effectiveness in various fields.
2. *Dendrimers*: Dendrimers are large molecules with repeating branches emanating from a central core and functional groups present on their outer surface. These groups can have a negative, neutral, or positive charge, which makes dendrimers an adaptable platform for modifying their structure and properties. The interior space of dendrimers can encapsulate therapeutic agents, or the surface groups can be used to attach them, enhancing their bioavailability and biodegradability. Researchers have found that dendrimers conjugated with saccharides or peptides display superior antimicrobial, antiprion, and antiviral properties.

They also exhibit better solubility and stability upon absorption of therapeutic drugs. Dendrimer-based polyamidoamine complexes (dendriplexes) have emerged as a promising candidate for gene delivery vectors. These complexes have the potential to facilitate successive gene expression, targeted drug delivery, and improve drug efficacy.

With their adaptable properties, dendrimers hold immense promise in biomedical applications, such as in imaging and drug delivery.

Due to their transformable nature, dendrimers have garnered significant attention from researchers for their potential to revolutionize drug development. They offer a novel way to overcome challenges in drug delivery and gene therapy by providing a platform for targeted and controlled release of therapeutic agents. As research continues, dendrimers are expected to emerge as a versatile tool for enhancing the efficacy of drugs and facilitating the development of novel treatments for various diseases.

3. *Quantum Dots*: Quantum dots (QDs) are nanocrystals made of semiconducting materials that exhibit fluorescence when excited by light. These tiny crystals, measuring between 1 to 100 nanometers, have shown great potential for use in several biomedical applications, including drug delivery and cellular imaging.

   Quantum dots possess a unique shell-core structure, with the core made up of elements from the II-VI or III-V groups of the periodic table. This structure imparts distinctive optical properties to quantum dots, making them highly stable and bright, allowing them to be used in the field of medical imaging.

   The ability of quantum dots to emit light of specific colors has made them ideal candidates for a range of biological applications. Researchers are exploring new ways to harness their unique properties to develop targeted therapies, visualize cellular processes, and track the delivery of drugs.

   The potential applications of quantum dots in biomedicine are vast, and researchers are actively investigating their properties to develop new methods of diagnosis and treatment. These tiny crystals hold immense promise as a tool for enhancing our understanding of biological processes and improving the efficacy of therapies for a range of diseases.

Nanomaterials in Drug Delivery and Gene Therapy

Understanding the molecular mechanism of drug - cell receptor interactions help to design a more efficient nano delivering system which can reach those cells without triggering drug resistant cells that inhibit the drugs from being effective, as shown in figure 1.

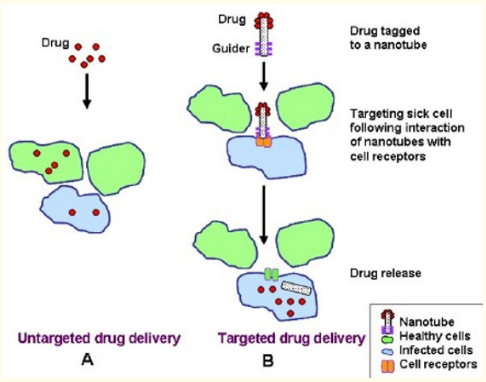

Figure 1: (Suri and colleagues).

Nano particles are also used as a gene expression control technique whereby short interfering RNA (siRNA) is employed. It tis theorized that the application of siRNA as a clinical tool would be a very effective delivery system. A significant drawback to this technique though is the difficulty in tracking and monitoring their delivery and efficiency, without a suitable tracking agent and marker, whereas designing a tracking agent that is efficient has proved to be quiet challenging. Recently, Howard et al [19] used such nanoparticles conjugated with siRNA specific to the BCR/ABL-1 junction sequence and found 90% reduced expression of BCR/ABL-1 leukemia fusion protein in K562 (Ph(+)) cells. Effective in vivo RNA interference was also achieved in bronchiolar epithelial cells of transgenic EGFP mice after nasal administration of chitosan/siRNA formulations. These findings highlight the potential application of this novel chitosan-based system in RNA-mediated therapy of systemic and mucosal disease [29].

Cardiovascular diseases are another area of research where the impact of nanoparticles is being considered, cardiovascular diseases (CVDs) refer to a group of disorders that affect the heart and blood vessels. They can range from mild conditions, such as high blood pressure, to life- threatening conditions, such as heart attacks and stroke. CVDs are a leading cause of death and disability worldwide, accounting for approximately 31% of all global deaths. Nitric oxide (NO) endothelial production impairment is linked to most cardiovascular risk factors, including hypertension, hypercholesterolemia, smoking, homocystinuria, and diabetes mellitus. Impaired endothelial function is known to be the first step in atherosclerosis. Gold and silica nanoparticles have been developed to enhance NO supply, potentially useful in cardiovascular diseases with low NO bioavailability [7].

To reduce the levels of pathological factors contributing to early atherosclerosis, the systemic administration of CREKA-peptide-modified nanoemulsion loaded with 17-βE has been shown to reduce lesion size, lower circulating plasma lipids, and decrease gene expression of inflammatory markers linked to the disease [8]. Furthermore, newly developed block copolymer micelles made from PEG and poly (propylene sulfide) have demonstrated excellent potential for atherosclerosis management by suppressing pro-inflammatory cytokines levels [35].

Liposome-mediated drug delivery has been shown to be effective in preventing platelet aggregation, atherosclerosis, and thrombosis. Prostaglandin E-1 (PGE-1) has a wide range of pharmacological properties, including vasodilation, inhibition of platelet aggregation, and leukocyte adhesion, as well as exhibiting an anti-inflammatory effect. Liposomal delivery of PGE-1 (Liprostin™) is currently undergoing phase III clinical trials for the treatment of various cardiovascular diseases, such as restenosis following angioplasty. Additionally, liposomes carrying the thrombolytic drug urokinase have also been assessed. Cyclic arginyl-glycyl-aspartic acid (cRGD) peptide liposomes encapsulated with urokinase can selectively bind to GPIIb/IIIa receptors, significantly improving the thrombolytic efficacy of urokinase by almost four times compared to free urokinase [4].

Application of Nanotechnology in Plastic Surgery

Surgery as a medical practice has had a long time coming from the days of nearly butchering the patients to the careful and meticulous art of saving a life it has now become. One of the hallmarks of improvements in surgery is the reduction in scarring after a surgical procedure has taken place. The integration of nanotechnology in surgery is a major win for the surgical field, as the use of nanotechnology causes less trauma on the patient, lessening the amount of scarring taking place, and in turn leading to reduced complications during the post-surgical healing process. Through nanotechnology, tiny biosensors could be constructed which could take these factors into account, thus shortening a patients recovery period and saving hospitals expenditure, reducing nosocomial infection rates, reducing the waiting lists for operation, and allowing doctors to treat more patients in the same period. A surgical nanobot, programmed by a human surgeon could act as an autonomous on-site surgeon inside the human body [11].

When it comes to some aspects of surgery, such as plastic surgery, an aspect of nanoscience called surface engineering is researched upon more intensely. In surface engineering, surface texture is repetitive or random deviation from the nominal surface that forms the 3D topography of the surface. Alterations in the surface roughness of implants influence cell response by increasing the surface area of the implant adjacent to soft tissues, thereby improving cell attachment to the implant surface [24]. Surface texture includes roughness (nano- and micro- roughness), waviness (macro-roughness), lay, and flaws [33].

Nanotechnology and Breasts Implants

In 2012, the procedures of breast augmentation and implant-based breast reconstruction following mastectomy were observed to be the most frequently performed surgical interventions within the field of plastic surgery. At present, the scientific community is engaged in the evaluation of a novel approach towards the deployment of breast implants, which involves the application of nanofiber coatings with the capability of releasing targeted and potent anticancer medications for the treatment of breast tumors. Most commercially available breast implants present some type of elastomer surface alteration to increase their surface roughness.

This is partly a result of the large number of in vitro and clinical studies demonstrating positive results and satisfactory outcomes of texturizing [Bern, Barnsley]. In fact over the last decades, known as "micro/macro texturization", several surface modification to increase roughness have emerged [Bern], such as Siltex texturing, a patterned surface created as a negative contact imprint off of a texturing foam, and the bio-cell surface, a more aggressive open-pore textured surface created with a lost salt technique in which the entire elastomer shell is placed on a bed of finely graded salt with light pressure. The size of the latter depressions is irregular, because created by salt with different particle sizes, ranging from 600 to 800 lm (0.6-0.8 mm) in diameter and from 150 to 200 lm (0.15-0.2 mm) in depth. An edge raised 70 to 90 lm around each of these depressions increases the total depth [6].

The distribution of these depressions is irregular on the surface. The surface characteristics constructed by these different technologies vary widely, and although they are not frequently compared with each other, as a group they enhance the process of bio integration when compared to relatively smooth surfaces, as previously mentioned by Barnsley and colleagues [2].

In the field of aesthetic and reconstructive breast surgery, use of breast implant often leads to different complications such as capsular contracture, double capsule, and late seromas. Different breast implant surfaces have been developed and proposed with the aim of decreasing those complications. The formation of capsular contracture is nowadays addressed with different breast implant surfaces together with a sterile, atraumatic technique, meticulous hemostasis, and local antimicrobial agents. A consensus has not yet been reached, but in literature the idea that textured surfaces decrease the incidence of capsular contracture prevails [6].

Application of Nanotechnology in "Wound and Burn" care

Another important aspect of clinical care that is already paying attention to nanotechnology is the area of "wound and burn care". Wound dressings constructed using nanoscale fabrication techniques can greatly improve wound healing. Nanofibrous structures can be fabricated from a variety of materials using manufacturing techniques that operate at the nanoscale. These nanofibers create a three-dimensional framework that emulates the natural extracellular matrix (ECM) while host tissue regeneration replaces the scaffold. Nanofiber scaffolds possess several properties that are vital for tissue repair, such as mechanical robustness, temperature regulation, fluid uptake, and gas exchange [21].

Collagen-based scaffolds made of nanofibers promote acute wound healing in rats by stimulating capillary and fibroblast growth. Choi et al. conducted a study in which recombinant human epidermal growth factor (EGF) was immobilized on biodegradable electrospun nanofibers to treat diabetic ulcers in rats. The effect of EGF nanofibers on the differentiation of human primary keratinocytes was investigated by cultivating them on the nanofiber matrix. The wound healing potential of EGF nanofibers was established in diabetic animals with dorsal wounds. In in vivo wound healing experiments, the EGF-nanofibers group outperformed control groups (conventional dressing, nanofibers alone, or EGF solutions). This study demonstrated that EGF- conjugated nanofibers have the potential to be used as a new wound healing material by boosting the proliferation and phenotypic expression of keratinocytes in diabetic wounds [5].

Chitin and chitosan nanofibrils are nanocrystals derived from the exoskeletons of crustaceans that are made up of natural polysaccharides. These fibrils have been used in various formulations to promote wound healing. Muzzarelli et al. demonstrated in murine models that different formulations of chitin nanofibrils promote near-normal physiological wound repair. They subjected various formulations of dibutyryl chitin (DBC), a modified chitin carrying a butyryl group at the three and six positions, to a series of in vitro and in vivo tests.

The DBCs were then included in a chitosan solution of 5-methylpyrrolidinone and freeze-dried to create a strengthened wound dressing material, which was subsequently tested in vivo in full- thickness wounds in rats. The rats had full-thickness dorsal wounds bilaterally and were treated with the experimental agent on one side and control on the contralateral side. The animals were examined at 7 or 14 days, and the skin of each surgical wound was excised. Using 4 mm × 4 mm pieces as wound dressings resulted in significantly less cutaneous scarring, as determined by collagen I/collagen III ratios and clinical measurements. Chitin nanofibrils/chitosan glycolate can be produced as a spray, gel, or incorporated into a dressing for wound care [17].

Application of Nanotechnology in Antibiotics

The impact of nanotechnology has unsurprisingly extended to the field of medical immunology, where nanoparticles have been hypothesized to act as an immune adjuvant to stimulate the immune response of the body or as a carrier to trap antigens for targeted delivery and activation induction. The utilization of nanotechnology in pharmacy has been particularly noteworthy, for instance, metal or metal oxide nanoparticles exhibit bactericidal effects and can function as bactericides. In addition, surface coating of nanoparticles can be exploited to target them, thereby improving drug efficacy, and reducing toxicity and side effects.

To improve stability, biocompatibility, and active targeting, it is common practice to coat nanoparticles with functional chemical groups. This approach holds great promise in enhancing drug solubility [29].

When confronted with critical situations, groundbreaking methods, tactics, or medications are frequently created to solve the situation. Otherwise, as bacterial resistance increases, making an already severe bacterial infection untreatable, with infectious diseases again posing a grave danger, endangering the well-being and lives of people worldwide. In recent years, only a limited number of new antibiotics have been uncovered, mainly due to the arduous and costly nature of drug discovery and development [22].

Using innovative technology to change the physical and chemical properties of existing antibiotics, thereby switching their mode of action, is a significant course of action to effectively combat MDR. Nanoparticles, with their unique size, properties, and high specific surface area, offer unparalleled benefits in the fight against bacterial infections and MDR. Research has demonstrated that bare nanoparticles have a relatively vulnerable core structure that is easily degraded and damaged by the in vivo physiological environment during actual physiological tests. However, applying a surface coating to the bare nanoparticles can significantly enhance their stability. Moreover, using coated nanoparticles loaded with antimicrobials can prevent superfluous interactions and drug degradation en route to the intended tissue or cell, while sustaining drug stability. Additionally, nanoparticles can achieve diverse targeting capabilities by altering their surface coatings.

Nanoparticles are tailored with specific chemical groups on their surface to enable accurate identification of targeted therapeutic sites. Once the site is reached, sustained antibiotic release results in the desired treatment effect. Moreover, nanotechnology can optimize drug properties, modify administration methods, and reduce patient discomfort. A remarkable feature of nanoparticles is their ability to package different antibiotics within the same nanocarrier [37].

Combining multiple antibiotics is a common strategy in treating infectious diseases for faster action and fewer side effects. Nanoparticles not only kill multi-drug resistant bacteria themselves but also act as adjunct agents with antibiotics to enhance their antibacterial capacity against resistant microbes. This approach helps restore the activity of older antibiotics to which microbes had developed resistance [34]. As a result, nanotechnology shows promising prospects in the treatment of infectious diseases and is currently a research focus. Although thousands of studies and papers have been published, the application of nanoparticles in the human body is limited due to their side effects.

Methods to assess the efficacy of antibacterial agents

1. The density of cells in a suspension of planktonic bacteria can be estimated by measuring its optical density, also known as turbidity, and relating it to the cell concentration. By measuring the cell density at various time points, this technique can also be used to estimate the rate of cell proliferation. As bacteria grow in cell culture media, their cell bodies increasingly obstruct the passage of light through the sample, resulting in reduced light penetration.
   To determine the optical density of a standard volume of samples, a spectrophotometer can be used to measure the light transmitted through them, which can then be compared to other samples. A higher density of bacteria in a sample result in less light penetrating it. While some studies report direct optical density values, others establish a standard curve to match experimental optical density values with cell density. The cell density can be determined by serially diluting a suspension of bacteria cells, measuring the optical density of each dilution, and then spreading each sample on an agar plate [28].
2. Crystal violet staining is a technique used to assess the formation of biofilms in bacterial colonies that may develop in a host. The staining is achieved by using crystal violet (hexamethyl pararosaniline chloride) to color the thick peptidoglycan layer of Gram-positive bacteria, the thin peptidoglycan layer of Gram-negative bacteria, and the components of the extracellular biofilm. When the biofilm is exposed to a crystal violet stain solution, the amount of absorbed stain is generally proportional to the amount of biofilm present. A standardized rinsing procedure can be used to remove the unabsorbed staining solution, leaving behind only the absorbed staining solution present in the biofilm. A solvent can then be used to remove the absorbed crystal violet, and the extent of the color change caused by the presence of the crystal violet stain can be measured using a spectrophotometer. The color change observed is proportional to the amount of biofilm present. By comparing the biofilm formation in the presence of nanoparticles to that of the control biofilm, this technique can be used to evaluate the impact of nanoparticles on biofilm formation [28].
3. The spread-plate technique is a method used to determine viable CFUs present after exposure to nanoparticles in bacterial suspensions. The process involves serially diluting the cell suspension samples, and then spreading a small volume of the sample across the surface of an agar plate, often using a Lazy-L Spreader™ or similar device.
   After an incubation period, CFUs are counted and calculations are performed to determine the cell density in the original sample, taking into consideration the dilution process. By comparing the results from plates spread from samples that did not contain nanoparticles, the percentage reduction in viable CFUs can be determined. It is important to note that a CFU counted on an agar plate may have arisen from a single bacterium or a larger cluster of many bacteria, which can introduce some uncertainty in the experimental results.
   To confirm the accuracy of the results, multiple techniques may be used. In some cases, low intensity ultrasound treatment may be employed to disrupt bacteria clusters into individual cells, which increases the number of CFUs and provides data that more accurately relates to the total number of viable cells present. However, one critique of this technique is that nanoparticle agglomeration may occur as the nanoparticles interact with intracellular components of lysed cells, preventing nanoparticle interactions with still-living cells, which can affect the accuracy of evaluating the antibacterial effect of nanoparticles in a liquid system [31].

Antibacterial nanoparticles

Various nanostructures have been studied for their antibacterial properties. It is important to note that while some metals like zinc, silver, and copper exhibit antibacterial mechanisms in their bulk form, other materials like iron oxide do not exhibit these properties in bulk form but may exhibit them in nanoparticulate form. The mechanisms behind this antibacterial activity vary from one nanoparticle to another, and are not yet fully understood. Some proposed mechanisms are related to the physical structure of the nanoparticles, such as their membrane-damaging abrasiveness, while others relate to the increased release of antibacterial metal ions from their surfaces. As the particle size decreases, the specific surface area of a dose of nanoparticles increases, allowing for greater interaction with the surrounding environment. Therefore, for inherently antibacterial materials, increasing the surface to volume ratio enhances their antibacterial effect. A nanoparticle of an inherently antibacterial material may have multiple mechanisms of antibacterial activity, such as the release of antibacterial metal ions from the particle surface and the physical properties of the nanoparticle that facilitate cell wall penetration or membrane damage.

1. *Zinc*: Zinc oxide (ZnO) has demonstrated a natural ability to decrease the activity of various types of bacteria (primarily Gram-positive strains) without the use of antibiotics [30]. Through the application of nanotechnology, the antibacterial properties of ZnO have been further amplified [9; 38].
   In one study, researchers added micron and nanoscale ZnO particles to bacteria suspensions in liquid cell suspensions to assess their antibacterial impact. The study found that nanoparticles had a greater antibacterial effect [14]. The researchers introduced ZnO nanoparticles (average mean diameter = 60 nm, zeta potential under experimental conditions = −5 mV) and micron scale ZnO particles to bacteria suspensions at a concentration of 20 μg/mL. After a 2-hour incubation period, the suspensions were added to agar plates to count the number of viable colonies. The study revealed a reduction in the viability of S. aureus and E. coli as the size of the ZnO nanoparticles decreased.
   However, the smallest diameter ZnO nanoparticle (40 nm) tested required a concentration of 5 mM (407.04 μg/mL) to reduce the viability of either bacteria species even after 24 hours. The study also observed that both bacteria species were impacted similarly by the nanoparticles. Additionally, the study noted that the exposed bacteria exhibited irregularities in their cell membranes. The researchers also discovered that the antimicrobial effect of ZnO nanoparticles on E. coli increased as the particle diameter decreased from 2 μm to 45 nm to 12 nm, which was attributed to the greater surface area to volume ratios and increased abrasiveness of the smaller particles, leading to more mechanical damage to the cells [19].
   In another study, researchers investigated the antibacterial effects of zinc ions and determined the minimum inhibitory concentration (MIC) for Pseudomonas aeruginosa, S. aureus, and Candida albicans at 48 hours to be 1917 μg/mL, 9 μg/mL, and 39 μg/mL, respectively [13, 14]. The study also found that S. aureus was more sensitive to lower concentrations of zinc ions than P. aeruginosa.
   Researchers attempted to elucidate the mechanisms behind the antibacterial effect of ZnO particles and found that the production of hydrogen peroxide, a reactive oxygen species that has bactericidal activity, was significantly increased in solutions with a variety of ceramic powder chemistries, particularly ZnO [26]. The study attributed the antibacterial effect of ZnO powders to this phenomenon. Other ceramic powders tested, such as magnesium oxide and calcium oxide, did not produce hydrogen peroxide. However, the mechanism of the antibacterial activity of ZnO nanoparticles is complex and not yet fully understood. Zinc ions have been shown to inhibit multiple activities in the bacterial cell, including glycolysis, transmembrane proton translocation, and acid tolerance.
2. *Silver*: Silver nanoparticles have been studied extensively due to their potential as a powerful antibacterial agent. The use of silver as an antibacterial agent has been well documented throughout history, and the development of silver nanoparticles is a logical progression in this field. One study found that silver nanoparticles with an average diameter of 21 nm were able to inhibit the growth of various types of Gram-negative bacteria, such as E. coli, Vibrio cholerae, Salmonella typhi, and P. aeruginosa, on agar plates. The bactericidal effect of these nanoparticles is attributed to several mechanisms. The presence of many nanoparticles inside the bacteria suggests that membrane permeability is affected, with interaction of silver particles with bacteria membrane and intracellular proteins causing interference with cell division and ultimately leading to cell death. The study also confirmed the presence of biocidal ionic silver released from nanoparticle surfaces. Although bacteria DNA conglomeration defense mechanisms protect against toxic environments, exposure to ionic silver compromises bacteria replication ability.
   Another study compared the morphological features of Gram-positive (S. aureus) and Gram-negative (E. coli) bacteria exposed to the same concentration of silver ions. Both bacteria species exhibited condensation of DNA, cell membrane separation from the cell wall, and cell wall damage. This suggests that silver nanoparticles are effective against a wide range of bacteria, regardless of their Gram classification.
   Further research has found that different shapes of silver nanostructures have varying levels of antibacterial activity. Truncated triangular silver nanoplates and nanospheres were found to be more effective at reducing E. coli viability than silver nanorods or ionic silver. Triangular silver nanoplates exhibited the greatest antibacterial activity at low doses, with a mere 1 μg of the nanoplates completely inhibiting colony formation on agar plates plated with bacteria cell suspensions. In comparison, 12.5 μg

of spherical nano particles was required to achieve a similar reduction in bacteria activity.

Concentration-dependent inhibition of bacteria growth was observed when silver nanoparticles with an average diameter of 12 nm were incorporated into agar plates at concentrations of 10-100 μg/mL. E. coli was added to the plates at population densities of 105 CFUs, and after 24 hours of growth, CFU populations on 10 μg/mL plates were 70% lower than on control plates. Concentrations above 50 μg/mL completely inhibited E. coli growth.

However, it is important to note that the effectiveness of silver nanoparticles is dependent on the seeding density of bacteria. One experiment found that for a fixed concentration of nanoparticles, the growth of low bacteria seeding densities was completely inhibited while higher seeding densities were not. These higher seeding densities were above and beyond cell densities relevant to infection. When grown in lysogeny broth medium suspension, growth curves were only slightly reduced at 10 μg/mL concentrations of nanoparticles and were reduced by about 50% after 9 hours in the presence of 100 μg/mL. As nanoparticle concentrations increased, some delay in growth was observed.

Silver nanoparticles have multiple mechanisms of antibacterial activity, making them a promising tool for combating bacterial infections. The ability of silver nanoparticles to inhibit the growth of various types of bacteria, regardless of their Gram classification, is a key advantage of this technology. The shape and concentration of silver nanoparticles also play a crucial role in their effectiveness against bacteria. Further research is needed to fully understand the potential of silver nanoparticles as a powerful antibacterial agent.

3. *Copper*: Copper, much like silver, has been found to possess antibacterial properties. When copper nanoparticles with a mean average diameter of 100 nm were added to agar plates, the survival rates of E. coli and B. subtilis were reduced by 90% at concentrations of 33.40 μg/mL and 28.20 μg/mL, respectively. The growth of both bacterial species was completely inhibited when the nanoparticle concentration exceeded 60 μg/mL. To compare the antibacterial effects of different metals, slightly smaller silver nanoparticles with a mean average diameter of 40 nm were also tested, but required higher concentrations of 58.4 μg/mL and 32.12 μg/mL to achieve a 90% reduction in survival rates for E. coli and B. subtilis, respectively.

   In another study, filter paper was impregnated with copper nanoparticles with a mean average diameter of 10 nm, which were then placed on inoculated agar plates. It was found that the minimum inhibitory concentration (MIC) of copper nanoparticles for E. coli ranged from 140-280 μg/mL depending on the strain, and was 140 μg/mL for S. aureus strains. The minimum bactericidal concentration (MBC) for E. coli strains ranged from 160- 300 μg/mL, while it was 160 μg/mL for S. aureus strains. B. subtilis was shown to be particularly sensitive to copper nanoparticles with an MIC of 20 μg/mL and an MBC of 40 μg/mL.

   In yet another study, the antibacterial effect of copper nanoparticles was observed and then eliminated by adding a copper ion-specific chelator, bathocuproine. This demonstrated the crucial role that copper ions play in the antibacterial mechanism. It is interesting to note that S. aureus, a Gram-positive bacterial species with a thick peptidoglycan layer that provides an additional structural barrier to harmful elements in the environment, was found to be more susceptible to the antibacterial effect of copper nanoparticles than E. coli, a Gram-negative species. This is somewhat surprising and counter-intuitive [27].

Application of Nanotechnology in Regenerative Medicine

Nanotechnology, an ever-evolving field at the intersection of science and engineering, has been demonstrated in the construction and restoration of various tissues that form the foundation of this surgical specialty. One of the most innovative developments in this field is the creation of electrospun nanofiber matrices, which have exhibited impressive results in both in vitro and in vivo experimental models for the regeneration of skeletal muscle tissue. The emergence of cartilage engineering, which has been successfully utilized in the realm of orthopedic surgery for many years, has paved the way for reconstructive plastic surgeons to utilize this technology in the regeneration of ear and nasal cartilage.

In particular, the engineering of auricular cartilage has proven to be a well-established technique for ear reconstruction, while the examination of nasal cartilage shows promising results for complex nasal reconstruction after cancer, trauma, or congenital defects. Moreover, the use of artificial skin for the treatment of skin defects has long been an important aspect of plastic surgery, and currently, scaffolds composed of polylactic and polyglycolic acids embedded with various growth factors are being used to enhance the healing process of skin tissues.

With precise manufacturing techniques and the utilization of novel biomaterials, the development of these products can provide an enhanced aesthetic appearance after reconstruction, which has been proven to be safe, reliable, and reproducible. As research in nanotechnology continues to progress, it holds significant promise for advancing the field of plastic surgery and improving patient outcomes.

Chapter 3. Drawbacks of Nantechnology in Medicine

Nanotechnology has certainly made its mark as both an innovative and groundbreaking solution in research and medicine. The application of nanotechnology in medicine has created new prospects in diagnosis, drug delivery, tissue engineering, and healthcare. Regardless of these diverse potentials, nanotechnology like anything else has its disadvantages and drawbacks in as a medical application.

A major limitation and source of concern with nanotechnology in medicine is its potential to become toxic. The application of nanotechnology in medicine causes concerns about their use as a biohazard, their biocompatibility and potential health hazards. The minute size of nanoparticles enables them to infiltrate many biological barriers and store up in vital organs, causing potential toxicity and long-term health defects. Also, the interesting properties of nanoparticles may interact with biological systems in unsee-able ways, which poses a challenge in the safe and effective use in medicine.

Another disadvantage of nanotechnology in medicine is the high cost associated with the development and production of nanomaterials and devices. The fabrication of nanoscale materials and devices requires specialized equipment, materials, and expertise, which may result in substantial costs. Furthermore, the regulatory requirements for the approval of nanotechnology- based medical products may also add to the expenses and time required for their commercialization.

Moreover, the lack of standardization in the characterization and evaluation of nanomaterials presents a significant challenge for the widespread adoption of nanotechnology in medicine. The characterization of nanoparticles is complex, and there are currently no standardized protocols for their evaluation. This presents a significant challenge for the reproducibility and comparison of results obtained from different studies, hindering the advancement of nanotechnology in medicine.

Additionally, there is a lack of understanding of the long-term effects of nanomaterials and devices on biological systems. The unique properties of nanomaterials may exhibit different behaviors in vivo compared to in vitro, which may lead to unexpected health consequences. Therefore, there is a need for long-term studies to evaluate the safety and efficacy of nanotechnology-based medical products, which may be time-consuming and expensive.

It is essential to note that, while nanotechnology holds immense potential in the field of medicine, we have to consider its limitations and disadvantages. The potential toxicity, high costs, lack of standardization, and unknown long-term effects are significant challenges that must be addressed for the safe and effective use of nanotechnology in medicine. Future research efforts should focus on overcoming these challenges to unlock the full potential of nanotechnology in medicine.

Chapter 4. Conclusion

The application of nanotechnology in medicine has brought about tremendous advancements in the field of healthcare. The integration of nanomaterials and devices in medicine has enabled the development of novel drug delivery systems, diagnostic tools, therapeutics, and tissue engineering scaffolds. These innovative technologies have the potential to improve patient outcomes and enhance treatment efficacy.

Regardless of its immense potential trough, the application of nanotechnology in medicine also presents certain challenges and limitations. The potential toxicity, high costs, lack of standardization, and unknown long-term effects are significant concerns that must be addressed to ensure the safe and effective use of nanotechnology in medicine.

To overcome these challenges, future research efforts should focus on the development of reliable and standardized protocols for the characterization and evaluation of nanomaterials. This would enable the reproducibility and comparison of results obtained from different studies, facilitating the advancement of nanotechnology in medicine. Additionally, efforts should be made to understand the long-term effects of nanomaterials on biological systems through extensive preclinical and clinical studies.

Moreover, regulatory agencies should establish guidelines for the approval of nanotechnology- based medical products, ensuring their safety and efficacy before their commercialization. Such guidelines should address the unique properties and potential toxicity of nanomaterials, as well as the requirements for their safe and effective use in medicine.

In conclusion, the application of nanotechnology in medicine has enormous potential to revolutionize the field of healthcare. However, its widespread adoption requires addressing the challenges and limitations associated with its use. Through collaborative research efforts, regulatory oversight, and technological advancements, nanotechnology can be harnessed to develop innovative medical technologies that improve patient outcomes and transform the field of medicine.

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