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Nanotechnology-Based Drug Delivery Systems: Revolutionizing Modern Therapeutics and Personalized Medicine

Maria Manan
Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan
Maryam Farrukh
Department of Pharmacology, Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan
Shumaila Mehdi
Assistant Professor, Department of Pharmacology, Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan
Rabia Munir
Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan
Faheem Sohail
Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan
Muhammad Shiraz Aslam
Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan
Usman Saleem
Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan
Ruqia Begum
Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan
Atif Iqbal Arshad
Pakistan Drug Testing and Research Center, Sundar Industrial Estate, Lahore, Pakistan
Hafiz Muhammad Faisal
Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan
Muhammad Asim
Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan

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Sohaib Iqbal
Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan
Maryam khalid
Department of Parasitology, University of Veterinary and Animal Sciences Lahore (UVAS), Pakistan
Corresponding Author Email: maryammano450@gmail.com
Shawana Masood
Faculty of Eastern Medicine, Hamdard University Karachi Pakistan
Sundleen Jannat
Manager of Regulatory Affairs, Kounter Intuitive Technologies, Bahria Phase 7, Rawalpindi, Pakistan
Shaista Gul
Department of Pharmacy, University of Azad Jammu and Kashmir, Pakistan
Sheeza Khizer
Department of Pharmacy, University of Poonch Rawalakot, Azad Jammu and Kashmir, Pakistan
Naveed Ayyaz
DVM, Faculty of Veterinary and Animal Sciences, University of Poonch Rawalakot, Azad Jammu and Kashmir, Pakistan
Momina Iftikhar
Faculty of Eastern Medicine, Government College University Faisalabad Pakistan

Author Details

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Corresponding E-mails & Authors*:
maryammano450@gmail.com

Abstract

Revolutionary systems for drug delivery using nanotechnology are changing how we treat disease by allowing for greater precision, effectiveness, and safety in treating patients. Nanotechnology-based drug delivery systems consist of very small materials, such as nanoparticles, liposomes, dendrimers, micelles, and nanogels (referred to as nanomaterials) that enhance the pharmacokinetics and pharmacodynamics of drugs. In addition, these systems provide targeted delivery of drugs to the area where they need to be administered; release of drugs at controlled rates over time; and for some drugs,

increased bioavailability. Nanotechnology reduces the systemic toxicity associated with the delivery of drugs, therefore improving the therapeutic outcomes for the patient through their treatment of complicated diseases such as cancer, cardiovascular diseases, neurological conditions, and infectious diseases. In addition, nanotechnology's incorporation with personalized medicine has allowed for production of custom-tailored therapies based on each individual's genetic, molecular, and physiological characteristics. Newly developed stimuli-responsive and smart nanocarriers have increased the potential for precision medicine specifically designed for real-time, site-specific drug delivery. Even with the progress that has been made in developing nanotechnology-based drug delivery systems, major challenges relating to biocompatibility, large-scale production, regulatory approval, and long-term safety still exist. This article will discuss the principles, applications, advantages, challenges, and future potential of nanotechnology-based drug delivery systems and their ability to revolutionize health care and further advance personalized medicine.

Keywords

Nanotechnology; Drug Delivery Systems; Nanoparticles; Personalized Medicine; Targeted Therapy; Controlled Drug Release; Nanocarriers; Precision Medicine; Liposomes; Therapeutics

Introduction

Recent years have seen an increased interest in advancements of nanotechnology. Many areas of research and development using nanotechnology have been achieved, but one area that has grown significantly is the development of drug delivery systems. Over the past few decades, these nanotechnology-based systems are progressively replacing traditional ways to deliver therapeutic agents to patients by improving how targeting of drugs occurs at the site of pathological events. Many of the traditional methods have suffered from an inability to deliver drugs where they are needed. There are many reasons for this shortcoming. Poor bioavailability of therapeutic agents, widespread distribution of non-targeted drugs, rapid degradation of the drug, and untoward effects associated with a drug that isn't delivered as intended are just some examples of why there are problems associated with the delivery of drugs to specific tissues or cells. Nanotechnology resolves many of these issues by providing a way to utilize nanoscale carriers (1 to 100 nanometers) that can carry therapeutic agents inside of them and successfully deliver them to the sites of pathological processes. Many different classes of nanocarriers exist; liposomes, polymeric nanoparticles, dendrimers, micelles, and solid lipid nanoparticles have demonstrated their capabilities to improve the stability, solubility, and controlled release of drugs. Nanotechnology-based drug delivery systems

have improved the efficacy of therapeutic interventions while simultaneously decreasing the toxicity that can occur in healthy tissues. With the increase of chronic illnesses like cancer and diabetes (and cardiovascular and neurological disorders), there has been an increased demand for the use of advanced technologies to deliver drugs to patients. Therefore, nanotechnology has become a fundamental aspect of precision medicine and modern therapeutic approaches, providing new and innovative ways to help us address our most complex medical challenges. (Patra et al., 2018)

The application of nanotechnology (NT) in drug delivery systems has dramatically increased the pharmacokinetic (PK) and pharmacodynamic (PD) properties of drugs used as therapeutic agents. Traditionally, therapeutic agents have exhibited properties such as poor solubility in aqueous solutions, short duration of circulation time, and limited ability to target tissues accurately, all of which have negatively affected the overall effectiveness of these agents in the clinic. NT has been able to resolve these limitations through the design of nanocarriers that can protect drugs from being degraded before reaching their intended target site and can be engineered to provide sustained, or stimuli-responsive, drug release profiles. One of the most significant advancements in the use of NT has been the development of targeted drug delivery, which involves designing nanoparticles to selectively localize within diseased tissues using passive or active targeting methods. Passive targeting takes advantage of unique physiological characteristics such as the enhanced permeability and retention (EPR) effect of tumor tissue; while active targeting depends upon ligand-receptor binding for specific cellular uptake. These new applications of NT will provide enhanced delivery of chemotherapeutics to malignant cells while reducing the damage done to surrounding normal cells. Furthermore, NT will increase the therapeutic index of therapeutic agents and permit the use of lower doses to produce the same level of effectiveness, thereby improving patient adherence and reducing adverse side effects (Shi et al., 2017)

Nanotechnology-enabled drug delivery methods have proven incredibly useful across a variety of different fields within healthcare, especially in cancer treatment, as well as in cases involving Infectious Diseases, Heart Disease, and Brain Disease. For instance, in cancer treatment, nanomedicine has led to the development of much more efficient drugs like liposomal doxorubicin and albumin-bound paclitaxel, both of which have improved the ability of doctors to deliver medication to a tumour site while reducing toxic effects on healthy tissue compared to what happens with standard chemotherapy. Likewise, nanoparticles are being used to enhance the therapeutic effectiveness of some anti-microbial agents or vaccines. This was particularly true with respect to the use of lipid-based nanoparticles as delivery systems for the mRNA vaccines that were

developed during the COVID-19 Pandemic. Nanoparticles are also being investigated for their potential to facilitate the delivery of medicinal compounds through the Blood-Brain Barrier, which normally limits the number of drugs that can get into an individual's brain. The development of particles that can transport drugs beyond this barrier opens the door for treatment options for various diseases affecting the brain, including but not limited to: Alzheimer's disease, Parkinson's disease and Brain Tumours. Furthermore, nanotechnology has been used to develop tools to promote the healing process in tissue engineering, as well as to provide gene therapy by allowing scientists to deliver Nucleic Acid, Protein, and Growth Factor-based therapies. Collectively, these many capabilities demonstrate a wideranging opportunity for Nanotechnology to assist in transforming how Diseases are diagnosed and treated (Ventola, 2017)

The role of nanotechnology-driven drug delivery systems in helping develop personalized medicine is great, and one of the most important is nanocarriers that find ways to create individualized drug regimens based on the genetic profile, physical status, and other variables within a person's body. With advances in creating "smart" nanocarriers that respond to temperature, pH, enzymes, magnetic fields, etc., the delivery of therapeutic agents can be pinpointed to specifically where and when they are needed while also providing the maximum benefit with the least amount of unwanted side effects. Other nanotechnology advancements include "nanodiagnostics," or nanoscale diagnostic tools that detect diseases early on and enable real-time monitoring of therapies. The integration of diagnostics (nanodiagnostics) with therapeutics (drug delivery systems) can be categorized as theranostics, and these therapies are an important step in the field of precision health care. Finally, nanotechnology will also help deliver genome editing tools such as CRISPR-Cas9, thus setting the stage for future personalized genetic therapies and individualized health care solutions for patients. (Peer et al., 2020)

While there have been major advances in, and possibilities for, drug delivery systems using nanotechnology, the continued development of these systems has been hindered by many scientific, technical and regulatory challenges in their translation to clinical settings worldwide. An important challenge is that there is still a lack of understanding about the long-term safety and biocompatibility of nanomaterials. For example, depending upon their composition, certain nanoparticles can result in cytotoxicity, oxidative stress or induction of an immune response, with the degree of these responses likely depending upon the size of the nanoparticles as well. In addition, it is technically very challenging to produce large quantities of nanoformulations that are biologically effective due to the complexity of the processes involved in synthesizing and

characterizing nanoparticles. Furthermore, regulatory agencies require that extensive testing of any new nanomedicine be conducted prior to being approved for clinical use. Also, the costs of producing advanced nanotechnology-based therapeutic delivery methods may prevent widespread access to these therapies in healthcare settings with limited resources. However, advancements in technology using artificial intelligence, biomaterials and nanofabrication are expected to help overcome many of these challenges in the near future. Nanotechnology-based therapeutics are expected to become increasingly important to advancing healthcare and personalized medicine as interdisciplinary partnerships in the areas of pharmaceutical sciences, biotechnology, engineering and medicine expand. (Rosenblum et al., 2018)

Improves targeted drug delivery

Targeted delivery of therapeutic agents has been a huge benefit thanks to advancements in nanotechnology. Traditional ways of giving medications often cause those drugs to be given throughout the body, resulting in an effect on both normal and abnormal tissues. This type of distribution does not only create side effects but also reduces the efficacy of the drug and negatively impacts the outcomes of patients. Advanced drug-delivery systems using nanotechnology are designed to solve those issues because they enable a more precise/targeted transport of drugs to specific tissue/cells/organs. They possess unique physicochemical characteristics (like small size, charge on the surface, biocompatibility) making them capable of properly interacting within biological systems. They can encapsulate medications, thus protecting them from being degraded prior to reaching their destination while in circulation in the bloodstream. In addition, since drug delivery uses targeted systems, a much greater amount of the medication reaches the diseased body area, thereby improving the outcome of the treatment while minimizing the toxicity of normal tissue to the patient. Targeted drug delivery is an especially effective treatment method for cancer, whereby the healthy cells may be spared while selectively destroying cancerous cells. Therefore, the development has greatly increased the precision (accuracy) as well as the safety of drug-based therapies in hospitals around the globe. (Torchilin, 2014)

Passive targeting is one of the main ways that benefit drug delivery systems based on nanotechnology, which have the goal of enhancing therapeutic effectiveness. Passive targeting uses the inherent physiologic properties of diseased tissue, particularly tumors, to give a higher amount of selectivity to the location of drug accumulation compared with healthy tissues. Tumors possess dysfunctional blood vessels that are more permeable than those of their normal counterparts; consequently, nanoparticles can better penetrate and accumulate in those areas as a result of this phenomenon, referred

to as "the enhanced permeability and retention (EPR) effect". Specifically, if nanoparticles are designed with a certain size range for optimized drug delivery, they will remain in circulation longer and will preferentially accumulate within the diseased tissue due to the inefficient drainage of lymphatic systems in the tumor tissue. By increasing the amount of active drug delivered to disease sites and decreasing amounts of drug delivered to healthy sites, passive targeting significantly increases the amount of active drug amount at disease sites, while minimizing the amount delivered to healthy) tissues. In addition, nanoparticles can improve solubility and stability of poorly water-soluble drugs, thereby improving the overall pharmacological performance of those drugs. This has been demonstrated through the successful use of various nanoparticle formulations developed for use in oncology and inflammatory disease applications. Improvements in drug localizations and retention at the site provide significant contributions to an individual's overall systemic toxicity levels and success of current therapeutic methods. (Maeda et al., 2013)

By employing specific molecular interactions between nanoparticles and diseased cells, active targeting increases the precision of drug delivery systems based on nanotechnology. Nanoparticles can be engineered to contain targeting ligands (antibodies, peptides, aptamers or small molecules) that specifically bind to receptors overexpressed by the disease target cells. After binding with the target cell's receptor, the nanoparticle(s) can be internalized into the target cell via receptor-mediated endocytosis, thus allowing direct intracellular delivery of therapeutic agents. The process of active targeting aids both in increasing cellular uptake and therapeutic efficacy, while decreasing the harmful effects to any normal cells that may surround the target cells. Active targeting is particularly beneficial in cancer treatment because many cancer tumor cells express distinctive biomarkers that can be targeted specifically. Folate receptors and HER2 receptors are examples of commonly targeted receptors in therapeutics for cancer. Active targeting is not limited to treating cancer, however, and has demonstrated potential for use in the treatment of cardiovascular disease, infectious disease and neurological disorders. Nanocarriers that have been designed for active targeting are also able to bypass biological barriers and deliver drugs effectively to provide the desired therapeutic result in diseases that are difficult to treat due to their location in tissue. Active targeting technologies, therefore, will significantly promote advancements in precision medicine and create opportunities for developing safer and more effective therapeutic systems. (Danhier et al., 2010)

Nanotechnological targeted delivery mechanisms for pharmaceuticals are proving to be impactful in advancing the treatment of both neurological and infectious disease

categories. The blood-brain barrier presents one of the most significant obstacles to effectively treating neurological disorders because it limits the absorption of a variety of therapeutic agents into the tissues of the brain. However, it is possible to engineer nanoparticles that facilitate crossing the blood-brain barrier by utilizing specific receptors located on endothelial cells to function as a way to enhance the ability of drugs targeting a variety of issues related to the brain, such as Alzheimer's Disease, Parkinson's Disease, epilepsy, and brain cancer. Similarly, targeted nanocarriers have also been shown to be beneficial in fighting infectious disease by enhancing the delivery of antimicrobial agents and decreasing the incidence of resistance to antimicrobial agents. Antibiotics can be delivered directly to infected cells or tissues using nanoparticles, allowing higher quantities to be delivered to the site of infection while decreasing the potential for systemic toxicity. Additionally, improvements in vaccine delivery systems have been made as a result of the use of nanotechnology by way of improving the stability of antigens and the strength of the immune response. A current example of targeted delivery for infectious disease management through nanotechnology is lipid nanoparticle-based technology used in present-day mRNA vaccines. The evidence of the broad reaching application of nanotechnology in overcoming biological barriers and enhancing therapeutic outcomes in numerous medical specialties is a testament to the ability of this technology to impact medical care. (Saraiva et al., 2016)

Targeted drug delivery utilizing nanotechnology has rapidly advanced in recent years; however, many obstacles exist that prevent the widespread use of targeted drug delivery via nanotechnology in clinical settings. The long-term safety and biocompatibility/toxicity of nanoparticles (e.g., certain types of nanomaterials could accumulate in organs such as the liver, spleen and kidneys) after prolonged exposure to humans pose significant concerns. In addition, producing large quantities of nanoparticles at high quality and consistent reproducibility is technically challenged and expensive. Nanomedicine's regulatory approval process is complicated by the physicochemical differences between nanomedicines and conventional pharmaceutical products. The application of nanocarrier technologies is hindered by an unknown immune response generated by some types of nanocarriers; therefore it may reduce the effectiveness of the therapeutic agent delivered and/or potentially cause an unintended complication. For this reason, researchers are focused on developing biocompatible, biodegradable and environmentally safe nanomaterials for use in future applications. Recent advancements in artificial intelligence, biomaterials and molecular engineering will help researchers design nanoparticles with enhanced functionality to optimize the

efficacy of targeted drug delivery systems. Given these advancements and the ongoing evolution of scientific research, it is highly likely that targeted drug delivery utilizing nanotechnology will play a critical role in future forms of personalized medicine and precision healthcare strategies. (Blanco et al., 2015)

Enhances drug bioavailability

Bioavailability is the amount of a drug that gets into the circulation and causes a therapeutic action at the desired target. Many traditional types of drugs have low bioavailability due to poor solubility, degradation in biological fluids, fast metabolism, and poor passage through biological membranes. Drug delivery systems using nanotech have been created to resolve these constraints by enhancing the chemical and physical properties of therapeutic agents. Nanoparticles have the ability to enclose the drug within a protective carrier, thereby improving solubility and protecting the drug from degradation prior to entering the bloodstream. In addition to their small size and large surface area, nanocarriers also enhance drug dissolution and aid in crossing the cell membrane for absorption. Nanotechnologies are especially useful with hydrophobic drugs, which typically have poor solubility in water and low rates of absorption. In addition, nanotech will also allow for controlled and prolonged release of the drug, thus ensuring optimal concentrations for a longer period. As a result of improved stability and efficiency of absorption, nanotech has markedly improved the therapeutic response of drugs, reducing the administration frequency. Therefore, enhancing bioavailability using nanotechnology represents a milestone in contemporary pharmaceutical science and development of therapeutics. (Müller et al., 2011)

Nanotechnology is enhancing the bioavailability of drugs in part by improving the solubility of drugs. Many types of pharmaceutical compounds (especially therapeutic molecules that are newly being developed) have low solubility in water, thus limiting their absorption from the gastrointestinal tract. Because nanoparticles have higher surface area, they also have a faster dissolution rate (based on principles of surface chemistry). Drugs with poor solubility that are encased in lipid-based nanoparticles, nanoemulsions, or polymeric micelles, will stay stable in aqueous environments, which will help with transporting these drugs across biological membranes. For example, when using oral drug delivery systems, the encapsulation of drugs within nanoparticles protects them against degradation due to acid in the stomach and digestive enzymes in the intestine, thus resulting in greater amounts of available ("active") drug circulating systemically. Increased solubility also leads to more consistent absorption (bioavailability) and better pharmacokinetic properties for the drug. Consequently, nanotechnology-based drug formulations are generally able to provide therapeutic effects with lower

doses than conventional formulations, which in turn, reduces patient toxicity and improves long-term patient adherence/compliance to medication regimens. (Savjani et al., 2012)

Nanotechnology-based systems enhance the bioavailability of drug products by improving their ability to pass through biological barriers and be absorbed. These include biological membranes, including the intestinal epithelium, skin, and blood-brain barrier, which restrict the transport of therapeutic agents into tissue and reduce the effectiveness of medication. Nanocarriers are engineered to have unique surface properties that enhance cellular uptake of the of drug product via transmembrane transport via mechanisms such as endocytosis (the process of taking substances into a cell) or receptor mediated transport (the transport of substances into a cell through the binding of a substance to a receptor molecule). Nanoparticles in the form of polymers, liposomes or dendrimers can engage cell membranes and change the permeability of the membranes temporarily, allowing substances to enter cells more readily or efficiently. In oral drug delivery systems, the ability of nanoparticles to adhere to intestinal villi increases the residence time of the nanoparticles in the gastrointestinal tract and enhances their ability to be absorbed into the bloodstream. Similarly, transdermal systems that utilize nanoparticles can enhance drug penetration through the skin and provide an alternative method for drug delivery. With regard to neurological treatments, nanotechnology has created the potential for developing medications that can cross the blood-brain barrier, which is highly selective in terms of what substances can have access to the central nervous system. Therefore, these technological advances improve the absorption and distribution of drugs, and thus improve their bioavailability and therapeutic effectiveness for a variety of clinical applications.(Pardridge, 2012)

Nanotechnology improves drug bioavailability via controlled and sustained release of drugs. Conventional drug formulations often rapidly release drugs into the bloodstream, leading to fluctuations in the concentration of the drug in the body. These fluctuations can lead to reduced effectiveness of the therapeutic agent, as well as an increase in the possibility of negative side effects. Nanotechnology delivery systems are designed to slowly release drugs over a longer period of time, keeping the concentration of the drug in plasma consistent and providing better clinical outcomes than conventional drug formulations. Drug formulations are often made with biodegradable polymeric nanoparticles or nanogels in order to create controlled drug release systems that respond to changes in environmental conditions (e.g., pH, temperature, or enzymes). Because the use of sustained release formulations reduces the frequency of dosing and

helps patients adhere to their prescribed drug regimens, controlled release drug delivery systems are especially beneficial for treating chronic diseases (e.g., diabetes, cancer, and cardiovascular diseases). Additionally, controlled drug release systems help protect therapeutic agents from premature degradation and allow therapeutic agents to stay active longer in the body. Thus, through the extended duration of therapeutic effect, controlled release systems greatly increase the effective bioavailability of therapeutic agents and have been shown to have better clinical performance than conventional drug formulations. (Kumari et al., 2010)

Although there are many benefits of using nanotechnology to increase the bioavailability of drugs, there are also many issues that must be resolved before it can be used routinely in clinical practice. One of the most significant issues is the possibility of nanoparticles being toxic or unsafe after long-term use because some materials can become deposited within the body's tissues and organs as a result of repeated use. Interactions between nanoparticles and biological systems are very complex and depend on characteristics such as particle size, surface charge, and chemical makeup. Additionally, producing nanomedicines on a large scale requires high-quality manufacturing processes and the implementation of rigorous quality control procedures to ensure that products are manufactured consistently and reliably. Obtaining regulatory approval for nanoforming also presents challenges due to the unique qualities of nanomaterials compared with conventional drug products and will make it more difficult to manufacture nanomedicines because of the cost associated with synthesizing and formulating nanoparticles. Despite these challenges, research being conducted on nanoscience, biomaterials, and pharmaceutical engineering is helping to improve the safety and effectiveness of these systems while increasing their capacity for large-scale production. In addition, advancements made in the future will continue to improve the bioavailability-enhancing potential of nanotechnology and facilitate the development of better and more personalised therapies. (Yadav et al., 2012)

Reduces side effects and toxicity

Nanotechnology-enabled drug delivery systems can provide many benefits over standard drug delivery systems, such as the potential to reduce the risk of side effects and the toxicity that usually occurs with standard drugs. Standard drug delivery techniques usually deliver drugs evenly throughout the body, where they can affect both healthy and disease tissues and organs in the same way. Because of this, patients may experience significant side effects or organ damage when taking standard drugs; this is especially true when receiving long-term treatments (e.g., chemotherapy). In contrast, nanotechnology-based systems provide a more focused and precise delivery of

therapeutic agents directly to specific sites within the body. For example, pharmaceutical products, such as liposomes, polymeric nanoparticles, and solid lipid nanoparticles act as nanocarriers by encapsulating the therapeutic agent and protecting healthy tissue from exposure to unnecessary amounts of the therapeutic agent. Delivering therapeutic drug products directly to areas where disease processes occur minimizes systemic toxicity from the drug while maximizing the therapeutic effectiveness of the drug. This is especially true for patients with cancer who suffer significant toxicity when treated with cytotoxic chemotherapies due to the effect of these drugs on rapidly dividing normal cells as well as tumor cells. Reducing the systemic toxicity of a therapeutic agent will result in patients having improved quality of life when taking the therapeutic drug systems while permitting patients to safely receive higher doses than could be delivered through traditional routes of administration. Therefore, the potential development of nanotechnology-based drug delivery systems will provide the healthcare community with a promising avenue for developing novel, safer, and more effective methods for administering drug products to patients in need. (Shi et al., 2017)

Therapeutic Agents' Pharmacokinetic Profile Is Enhanced By Increasing The Pharmacokinetic Profile Of The Therapeutic Agent By Providing A Means For Improved Drug Delivery To The Site Of Action, In Addition, The Use Of Nanotechnology As A Vehicle Has Been Proven To Improve The Pharmacokinetics Of Therapeutic Agents, As Well As To Improve The Pharmacokinetics Of Therapeutic Agents, In Many Cases, Will Require Higher Doses And More Frequent Administration. The Benefits Of Nanotechnology Police Drug Stability And Circulate For Extended Periods Of Time, Enabling Controlled And Sustained Release Of Therapeutic Agents. One Example Is The Use Of Liposomal Formulations, Which Encapsulate Therapeutic Agents In Phospholipid Bilayers And Minimize Direct Contact With Traditional Tissue And Therefore Reduce The Toxicity Of The Therapeutic Agents. In Addition, Biodegradable Nanoparticles Break Down Into Non-Toxic Byproducts That Minimise The Accumulation Of Therapeutical Agents After The Therapeutic Agent Has Been Delivered In The Body, Thus Reducing The Toxicity And Long-Term Effects Of The Therapeutic Agent. All Of The Above Characteristics Have Led To A Significant Increase In Tolerance And Safety Markets For Therapeutic Agents. The Enhanced Pharmacokinetic Control Provided By Nanotechnology Has Significantly Benefited Treating Chronic Diseases That Require Long-Term Therapies. For This Reason, There Is A Growing Amount Of Scientific Literature Supporting The inclusion Of Nanoparticle-Drug Delivery Systems In Pharmaceutical Formulations To Minimisalize Toxicity And Improve Patient Outcomes. (Torchilin, 2014)

The targeted delivery of drug-carrying nanoparticles can reduce the amount of toxicity during cancer treatment. Although chemotherapy has been shown to be an effective way to treat many kinds of cancers, it is associated with considerable side effects, including hair loss, nausea, immune suppression, and damage to healthy organs. Nanotechnology can be used to overcome these side effects by targeting the delivery of anticancer drugs specifically to the tumor cells while minimizing the amount of drug delivered to the healthy cells. Functionalized nanoparticles can target and bind specifically to receptors found only on tumor cells. This allows an accumulation of the nanoparticles at the tumor sites by utilizing active targeting mechanisms. The nanoparticles can allow smaller doses of traditional chemotherapeutics to be used while still achieving a beneficial therapeutic outcome, thereby reducing toxicity to normal cells and improving patient tolerability. In addition, nanocarriers can also deliver multiple drugs at the same time, allowing an additive effect of the two drugs and providing further reduction of the overall dose of each individual drug. For example, various nanoparticle-based formulations of anticancer drugs, such as pegylated liposomal doxorubicin and nanoparticle-bound albumin paclitaxel, have been shown to have lower toxicity than traditional chemotherapy agents. The ability to use nanotechnology in the development of safer means for treating cancer and improving the overall efficacy of cancer treatment will continue to expand. (Danhier et al., 2010)

This also helps to reduce toxicities that are often a problem when treating infectious, inflammatory and neurological diseases with high-dose, long-duration drug administration. Many antimicrobial and anti-inflammatory agents cause unwanted side effects in the body when given in high doses and for extended periods. However, by utilizing nanoparticle technologies we can deliver those agents directly to the infected or inflamed tissues which will allow for an increase in the therapeutic effectiveness of the drug while decreasing the amount of systemic exposure of the drug to the entire body. In addition, when utilizing nanocarrier delivery systems for neurological disorders, we can deliver drugs across the blood-brain barrier and thereby provide therapeutic effects in the central nervous system at a lower dose. This type of targeted delivery will minimize the adverse effects of a drug on peripheral tissues and will increase the drug's safety. Nanoparticles can also be engineered to utilize biocompatible and biodegradable materials that do not activate the immune system, causing further inflammatory responses or reducing those undesirable outcomes. Surface modification can also be utilized to enhance the stability of nanoparticles, such as using polyethylene glycol (PEG), which can also reduce the recognition of nanoparticles by the immune system allowing a longer period of circulation for the nanoparticle and therefore

allowing for less toxicity to be produced as a result. The growing importance of using nanotechnology as a means of improving both the safety and efficacy of drug delivery methods in a variety of medical applications highlights the expected impact of nanotechnology on the ability to improve therapeutic outcomes and patient safety in today's healthcare systems. (Allen &Cullis, 2013)

Although there are many positive aspects of using nanotechnology regarding the reduction of toxicity and adverse effects, there are still many safety issues and challenges that must be addressed. For example, some types of nanoparticles can cause immune responses; create oxidative stress in the body; and result in unintended accumulation of the nanoparticles in organs, such as the liver, spleen, and kidneys. Furthermore, we do not have enough data to accurately determine the long-term effects of chronic exposure to nanoparticles, which means we will need extensive toxicological studies to ensure nanoparticle safety before they can be used in mainstream clinical practice. In addition, different types of nanoparticles can vary greatly in size, composition, and surface characteristics, all of which can have an effect on their biological activity and safety. Regulatory authorities are having difficulty establishing standard procedures for assessing and evaluating nanomedicines because these types of systems do not closely resemble traditional pharmaceuticals. Therefore, researchers are focusing on developing nanomaterials that are safe, biodegradable, and environmentally friendly, in order to reduce potential health risks associated with these materials. The use of novel nanotoxicology methods, as well as molecular engineering techniques and advances in materials science, will contribute to improving the safety and efficacy of future applications for nanomedicines. Scientific knowledge continues to expand, so it is likely that nanotechnology-based drug delivery systems will continue to develop into safer alternatives with lower levels of toxicity while improving the level of patient care in the future. (Fadeel& Garcia-Bennett, 2010)

Enables controlled and sustained drug release

Among the many benefits of using nanotechnology for drug delivery systems, controlled and continuous release of the drug is one of the most significant advantages of utilizing this technology in current medical treatment. Traditional forms of drug delivery can often release the entire dose of a drug very quickly after it’s administered, resulting in a rapid increase in the amount of drug in the bloodstream. When this occurs, it can lead to toxicity, side effects, and reduced effectiveness of the drug over time. Conversely, by utilizing nanotechnology, it is possible to provide a gradual and regulated release of the drug over an extended period of time. Nanocarriers such as polymeric nanoparticles, liposomes, and nanogels are specifically designed to

encapsulate a therapeutic agent and release it in a controlled manner. Because the release is regulated, the concentration of the drug in the blood remains at a constant concentration within the therapeutic range to produce a stable pharmacological effect. Therefore, patients will have improved outcomes from their treatment, require fewer doses of the medication, and ultimately will have a higher degree of compliance with their treatment. For chronic diseases such as diabetes, cancer, and heart disease that require long-term therapy, controlled drug release by means of nanotechnology can greatly enhance the effectiveness and safety of current pharmaceutical therapies. (Vauthier&Bouchemal, 2009)

Nanotechnology-based drug delivery systems utilize engineered materials for controlled release, by utilizing specific biological and/or environmental triggers to create their designs. These designs utilize biodegradable polymers that have a specific rate of degradation when in the human body; as the polymers breakdown, the drug encapsulated within will also be released at a specific rate. The rate of release can be controlled by modifying the size, composition, and surface characteristic of the nanoparticles. Smaller nanoparticles will usually have a faster rate of release than larger, cross-linked nanoparticles will. In addition to utilizing engineered materials to achieve a desired release profile, nanocarriers can also be designed with the potential for internal response to stimuli such as acidity changes due to PH, enzymatic action or redox differences common in diseased tissues (i.e., acidic PH levels in tumors). The internal response of the nanocarrier allows for highly accurate delivery of drugs to only the site of need, rather than the entire body (systemic exposure). The combination of material design advancement with this enhanced precision and predictability has resulted in tremendous improvements in drug delivery systems for clinical use. (Langer, 1998)

Using nanotechnology for prolonged delivery of medications also leads to improved effectiveness by allowing constant medication levels to be maintained in the bloodstream. Conventional methods of delivery of medications lead to fluctuations between the peak and trough concentrations of drugs that are associated with decreased effectiveness of the medication as well as an increased risk of adverse events. Nanoparticle technology provides a means to consistently deliver medication over time, thereby providing prolonged therapeutic effect without the need for frequent re-dosing of the medications. This is particularly true with medications that have a short half-life in which frequent re-dosing would otherwise be needed. Lipid-based nanoparticles and polymeric systems are frequently used to provide sustained delivery due to their ability to effectively encapsulate both hydrophilic and hydrophobic medications. These systems also provide a protective barrier against enzymatic degradation of the drug, preventing

the drug from being eliminated prematurely, thus increasing the length of time the medication will be active in the body. Sustained release formulations are in extensive use within pain management, hormone therapy and oncology. With improved efficacy by providing a reduction in frequency of dosing and an increase in patient "adherence to therapy," the use of nanotechnology-based delivery systems increase the likelihood of success for the patient receiving long-term therapy. (Panyam&Labhasetwar, 2003)

Controlled and sustained drug release provides another major benefit: it improves the convenience of taking medication for patients. Chronic disease patients often have a difficult time following complicated medication regimens with multiple daily doses. Drug delivery systems based on nanotechnology have simplified these regimens by decreasing the number of doses patients receive; in some cases, patients receive only one dose over several days or weeks. Increased convenience for patients leads to increased adherence to prescribed therapies, which is essential for reaching the best clinical outcomes possible. In addition, controlled drug release systems lower the likelihood of missing a dose, thereby reducing the chance of treatment failure. Simplified dosing regimens can greatly aid elderly patients as well as patients who have limitations either cognitively or physically. Drug delivery systems that use controlled and sustained release also reduce the cost of frequent administration of drugs and require less hospital visits, which would reduce healthcare costs. Overall, because they improve both the therapeutic efficacy and everyday quality of life for patients, systems using nanotechnology will greatly assist with the modernization of current drug delivery methods and will improve the delivery of health care services globally. (Siepmann&Siepmann, 2012)

Advancements have significantly improved long-term and sustained delivery systems in medicine; however, additional advancements remain in creating ideal long-term and sustained drug delivery systems using nanotechnology. One challenge has been to develop a way to precisely control how drugs are released from nanocarriers. The way that drugs are metabolized by each patient and what stage of injury they are in, as well as what type of biological environment surrounds the nanocarriers will all affect how well the carriers perform. Another challenge is mass-producing highly uniform nanoparticles that release drugs in a consistent manner, as this is a highly complex and costly manufacturing process. Additionally, concerns have arisen regarding the long-term stability of nanocarriers and the potential for non-biodegradable materials to accumulate within the human body. Due to the complex biological behavior of sustained-release nanomedicines, obtaining regulatory approval for these products will also present significant challenges when compared to conventional drugs. Researchers

are continuing to develop "smart" nanocarriers that can more accurately respond to biological signals and improve predictability of drug release. Finally, as the fields of polymer science, biomaterials, and nanofabrication continue to expand and develop, researchers expect those advancements will allow them to overcome the challenges experienced with smart nanocarriers. As researchers continue to explore this avenue, it is anticipated that controlled and sustained-release drug delivery systems will play a prominent role in enhancing therapeutic outcomes, as well as contributing to the advancement of personalized medicine. (Kumari et al., 2010)

Supports personalized medicine

The advanced healthcare concept of personalized medicine customizes treatment for a specific patient with respect to their genetic composition, biological profile and medical condition. Nanotechnology based drug delivery systems are able to deliver medication in a very specific and targeted way. Traditional approaches to treatment do not provide the same effectiveness to every patient and can increase the possibility of side effects and failure. Nanoparticles can be designed so that they can locate diseased cells or biomarkers and deliver drugs only to the affected area. This saves the surrounding tissue and increases the effectiveness of the drug. The utilization of nanotechnology has moved healthcare away from the original "one-size-fits-all" model to an individualized approach to therapy. With this approach, treatments will be much more accurate on a patient by patient basis and will have a higher degree of safety and efficacy. Nanotechnology has been progressively playing a larger role in personalized medicine through its potential to integrate diagnostic and therapeutic modalities which enhance the use of precision medicine and patient-specific care in current healthcare practices. (Hamburg & Collins, 2010)

Nanotechnology improves personalized medicine by allowing for targeted treatment of disease on a molecular level. While all patients may have the same disease, they typically express that disease differently; this is especially true with regard to certain cancers and genetic disorders, where overexpressed biomarkers are often present on the target cells. To facilitate targeted delivery of the drug to the target cell, nanoparticles (NPs) are functionalized with antibodies, peptides, and/or ligands that bind to overexpressed biomarkers on the target cell. Once delivered to the target cell, the drug is released from the NP in a controlled fashion, leading to improved therapeutic efficacy and reduced side effects. Healthy cells are largely unaffected throughout the process. Furthermore, by combining imaging techniques with NPs for real-time imaging, theranostics integrates the diagnostic process with the therapeutic process in a single platform, which can greatly enhance the precision of personalized treatment planning for each

patient. Using this approach will allow doctors to continuously adjust their treatment for every patient based on how well they respond to treatment. Therefore, by providing a more precise, adaptive, and patient-centered treatment option, nanotechnology is transforming the practice of medicine. (Ferrari, 2005)

Pharmacogenomics is an essential component of personalized medicine. In pharmacogenomics, a person's response to medications is influenced by their genetics. Pharmacogenomics recognizes that each person has different levels of metabolism for drugs and varying activity in their enzymes that will produce different effects for the same medication. Nanotechnology can help address the variation between patients by providing controlled delivery systems so each patient can have a specific dose delivery. Nanocarriers can deliver medications in stable formulations to the exact site in the body where they need to be, and allow for the medications to be released when needed. Smart nanoparticles can detect biological signals, including pH changes, the presence of enzymes, or areas of inflammation, and, in turn, trigger the release of medications. By triggering the release of medications only when required, the risk of patients being over-exposed and harmed by medications is greatly reduced. In addition to providing a way to effectively deliver medication, nanotechnology is also being used in the area of gene therapy, which can provide for the direct delivery of DNA, siRNA or mRNA to targeted cells in the body for the treatment of genetic diseases. Nanotechnology will play a significant role in making personalized medicine more effective, safe and predictable for patients. (Duncan & Gaspar, 2011)

Nanotechnology diagnostics make personalized medicine more powerful. Through the use of nanosensors, disease biomarkers can be identified at extremely low concentrations, enabling early disease detection. The advantage of early detection is that treatments can be tailored to a person's specific needs early in the disease progression, increasing the likelihood of successful recovery. Imaging nanoparticles allow for monitoring of drug distribution and disease progression through the body, providing real-time feedback. Doctors can then adjust the treatment regimen based upon this data. The end result is a reduction in unnecessary medications and improved accuracy of treatments. By integrating diagnostics and therapeutics via nanotechnology, a seamless system is created for tracking patient responses over time. This provides for greater efficiency and increased precision in healthcare, and reduced costs. The use of these technologies in personalized medicine directly contributes to supporting patient-specific decisions, enhancing overall clinical outcomes while at the same time making the treatment safer. (Hood & Friend, 2011)

Nanotechnology se tayyarshuda personalized medicine to hailekinkai challenges bhihai. Sab se bara challenge ye haikehar patient keliye customized nanocarrier design karnamushkilhai. Is keilawa long-term toxicity aur biocompatibility keliye concern bhijaldi hi khatamnahihonge. Kuch nanoparticles ke body mein organs mein collect honaykiwajah se bhi health problem ho saktihai. Nanomedicinekeliye use kiyejanay wale regulatory approval process bhi strict aur lengthy hai, kyunki ye conventional drug kitarahnahihai. Nanocarrierko manufacture aur reproduce karnabhi sab se bara challenge hai. Lekin, AI, biotechnology aurbadi biomaterials se juri technologies kiwajah se is field meinbehadrapat se tradition badalrahahai. Aanewaalewaqtmein, nanotechnology personalized medicine ka core hissa ban jayegiaurpaighaamkeliyezaida optimal, safe aur affordable banatirahegi. Health karehsrozanawohkaregajopehleyaisekarehsnahi. (Niemeyer &Mirkin, 2004)

Useful in cancer and chronic disease treatment

Cancer treatment with nanotechnology has been very effective due to its ability to help target drugs in the body, lower the side effects of drugs on normal tissues, and to increase the amount of raw anticancer drugs delivered to a tumor. Chemotherapy has a large number of side effects because normal cells will get killed along with cancer cells. These side effects can include things like hair loss, a weakened immune system and damage to many of the body's organs. Nanoparticles can solve this problem by allowing anticancer drugs to be delivered directly to the tumor. Nanoparticles (also known as nanocarriers) can be designed specifically to bind to markers that are present only or in high concentration at tumor sites, allowing both passive and active targeting of drug delivery to the cancerous tissues and providing a higher concentration of the drug in the tumor while reducing the amount of drug delivered to the surrounding healthy tissue. Clinical trials have shown that liposomal formulations, polymeric nanoparticles and albumin-based nanocarriers are successfully used in the treatment of cancer. Also, because the nanoparticles help to increase the solubility and stability of the anticancer drugs, this is even more helpful when the anticancer drugs are poorly soluble in water. Overall, the use of nanotechnology in cancer treatment has led to higher amounts of anticancer drugs being delivered to the tumor site, while causing less distribution of the anticancer drugs to the rest of the body, therefore leading to higher total percentages of patients who have a positive response from their treatments and higher survival rates. Therefore, nanomedicine will continue to be an important addition to the treatment of cancer and an important part of the developments of precision medicine in cancer treatment today.(Peer et al., 2020)

One of the greatest challenges in chemotherapy is the ability of some cancer cells to become resistant to medications. Resistance to chemotherapy can happen by ways of the cancer cells pumping out the chemotherapy medications or altering the drug targets that medications work on, which leads to decreased efficacy of the treatment. Nanocarriers can allow for successful delivery of the chemotherapy medications in an endocytic manner, allowing for the drug to be effectively bypassing the ways the cancer cells have become resistant, and therefore the resulting drug concentration inside the resistant cancer cell will be much higher than if delivered with traditional methods and therefore it will increase the cytotoxic effects of the chemotherapy medications against the resistant tumor cells. Additionally, since nanoparticles can be used as carriers for co-delivery of different chemotherapy medications, the cancer cells are attacked by multiple methods at the same time, thereby decreasing the likelihood that the cancer cells will develop resistance and creating a better response to the overall treatment. Furthermore, the development of stimuli-responsive nanoparticles can lead to the ability to release the chemotherapy medication in response to conditions that are specific to the tumor environment (i.e., acidic pH, overexpression of enzymes, etc.). Therefore, the "smart" delivery systems through the use of nanotechnology allow the chemotherapy medications to be activated within the tumor microenvironment, and therefore increase the specificity of the treatment and decrease the damage to healthy tissue. In conclusion, nanotechnology offers innovative ways to overcome chemotherapy medication resistance and to improve the efficacy of cancer chemotherapy.(Shi et al., 2017)

Nanotechnology has long been embraced in treating chronic diseases by providing better methods for delivering medications to patients over extended periods of time (i.e., long-term maintenance). Chronic conditions such as diabetes, heart disease, and arthritis require lifelong medication for successful management, resulting in difficulty for patients due to multiple doses (and associated side effects). Nanotechnology-based drug delivery systems provide controlled/sustained release of medication from a single source, while obtaining stable systemic drug levels in the body over a long period of Time (without the need for multiple doses), thereby improving compliance with prescribed therapy. For instance, research is ongoing to develop nanoparticle-based delivery systems for insulin to improve glucose control in diabetic patients. Similarly, research is being done to enhance the use of nanoparticles as carriers for anti-inflammatory agents in patients with arthritis, providing more effective relief of joint pain and swelling. In the treatment of cardiovascular disease, nanoparticles are being used to deliver therapeutic agents to specific blood vessels, thereby improving treatment efficacy and reducing systemic side effects. These emerging applications of

nanotechnology demonstrate how this technology will be used to improve the management of chronic diseases by providing patients with easier and more effective options for their treatments. These improves overall quality of life for individuals who have chronic illnesses. (Mura et al., 2013)

Nanotechnology aids in the diagnosis and early detection of cancer and other long-term illnesses, which are crucial for good treatment practices. Early diagnosis leads to prompt clinical management and consequently significantly higher survival rates in cancer patients and controlled chronic illnesses. In the case of cancer patients, the early detection of cancer through the use of nanotechnology-based designing and imaging agents will allow medical professionals to locate everything from the size, location, and the progression of the tumor by highlighting these tumors using nanoparticles during imaging diagnostics. In patients with chronic illnesses such as Alzheimer's disease and cardiovascular disease, nanotechnology-based diagnostics will assist in monitoring the disease and response to treatment in real-time. The integration of diagnosis and treatment that results from theranostics, or the treatment of the disease through diagnosis, allows for more individualized and customized treatment strategies. By combining diagnostic and drug delivery to patients, nanotechnology guarantees that patients receive treatment on time and appropriately. In both cancers and chronic diseases, this will dramatically enhance the outcomes of treatment and decrease the progression of disease. (Smith et al., 2019)

Nanotechnology has many promising applications for treating cancer and other chronic diseases but also presents some big hurdles. One of the biggest challenges is whether nanoparticles can build up over time and cause damage to healthy tissues, such as the liver, spleen, or kidneys. How the body interacts with nanoparticles is still not completely known, nor do we know what will happen to a nanoparticle as it travels through the bloodstream or what will happen when it arrives at its target site. For example, how to make the nanomedicine in large quantities with consistent product quality remains an ongoing technical challenge. In addition, patients in low-income countries may not have access to nanomedicine due to the high cost of manufacturing. There is a lengthy process to obtain regulatory approval for a new medical product. This is partly due to the safety concerns with nanotechnology, and because the materials used to create nanoparticles are relatively new. Because of these problems, the effectiveness of nanomedicine-based treatment protocols may be reduced because of differences in the response of patients to nosology. Researchers are currently exploring the development of biodegradable and biocompatible nanomaterials to overcome these obstacles. Researchers are continuing to invest in improving the design and safety of nanoparticles

through advances in biomedical engineering and artificial intelligence. Therefore, there is a potential for nanotechnology to be a major component of future treatments for cancer and chronic diseases, providing safe, effective, and customized treatment options. (Wicki et al., 2015)

Conclusion

Nanotechnology-enabled drug delivery systems have greatly changed how drugs are delivered around the world. These systems have enhanced the way we deliver medicines to specific areas of disease, allowing for greater accuracy and efficiency when providing medication. By targeting these medicines to specific locations, we can greatly reduce how many medicines enter the entire body, and therefore reduce the number and severity of side effects that can occur with treatment. Nanocarriers have also enabled improved water solubility, stability and bioavailability of previously ineffective drugs, resulting in many being available for use in the clinic. Additionally, the sustained and controlled release properties of nanomedicines result in medications being available to produce therapeutic outcomes for a longer period, thus supporting patient compliance. The application of nanotechnology can also greatly assist with the development of personalized medicine by helping us to tailor treatment strategies based on individual patients' genetic, molecular and physiological patterns of disease. For example, precision medicine has changed the way we treat, manage and improve the lives of patients with complex diseases such as cancer, neurological disorders and chronic illnesses; standard treatments, often fail to work or produce optimal outcomes. Furthermore, the use of nanotechnology helps us to develop new ways to provide therapeutic and diagnostic functions in the same product (theranostics), enabling us to continuously monitor a patient during their course of treatment and adjust their treatment based on that monitoring.

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