Chapter 6: Nanotechnology applications in drug delivery and therapeutics

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Abstract-

Nanotechnology or nanoscience addresses the examination and inferred applications created at nano level. In traditional drug development and delivery systems, methods typically involve either oral ingestion or intravascular injection. Currently, pharmaceutical companies face various challenges in drug development and delivery such as low solubility, low bioavailability etc.to overcome these the nanotechnology is used in medicines. The nanoparticles are frequently used in nanotechnology. They are used in treatment of various diseases and disorders. But they have some challenges in market growth. the rising number of fatalities from cancer is what is mostly responsible for the anticipated growth in the size of the worldwide nanomedicine market in the upcoming years.

Key words: Nanocarriers, Targeted Drug Delivery, Controlled Release, Theranostics

Introduction

The study and deduced applications developed at the nanoscale are the focus of nanotechnology or nanoscience. Scientist defined it as the "processing, separation, combination, and disfigurement of materials by one atom or molecule." [1-3].
1) Nanomaterials and electronics for advanced diagnostics and biosensors are the three powerful molecular improvements used as nanotechnologies.
2) Molecular drugs having applications in microbial robotics, proteomics, and genomics
3) Clinical tiny robots that increase normal physiological functions and provide prompt diagnosis and therapy. [4]

Nanostructured materials are prepared by two fundamental methodologies:

1) Bottom-up approach- The development of nanostructures is accomplished by collecting of atoms or molecules which are known as as building blocks. Self gathering of building blocks are acquired by controlled chemical reaction to yield nanostructures like nanotubes and quantum dots.
2)Top-down approach- It is accomplished by taking on procedures like carving or breaking where mass materials are diminished to frame nanostructures. Mass machining, surface machining and mold machining are utilized for diminishing mass materials.[5]

Limitations of Conventional drug delivery system-

Traditional medication development and delivery techniques usually include oral intake or ventricular injection. The systemic circulation distributes the medication throughout the body. Currently, pharmaceutical companies face various challenges in drug development and delivery mentioned below:

1)Low Solubility: A significant challenge encountered during the development of specific drug formulations is poor aqueous solubility. This issue negatively impacts the bioavailability of the drug , presenting a major hurdle for newfangled chemical entities.
2)Low Bioavailability: Bioavailability, a critical pharmacokinetic property of drugs, refers to the segment of a drug dose accessible for universal flow. Intravenous administration results in 100% bioavailability, while bioavailability decreases with other routes of administration (e.g., orally) due to incomplete absorption. Therefore, ensuring adequate bioavailability is essential.

3)Low efficacy- Efficacy is the maximum effect of drug achieved from administered dosage form. Low affinity results in low efficacy results in more time required for treatment of disease.

4)Fast excretion- Excretion is the process in which drug is thrown out from body. If the rate of excretion is high the drug remains in body for short period of time resulting in decreased effect of drug.[6]

Nanotechnology in drug delivery-

Researchers have used nanotechnology to create innovative medicine delivery methods and nanocarriers for the drug molecules are successfully delivered to the scene of the action. [6]

Mechanism of action of nanoparticles

One of the three general physico-chemical ways by which the drug is delivered to the tissue location by the polymeric drug carriers is: By the polymer nanoparticles expanding as a result of hydration and then diffusing out. Through an enzymatic reaction that causes the polymer to rupture, cleave, or degrade at the delivery site, freeing the medication from the inner core that was imprisoned. by the medication dissociating from the polymer and being released from the swollen nanoparticles through de-adsorption.

Release of Drugs using Nanoparticles: One of the following methods could be involved in the drug release from nanoparticles: Drugs that are adsorbed or surface bound desorb.

When compared to other bigger structures, the medication release rate from nanoparticles is higher. They might have a greater specific surface area for this reason. The kind of system (vesicular or matrix) and the drug loading process determine how the drug is released from the nanoparticles. Therefore, nanoparticles are typically not intended to prolong the drug's release.[7]

Advantages of Nanoparticles

Compared to other innovative medication delivery technologies, nanoparticles provide a number of benefits, including:

Unlike other colloidal systems that obstruct both capillaries and needles, their nanometric size enables them to be injected intravenously. Unlike other systems like liposomes and microspheres, they are tiny enough to fit through the sinusoidal gaps in the spleen and bone marrow. As a result, their blood circulation time is prolonged. Nanoparticles have a higher loading capacity because of their increased surface area.

The polymeric makeup of nanoparticles determines whether they function as a controlled release system. Because of their polymeric makeup, nanoparticles are more stable than liposomes and nanoemulsions, which are brittle by nature.
Additionally, nanoparticles aid in making medications and proteins more stable. To improve the specificity of nanoparticles, targeting moieties such as monoclonal antibodies can be affixed to them. When it comes to targeted and site-specific medication delivery, nanoparticles are secure and efficient. Nanoparticles have drawbacks. high surface energy that might cause biological systems to aggregate more. Low biological half-life due to rapid scavenging by the body's RES system. Any organic solvent that is left over after creating nanoparticles might be harmful. inadequate location and target specificity. high foreignness or immunogenicity.[7]

Applications of Nanotechnology

1) Nanotechnology in cancer treatment- Ethylene glycol mol. 1.0 has been employed by many nanoscientists to deliver therapeutic drugs to cancer patients. Cello-ethylene glycol enables NPs to bind to cancer cells and circulate in the bloodstream by preventing WBCs from identifying them as foreign mothers. Drug delivery using hydrogels was shown by IBM researchers. Thus, studies are being conducted to improve the capacity of medication-carrying nanoparticles to enter tumours.[13]
2) Nanoparticles as Anti-inflammatory- The ability of macrophages to identify and eliminate foreign particles quickly has given rise to a sensible method for macrophage-specific nanoparticle targeting.Macrophages are able to control inflammation in a variety of disorders due to their capacity to release a wide range of inflammatory mediators. As a result, in many human and animal disorders, macrophages are viable targets for therapeutic intervention.[14]
3) Regenerative Health Care: Its primary goal is to support the body's natural ability to heal itself. There are three primary methods in Regenerative Medicine: 1. Cell band 2. Based on biomaterials 3. The combination of tissue engineering techniques. Stem cells are capable of renewing themselves. Bioactive substances are applied to the regeneration of hard tissue.[13]
4) Bone regeneration: nanoscaffolds are offered for the formation of bone tissue. Nanostructured supports biomineralization As previously mentioned, carbon nanotubes are also utilized for osteoblast-like cell selection.[13]
5) Nanotechnology in CVS diseases- Protein nanoparticles are applied to the affected area of the artery in heart disease nanotechnology.Particles of super iron oxide (SPIO) are also utilized in this proposal. It fixes the faulty cardiac valve. Recognize and handle arterial plague Heart valves that have the incorrect

amount of collagen will be stiff and floppy. Thus, collagen and gold nanoparticles alter valve characteristics and replace a damaged heart valve without the need for surgery. (South Carolina University)[13]

6) Nanotechnology in Aging: Nanoparticles stand out as an excellent option for combating aging.
7) By incorporating drug molecules with nanodiamonds embedded in contact lenses, which come into contact with tears, they offer a more uniform delivery compared to eye drops.
8) Nanotubes: These tiny tubes are utilized in capsules designed to release insulin whenever there's an increase in glucose levels, helping to regulate blood sugar. Additionally, nanoparticles play a crucial role in treating autoimmune diseases by delivering medication directly into the bloodstream to target specific diseases.[13]

Market Status of Nanomedicines-

In the field of nanomedicine, research laboratories in academia are continually making progress. One important consideration is the extent to which these advancements lead to the creation of patents that can be licensed to new or existing startup companies. The rising costs associated with pharmaceutical development mean that not all improvements in drug delivery necessarily lead to the approval of new medications. However, it is evident that healthcare accounts for a growing portion of the gross domestic product in many developed nations. It is both cost-effective and patient-friendly to diagnose and treat patients as efficiently and non-invasively as possible. A significant recent trend is the emergence of "personalized medicine." Breakthroughs in genetics and proteomics have shown that individual patients who appear to have the same illness may differ significantly at a molecular level.

The precise nanoformulation may be customized according to laboratory tests and biomarkers. This movement has been initiated by companies such as Cerulean Pharma Inc. and Calando Pharmaceuticals . Combination nanomaterials, as mentioned previously, are poised to become the future cornerstone of the global medical market due to their enhanced overall performance.

Challenges for Nanomedicines-

Regarding financial challenges, most academic labs lack the necessary funding , leading to the termination of basic research studies at the lab level due to financial

constraints. Without financial backing, no basic formulation can advance to clinical trials. Hiring experts, acquiring bulk raw materials, scaling up production methods, compensating volunteers, and conducting precise measurement and evaluation all require significant financial investment. According to a survey, the majority of basic nanomedicine researchers agree that it is challenging to gain the interest of commercial companies . One researcher stated that companies are reluctant to get involved and are unwilling to jeopardize their investment in a competing product, as they often have their own product in development. Ethical concerns are present in all medications, including nanomedicines, and often revolve around cost-benefit analysis. Human clinical trials for nanomedicine are typically conducted on individuals with incurable diseases or those who have not responded to previous treatments . Despite the valuable information gained from these trials, most participants are unlikely to experience any direct benefits from their involvement in such research.

During this phase, numerous ethical concerns will emerge, including the overly cautious approach of ethical committees, the challenge of providing accurate information about risks, benefits, and potential outcomes of the trials, and other humanitarian issues that need to be addressed. These ethical considerations can significantly impede the progress of clinical trials

Additional obstacles in the development of new nanoformulations stem from the established regulations set by drug authorities, which can sometimes be unwelcome. Furthermore, differences between the regulations of the EMA and the FDA, which are subject to periodic changes, pose a further challenge. Once it's determined that a clinical trial for a new nanoformulation is necessary, various drug regulatory bodies, each with their stringent rules, will step in. While they can offer crucial insights and guidance, particularly in the planning and execution of clinical trials, their rules often differ based on national and ethnic backgrounds, and there might be a need for separate trials involving individuals from various national or ethnic groups. Sharing accurate and comprehensive data on the nanoscale properties and safety of nanomedicines to these regulatory bodies might also present challenges.

These obstacles can dampen the enthusiasm of researchers in academia to pursue or continue their foundational studies on nanodrugs, potentially leading to a decrease in the number of nanomedicines available in the market. Offering sufficient financial backing, greater focus on ethical considerations, and creating robust ethical review mechanisms, along with aligning regulations across different nations, could all streamline and enhance the transition from laboratory to market.[16]

Future Perspective

Growing healthcare costs have been a cause for concern for most industrialized and even emerging nations in recent years. The confidence that patients, the general public, and physicians have in the viability and safety of nanomedicines is crucial to the market's advancement. The public has to be better informed of the advantages, dangers, and safety concerns associated with nanopharmaceuticals in order to overcome this obstacle in the future. These uses could include both up- and down-regulating the immune system to combat allergies and autoimmune illnesses, as well as boosting the immune system to combat infections and cancer. All things considered, we think that the rising number of fatalities from cancer is what is mostly responsible for the anticipated growth in the size of the worldwide nanomedicine market in the upcoming years.

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