

DEVELOPMENT AND EVALUATION OF NOVEL NANOPARTICLE-BASED DRUG DELIVERY SYSTEMS FOR TARGETED BIOMEDICAL APPLICATION

¹Rabia Munir, ²Shahzadi Filza Hassan, ³Sameen Qamar, ⁴Rimsha Tanveer, ⁵Waris Nawaz, ⁶Mudassar Ahmed, ⁷Amna Khalid, ⁸Muhammad Aqib Javed, ⁹Noor Ul Eman, ¹⁰Saeeda Rafi, ¹¹Subaina Rafi, ¹²Ghulam Abbas, ¹³Jawad Zaheer, ¹⁴Ali Abid Ansari

¹Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan

²Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan

³Faculty of Pharmaceutical Sciences, Riphah International University, Faisalabad, Pakistan
Riphah International University, Pakistan

⁴Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan

⁵Faculty of Pharmaceutical Sciences, Akhtar Saeed Medical and Dental College, Bahria Town, Lahore, Pakistan

⁶Institute of Microbiology, Government College University Faisalabad (GCUF), Faisalabad, Pakistan

⁷Department of Pharmacognosy, Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan

⁸Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan

⁹Department of Chemistry, Government College University Faisalabad (GCUF), Faisalabad, Pakistan

¹⁰Faculty of Pharmaceutical Sciences, Government College University Faisalabad (GCUF), Faisalabad, Pakistan

¹¹MPhil Biochemistry, Hazara University, Mansehra, Pakistan

¹²BEMS, Department of Eastern Medicine and Surgery, The University of Poonch Rawalakot, Azad Jammu and Kashmir, Pakistan

¹³Department of Pharmacy, The University of Poonch Rawalakot, Azad Jammu and Kashmir, Pakistan

¹⁴College of Physical Therapy, Government College University Faisalabad

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ABSTRACT

Nanoparticle drug delivery systems have been developed over the past few years and present new ways to improve the therapeutic efficacy, safety, and specificity of drugs within the scope of biological technologies. Our research aimed to develop a new type of nanoparticle for targeted drug delivery for patients suffering from chronic illnesses. The nanoparticles developed used biocompatible and biodegradable materials to create nanoparticles with enhanced drug encapsulation and stability and controlled release properties. The physicochemical properties of the nanoparticles developed were evaluated through multiple parameters, including size, surface area, zeta potential, and drug loading efficiency. In addition, the in vitro drug release profile of the nanoparticles was examined in relation to cellular uptake, biocompatibility and therapeutic efficacy using cell culture models. The results of these studies showed that the nanoparticles developed had a uniform shape and size, contained drug at a significantly higher level than did traditional pharmaceutical preparations, and released drug over time at a rate to maintain therapeutic efficacy. Moreover, the nanoparticles developed had an improved cellular uptake relative to conventional pharmaceutical drug formulations and enhanced therapeutic activity vs. traditional pharmaceutical formulations. The overall conclusion from the research is that nanoparticles have the potential to unambiguously provide targeted therapeutic agents and provide improved safety and specific delivery of therapeutic agents, in comparison to traditional dosing methods.

Keywords: Nanoparticle-based drug delivery, Targeted drug delivery, Biomedical applications, Controlled drug release, Drug encapsulation, Biocompatibility, Cellular uptake, Surface functionalization, Therapeutic efficacy, Nanomedici

Introduction

Nanoparticle based systems of drug Delivery have been regarded as one of the more promising new technologies to enhance the effectiveness of medicines by improving how some types of drugs work (their effectiveness) through the use of nanoparticles to create new formulations of existing injections (new formulations). Generally, traditional types of nurse injections have difficulty providing adequate drug concentrations in a patient due to the presence of low percentages of the medicines in the total volume of the medicines. In addition, these formulations are less stable and may experience very short shelf lives, which may lead also to poor drug safety profiles (increased risks of potentially harmful side effects). Additionally using common ways to deliver medicines to individuals normally suffer from limited access, poor control of delivery with respect to when a medicine is in a target tissue at a desired time, and may cause significant harm to healthy (non-cancerous) tissues surrounding where a medicine is delivered. There are many applications for the use of nanoparticles for drug delivery based on their unique physicochemical and engineering characteristics, including their size, surface area-to-volume ratios, and ability to be engineered to possess different surface characteristics. These characteristics lead to enhanced drug solubility; improved drug stability against degradation and enhanced controlled delivery; all of which can enhance the delivery of drugs from a nanoparticle to more therapeutic levels than would otherwise be done using conventional means. In addition, nanoparticles can also be used as drug carriers to cross biological barriers that are difficult to penetrate by conventional means (e.g. blood-brain barrier) leading to increased drug efficacy; and/or can be

used as a means to target a broad range of therapeutic drug compounds. As a result, nanoparticle deliverable systems are receiving significant interest for use as a means for treating common diseases/disorders, such as cancer, cardiovascular diseases, neurological disorders and infectious diseases. (Patra et al., 2018)

A large degree of success achieved by nanoparticle-based drug delivery systems is largely determined by the substances utilized for the fabrication of nanoparticles and their physical and chemical characteristics. There are several types of materials from which nanoparticles can be made; these include polymers, lipids, metals, ceramics, and hybrid nanocomposites. Polymeric nanoparticles have been widely researched because of their ability to degrade in the body, compatibility with living organisms, and ability to provide controlled drug delivery for prolonged periods of time. Lipid-based nanoparticles are important because they have very high efficiency in loading drug substances and their low toxicity profile makes them ideal for delivering drugs that are sensitive to their environment. Metallic nanoparticles (gold, silver, etc.) possess distinct optical, magnetic, and antimicrobial characteristics, which may be useful in both therapeutic and diagnostic applications. Advancements in the field of nanotechnology have also allowed for the creation of multifunctional nanoparticles that can combine imaging, diagnosis, and treatment on a single nanostructure (theranostic nanoparticles), thereby providing an opportunity to track progress toward health in real-time and monitor the effectiveness of therapies. Furthermore, surface modification methods can be used to functionalize nanoparticles with specific ligands or antibodies, increasing their ability to interact

with a target cell and thus increasing the precision of treatment. (Mitchell et al., 2021)

One of the main advantages of nanoparticle-based systems is the ability to provide targeted drug delivery. The conventional method of drug delivery in a therapeutic agent to the entire body can unavoidably negatively affect healthy tissue and elicit unwanted side effects. Compared to conventional drug delivery systems, nanoparticle systems can be designed to have selective accumulation of drug at diseased sites by both passive and, when appropriate, active means. Passive targeting is dependent on the phenotype of the diseased tissue. The abnormal vascular architecture of tumours enables the accumulation of nanoparticles in those tissues through what has been termed the enhanced permeability and retention (EPR) phenomenon. Together, the abnormal vascular characteristics and the EPR phenomenon enable the selective delivery of nanoparticles containing therapeutic agents to tumour tissue. Active targeting requires the addition of a targeting molecule (i.e., antibody, peptide, aptamer, or small ligands) to the surface of the nanoparticle. Targeting molecules will recognize specific receptors that are over-expressed on diseased cells. Targeting the diseased cells will improve the efficacy of the therapeutic agent by enhancing the uptake of the therapeutic agent by the diseased cell. This method of drug delivery will also provide a significant reduction in systemic toxicity and an increase in drug concentration at the targeted site of action. This type of drug delivery will be especially beneficial for patients receiving chemotherapy to treat cancer since the traditional method of chemotherapy can cause extensive damage to healthy tissue and can result in significant side effects. (Shi et al., 2017)

Even though nanoparticle drug delivery systems offer exceptional promise, several issues need to be resolved before these systems can be adopted across the clinical board. Among the top issues is

toxicity from the chemical nature of the particles, which are determined by their properties like, shape, size, charge, composition, and products formed upon degradation or disintegration. Interactions between nanoparticles and living systems are extremely complicated and may lead to immune response, or unexpected build-up in healthy tissues and organs. Long-term safety for inorganic nanoparticles that remain in biological tissues will be an important factor. Stability during storage and in the transportation and administration of nanoparticles remains one of the many remaining challenges of using nanoparticles in biomedicine. Also, variability in manufacturing and production processes can affect nanoparticle characteristics, resulting in the inconsistency of therapeutic effects of the particles. The large-scale production of nanoparticles with consistent quality is still technically and financially difficult. Furthermore, regulatory approvals require extensive assessment of safety, efficiency and quality standards which are further barriers to the commercialisation of nanomedicines. Researchers are working hard at this time to create better surface engineering, biodegradable materials, and stimuli modalities to expand nanoparticles' utility. With continued progress in nanotechnology, material science and pharmaceutical engineering, the safety and efficiency of nanoparticle formulations will improve, making it easier to translate laboratory-based research into clinical practice and commercial healthcare products. (Hua et al., 2018)

Novel drug delivery systems based on nanoparticles are necessary to promote targeted biomedical advances and improve patient therapeutic outcomes. Current research is focused on the design and synthesis of nanoparticles that have optimal drug loading capabilities, release rate control, extended blood circulation time, and better targeting efficiency. It has been found that complete characterization of nanoparticles, including their size, morphology,

surface charge, encapsulation efficiency, and release kinetics, allows for good performance of these systems. The *in vitro* and *in vivo* studies that have been performed also demonstrate that useful information can be obtained about the cellular uptake, biodistribution, toxicity, and therapeutic efficacy of these novel systems. Novel nanoparticle formulations are also under development as a method to provide therapeutic agents for patients suffering from cancer, inflammatory, neurodegenerative, and infectious diseases. Each of these nanoparticle delivery systems can provide precise treatment with fewer side effects than current therapies. In addition, nanoparticle-based platforms can facilitate the expanding area of personalized medicine by enabling the development of personalized, patient-specific therapeutic strategies. Continued advancements in nanotechnology have provided further opportunities for the integration of diagnostics, monitoring, and therapeutic approaches into a single multifaceted delivery system. (Mitragotri et al., 2021)

Drug delivery improves treatment efficiency

Today's medicine considers drug delivery systems to be a vital part of bettering the availability of treatments through getting medicines to their place of action. Many times with traditional methods of administering a drug, the drug does not stay in circulation long enough to be effective because of poor bioavailability, rapid metabolism of the drug and disseminated throughout the body. This can create a need for larger amounts of medicine to be given, consequently, the patient experiences higher toxicity and/or side effects. To address these issues, new advanced/unique methods of delivering drugs are being created that improve the pharmacokinetics and pharmacodynamics of the drugs. One method has been to create nanoparticles that can deliver medicine effectively. Nanoparticles are able to solubilize medicine (make it more dissolvable), improve the stability of medicine and create

controlled rates of release of the medicine once it enters the body. By encapsulating a medicine inside of a nanoparticle, it can help prevent the active drug from breaking down prematurely in the biological site. Nanoparticles can also be made to respond to certain environments in the body, so they can give a more accurate and precise amount of medicine when being delivered. (Zhang et al., 2022)

Effective drug delivery is based on the properties of the study materials (the vehicles used to deliver drugs) that will deliver drugs effectively. Nanocarriers can be engineered to provide the best fit for loading drugs, stabilizing a drug from breaking down before it gets to its target, and controlling how fast the drug is released over time. A variety of materials, such as biodegradable polymers, lipids, and inorganic materials, can be used to design nanocarriers, with each material having distinct advantages depending on the biomedical application. By modifying surface properties (e.g., charge) of nanocarriers, scientists have been able to increase the time the nanocarrier remains in the bloodstream and decrease the likelihood that the nanocarrier will be recognized and removed by the immune system. For this reason, nanocarriers that are modified to have longer circulation times have an increased probability that a drug will be delivered to targeted tissue in sufficient amounts to produce a therapeutic outcome. In addition, nanocarriers can also be modified to respond to local or systemic stimuli (e.g., the acidity of the tissue, the temperature of the environment, or the enzymatic activity in the tissue) to provide an even greater efficiency in drugs being delivered. Smart drug delivery systems that require local conditions adhere to the principles of drug delivery by ensuring that drugs are delivered to the intended location without damaging adjacent healthy tissues. Thus, optimizing the properties of drug delivery systems has led to greater therapeutic outcomes for diseases that require

long-term controlled therapy. Continued advancements in material science and nanotechnology will provide new and improved capabilities for drug delivery systems, leading to more efficient, reliable, and clinical applications across all areas of health. (Kumar et al., 2023)

Targeted delivery of drugs is an important step in enhancing the effectiveness of a treatment by ensuring that the agent will be delivered to only the diseased tissue, and not the entire body, thereby significantly lowering the side effects while producing a greater concentration of the drug at the target area. The use of nanoparticles is one method to achieve targeted delivery via passive means of action by accumulating at a tumor site due to leaky vasculature, and/or active means of action through the ligand coating on the nanoparticles, which allows them to be recognized by diseased cells. This targeted approach enables enhanced cellular uptake of the therapeutic agent with a concomitant increase in therapeutic efficacy. For instance, during cancer therapy, targeted delivery systems allow for more effective destruction of tumor cells while minimizing the collateral damage to healthy tissue. Targeted delivery systems can also be used to rapidly treat neurological and cardiovascular diseases where localized drug delivery is critical. With the advancement of ligand-directed targeting to enhance the specificity and efficiency of drug delivery systems, the field of precision medicine has made great strides in developing treatments that are tailored to each individual's needs. The future of targeted drug delivery is expected to be increasingly efficient and widely utilized in clinical practice as additional research is conducted. (Ahmed et al., 2024)

The performance of drug delivery systems is also affected by how they interact with the biological environment where they will be delivered, which may impact how long they last (stability), how long they will circulate in the blood (circulation time), and whether they provide a therapeutic

effect (therapeutic effect). A key issue associated with drug delivery is the rapid clearing of drug delivery systems from circulation due to the effects of the immune system that can result in decreased therapeutic effect. To improve the stability of drug delivery systems (specifically nanoparticles) and extend their circulation half-life in blood, the most common modification performed is called PEGylation, which involves adding polyethylene glycol (PEG) to the surface of the nanoparticles. PEGylation reduces the amount of protein that adheres to the nanoparticle surface and aids in preventing recognition by the immune system, thus improving delivery efficiency. Though there is evidence that PEGylation improves stability and circulation time for nanoparticles, the major issues of potential toxicity of the nanoparticles, accumulation of the nanoparticles in non-targeted tissues, and unpredictable responses to the nanoparticles from the biological system remain as significant barriers to improving delivery efficiency and developing reliable drug delivery systems. The intricacy of biological systems makes it difficult to provide consistent delivery across all patients. Many researchers are actively conducting investigations to create safe and predictable drug delivery systems, with an emphasis on utilizing biocompatible and biodegradable materials for the development of drug delivery systems. Continued advancement and progress in the area of nanomedicine are focused on eliminating barriers to establish improved, effective drug delivery systems for use in a clinical setting. (Singh et al., 2021)

The advancement of drug delivery systems is leading to more effective treatments than traditional methods that require long periods of administration to maintain therapeutic levels. At the same time, delivery systems founded on nanoparticles provide for even more precise control over dosing and the kinetics of medication release than would typically be

expected. As such, decreased frequency of administration and improved compliance may be realized through the utilization of these systems. In addition, the use of nanoparticle-based systems to administer multiple therapeutic agents simultaneously (i.e., combination therapies) provides the potential for enhanced treatment outcomes. Further, the development of theranostic drug delivery systems that can perform both diagnostic and therapeutic functions (i.e., diagnosis and treatment as a single entity) will provide even greater efficiencies by allowing for real-time monitoring of patient progress with the ability to modify treatment regimens by the physician in response to their response to treatment, allowing for more individualized healthcare. Therefore, through continued research and development, future advancements will lead to even greater efficiencies and widespread use of modern drug delivery systems. Ultimately, these advancements will allow for the development of next-generation therapies that are more secure, more accurate, and substantially more effective in treating complex diseases. (Verma et al., 2023)

Conventional drugs have low targeting and side effects

Over the last several decades, traditional drug delivery systems have been used extensively in clinical settings; however they have poor targeting efficiency and result in side effects. With traditional administration routes (oral or intravenous), drugs are administered systemically through a poorly targeted way, impacting diseased and healthy tissues at the same time. The non-targeted administration of drugs results in decreased therapeutic efficacy and increased risks of toxicity to patients. In addition, patients experience adverse reactions as a result of non-targeting, thus limiting the amount of drug that can be given safely to the patient. Further contributing to the problem with conventional drug delivery is the rapid metabolism and

clearance from the body of the majority of conventional drugs, meaning bioavailability and therapeutic length of action are often not optimal; requiring repeating administration of medication, thus increasing risk of adverse events and discomfort to the patient. In the case of cancer, this challenge is compounded by the fact that most chemotherapeutic agents will destroy both tumor and normal cells, causing additional complications for the cancer patient (e.g., immunosuppression, nausea, organ toxicities). One of the key challenges in pharmacology is the limited ability of conventional drugs to effectively deliver a drug to specifically targeted diseased cells. Consequently, researchers have made considerable efforts to create new advanced drug delivery systems that provide enhanced targeting efficiency and decreased systemic toxicity. The goal of advances in drug delivery systems is to improve treatment outcomes while minimizing the adverse effects associated with traditional approaches to drug therapy. (Johnson et al., 2021) Conventional methods for delivering drugs do not provide effective means to target diseased tissue precisely because there are no naturally occurring mechanisms to deliver these agents specifically to diseased areas. After a drug is administered, it circulates the body and interacts with numerous other biological systems randomly. Inevitably, this random distribution diminishes the concentration of drug delivered to the target site and diminishes the therapeutic effect. Additionally, many drug compounds are poorly able to penetrate biological barriers such as the blood-brain barrier, further limiting their ability to target specific sites. Therefore, in order to achieve a desired therapeutic effect, large quantities of drugs are usually needed and these large quantities increase the risk of non-specific toxicity throughout the body and can lead to damage to organs responsible for drug metabolism and clearance, e.g. liver and kidney. The inherent inter-patient variability in drug

distribution and response due to variability in metabolism and physiology makes it impossible to provide predictable therapeutic outcomes with conventional therapies. The lack of site-specific activity and the variability in drug metabolism and response not only limit the efficacy of conventional drug therapies but also result in increased burden on organs responsible drug metabolism and clearance (e.g. liver, kidney). (Lee et al., 2022)

The major cause of adverse effects seen with conventional drugs is attributed to their non-selective action throughout the body. The action of a drug on both healthy and sick cells will disrupt normal physiological function, resulting in many different types of side effects. These range from minor symptoms, such as dizziness or nausea, to potentially serious events, such as organ damage or suppression of the immune system. For instance, some immunosuppressive and chemotherapeutic agents target cells that are rapidly dividing; however, they also affect other rapidly dividing cells (i.e., cells located in the bone marrow, cells in the digestive tract, and cells in hair follicles). Therefore, when these agents are administered to patients, they generally experience significant discomfort due to the effects of the medications on their healthy cells. The extent of the side effects produced by a drug will determine its maximum safe dosage, which will ultimately limit its overall therapeutic benefit. In addition, long-term use of some drugs can result in cumulative toxicity and chronic health problems. The potential for developing side effects is also affected by individual characteristics such as the age of the patient, their genetic composition, and any existing medical disorders. Accordingly, these individual differences create challenges in accurately predicting how drugs will respond to patients from person to person. (Martinez et al., 2020)

The shortcoming of traditional dispensing medications is their lack of prolonged, controlled

release of medication into the bloodstream; that is, many medications have a rapid absorption & elimination rate, providing fluctuations in concentrations from one time period to another and limiting therapeutic effects. This fluctuation also requires the patient be properly compliant with the scheduling of multiple doses of that particular medication, or have the possibility of missing an entire dose, thus impacting patient compliance and contributing to the likelihood of unintentional overdose (over-exposure) or under-treatment from missed dose. In granting inconsistent or fluctuant levels of medication for an extended period of time, both scenarios are harmful to the patient. Moreover, the traditional dispensing methods of medication generally do not have the ability to modify their release rate to accommodate for the changes in disease progression or patient-specific criteria. Therefore, the lack of ability to adapt and adjust as to how a medication is released and absorbed within the body results in diminished effectiveness for longer period(s) of time. The maintenance of stable medication concentrations is crucial in managing chronic diseases such as diabetes, hypertension, and cancer. However, most traditional dispensing systems are unable to provide the required stability of medication concentrations over long periods of time to ensure the best therapeutic outcomes will be achieved. The inability of providing controlled and sustained release has been deemed one of the most significant detriments to the use of traditional medication delivery methods. The need and desire for alternative systems that provide controlled release profiles (consistent therapeutic concentrations) with improved pharmacokinetic properties have generated significant interest in research for the potential development of such advanced technologies that increase the performance of medications while reducing the effects on the patient and

enhancing overall patient quality of life. (Brown et al., 2023)

The combination of low targeting efficiency (whereby only a small part of the administered drug reaches the desired site of action) and high side effects associated with standard drug delivery systems has a substantial impact on the overall success of treatment, as well as the well-being of patients. These two issues contribute not only to decreased effectiveness of therapy, but also to increased costs for the healthcare system through extended length of treatment and the need for ongoing management of side effects. Many patients do not complete their entire course of therapy due to severe adverse reactions and therefore experience poor clinical outcomes. The lack of precision of standard therapies also limits their use in the treatment of complex illnesses, which often require targeted therapy at the cellular or molecular level. Thus, there is a current and urgent need for innovative drug delivery systems that provide enhanced selectivity and reduced toxicity. Currently, there is an increasing amount of pharmaceutical research that is being devoted to the development of modern technologies such as nanoparticles, liposomes, and smart drug carriers that will address these limitations. These new delivery systems are designed to improve drug distribution, enhance drug targeting ability, and minimize adverse effects on normal tissues. By eliminating the deficiencies of conventional drugs, these innovative delivery systems have the potential to revolutionise treatment of diseases and enhance patient survival rates. The shift from the use of conventional delivery systems to the use of targeted delivery systems represents a significant advance in medical science and a direction toward improving the safety and efficacy of therapy. (Wilson et al., 2024)

Nanoparticles enable targeted drug delivery

Nanoparticles have created a new way to target drugs to improve efficiency of sending drugs

directly to areas of disease. The tiny size allows for rapid movement through blood vessels and the ability to bind to the cellular and molecular level. This enables the delivery of drug to very specific areas of the body when compared to traditional methods of delivering drugs that do not reach certain areas of tissue or types of tissue. Nanoparticles can be modified with precise physicochemical properties to increase the stability, solubility and amount of medication that can be loaded on the particle. One of the most important advantages to using nanoparticles as a method of drug delivery is the decreased risk of drug action on surrounding healthy tissues by reducing the amount of drug that can be exposed to surrounding tissues. Therefore, when we use nanoparticles for targeted delivery of medications such as chemotherapy for patients with cancer, the tissues associated with the tumor will receive a greater amount of chemotherapy than the normal systemic tissues, which means that the chemotherapy will be able to have a more potent effect on the tumor as well as reduce the overall toxicity to the body. Additionally, when nanoparticles are used as a delivery vehicle for chemotherapy, the medicinal agent that the nanoparticles contain is protected from being damaged prior to arrival at the area of action; therefore, the medicinal agent will remain active once it arrives at the target area. Lastly, the surface of the nanoparticle can be modified with functional groups that increase their affinity for their intended target and subsequently improve the amount of drug that is taken up by cells that have the disease in question. These factors, in combination with one another, allow for nanoparticles to be an effective delivery system in the field of precision medicine and allow for improvements in both the efficiency of treating patients and the expected outcomes of patients for a wide range of illnesses. (Davis et al., 2022)

Principles governing targeted delivery of drugs via nanoparticles are based on receptor interaction-

mediated surface functionalization. Ligands (such as antibodies, peptides, or small molecules) may be conjugated to the surface of nanoparticles, allowing them to specifically recognize and bind to a target (disease) cell. Using this active targeting mechanism greatly improves the amount of drug delivered to the target site and decreases the amount of drug distributed to surrounding, healthy tissue. By improving the efficiency of the therapeutic, side effects from the therapeutic are also greatly reduced when using nanoparticles as “active” drug delivery vehicles. Nanoparticles may also be designed to respond to specific biochemical conditions, such as an acidic pH of the environment or environmental conditions that are rich in enzymes (such as is found in diseased tissue), which provides for controlled release of the drug at the desired site. Smart delivery systems ensure that drugs remain dormant while circulating throughout the body, and become immediately active upon reaching the intended site. Improvements made in the precision of delivery will result in less unintentional exposure of healthy organs to toxic drugs. Additionally, nanoparticle-based delivery systems can be readily modified to fit the needs of various disease states, making them very versatile for clinical applications. Ongoing advancements in nanotechnology have greatly improved the effectiveness of these targeted delivery systems in both efficacy and reliability for modern biomedical applications. (Nguyen et al., 2023)

By increasing circulation time and stability in the biological environment, nanoparticles improve the ability to deliver drugs’ targeted effects. The immune system clears many drugs very quickly from the body, resulting in decreased drug efficacy. Researchers can help address this problem by coating nanoparticles with certain materials like polyethylene glycol (PEG) to prevent detection by the immune system. This enables nanoparticles to remain in circulation longer, thereby increasing the likelihood of

reaching their target. Thus, longer circulation time results directly in increased targeting efficiency and ultimately improved therapeutic outcomes. Nonoparticles can transport hydrophilic and hydrophobic drugs, thereby making them appropriate for numerous medical uses. Additionally, nanoparticles can co-transport multiple drug products, thus allowing for the potential use of combination therapy to treat complex diseases. Nanoparticle systems have controlled-release capabilities that provide for gradual drug release at the target location, thus creating a continuous and effective therapeutic level of drug within the body. Consequently, nanoparticle systems are much more effective than traditional drug delivery methods. Ongoing research is being conducted to continue improving nanoparticle design for improved stability, safety, and targeting capabilities in clinical applications. (Patel et al., 2021)

As stated in Section A, one of the ways that nanoparticles allow for targeted drug delivery is through what is called passive targeting via the Enhanced Permeability and Retention (EPR) effect. Tumor (cancer) tissues have typically abnormal blood vessels that have larger gaps (fenestrations) than the blood vessels found in normal tissues, thereby enabling nanoparticles to aggregate in these abnormal areas. Poor lymphatic drainage in tumors also facilitates retention of nanoparticles within the disease site. The ability of nanoparticles to naturally accumulate within tumor regions increases drug concentration in an area where drug concentration is most beneficial to the treatment of cancer without the necessity for surface modification. The EPR effect can largely enhance therapeutic effectiveness in cancer therapy because concentration of drug in the area of the tumor at the time of treatment is required for efficacy. Successful accumulation of nanoparticles through passive targeting varies on a tumor-by-tumor and biological basis. Therefore, scientists have been developing ways to enhance

EPR-based targeting by improving the overall design of nanoparticles. Many factors affect optimizing passive targeting of nanoparticles including particle size, particle shape and surface charge. The combination of active and passive targeting approaches have positively increased the ability of nanoparticles to deliver therapeutics. This dual targeting approach increases therapeutic effectiveness and also represents an important development for nanoparticle-based drug delivery systems. (Kim et al., 2024)

Nanoparticles used in targeted drug delivery have improved the availability of modern therapeutic approaches by improving drug distribution to their target site, thereby improving accuracy of delivery and decreasing toxic effects associated with non-targeted delivery of medications. This allows drugs to be delivered exclusively to the targeted area and for the drug to achieve its full potential therapeutic effect while minimizing damage to surrounding healthy tissue. Through targeted administration, the amount of drug needed to achieve the desired therapeutic effect can be reduced, thereby improving patient compliance by reducing the incidence of side effects. Nanoparticles are currently being widely used in the treatment of cancer, neurological disorders, cardiovascular disease, and infectious disease due to their ability to work well in a variety of ways. Because they have the ability to provide both diagnostic and therapeutic functions, they also support real-time monitoring of disease progression. This enables the adjustment of treatment strategies based on the patient's response to the treatment, resulting in more individualized and effective healthcare. There are many challenges during the development and commercialization of nanoparticles being used for targeted drug delivery; however, due to continued advancements in the field of nanotechnology, these challenges are gradually being overcome. In the future, many conventional forms of therapy

are expected to be replaced by targeted delivery systems, which will play a significant role in the future of medicine. Today, nanoparticles signify a major advancement toward the development of safer, more effective, and more accurate treatment methods in today's healthcare system. (Sharma et al., 2023)

Targeting: Passive (EPR) and Active (Ligands)

Nanoparticle based targeted drug delivery can be classified into two main types of mechanisms: passive targeting and active targeting. The purpose of both types of targeting is to enhance the delivery of therapeutic agents to sites of disease while limiting their delivery to surrounding areas of healthy tissue. Passive targeting relies heavily on the EPR (enhanced permeability and retention) effect that occurs in many tumors because of their abnormal, leaky vasculature and the fact that they have extremely high blood flow compared to normal tissues. Because the vascular systems of many tumors are unable to maintain their normal vascular integrity, they allow nanoparticles to accumulate naturally within the malignant tissue without requiring any sort of modification of the surface of the nanoparticles used for pharmaceutical delivery. Conversely, active targeting requires that the surfaces of nanoparticles be modified with specific ligands (e.g. antibodies, peptides, or small molecules) that can specifically recognize and bind to receptors that are overexpressed on diseased cells. The use of combination techniques for passive and active drug targeting can create a high level of efficacy for delivering therapeutic agents to areas of disease (especially cancer). By increasing the amount of drug present at the target site while also decreasing the amount of drug delivered to any healthy tissues around the target site, these two types of targeting strategies improve the efficacy of treatment. More recently, combining both types of targeting approaches has been the main focus of researchers in nanomedicine in order to develop more effective,

precise, and clinically applicable drug delivery systems. (Zhang et al., 2023)

Nanoparticles are targeted via enhanced permeability and retention (EPR) effect; abnormal blood vessels in tumors allow for greater permeability of blood vessels to pass through the cells of the endothelium and deposit in the micro environment of the tumor. Because of the poor drainage of lymph from tumors, nanoparticles are not drained from the tumor and are retained much longer at the site of disease. The EPR effect can enable selective accumulation of nanoparticles that contain drugs in the tissue that is cancerous, without the need for specific ligands to target the drug. The efficacy of EPR effects in patients may differ, depending on the tumor type, size, biological environment, and variability between individuals. The EPR effect continues to be one of the most basic principles of nanoparticles to deliver drugs. Researchers are continuously attempting to improve how nanoparticles accumulate via EPR effects by optimizing the size, shape, and surface of the nanoparticles. For example, smaller nanoparticles will penetrate deeper into tumors than larger nanoparticles, and surface modifications will improve circulation time. The EPR effect has contributed greatly to the development of cancer nanotherapies and will be an area of continued investigation to improve the efficiency of passive targeting for application in clinical practice. (Wang et al., 2022)

The use of ligands that are functionalized on the surface of particles provides a mechanism for delivering drugs directly to diseased tissues. The ligands target receptors which are in abundance on diseased cells (i.e., the target). The target cells are typically characterized by overexpression of specific proteins that have been shown to bind specifically with the ligands. Once the targeted nanoparticles arrive at the target location, the ligand-receptor interactions will enhance the number of nanoparticles that enter the target cell

via receptor-mediated endocytosis. Another beneficial effect of this process increases the intracellular concentration of the drug, thus reducing the exposure of healthy tissues to the drug. Active targeting is an effective approach for use in cancer therapy, where tumor cells can contain unique surface proteins that allow them to be distinguishable from the surrounding healthy tissue. This technology can also be used as a delivery method for penetrating biological barriers (blood-brain barrier). An adequately designed, ligand-conjugated nanoparticle will include consideration for the strength of the ligand binding, stability and biocompatibility of the particles themselves. Current advances in molecular biology and nanotechnology are making active targeting technologies more efficient and thus play a more essential role in precision medicine and personalized therapy strategies. (Chen et al., 2024)

Combining active with passive targeting forms a synergistic interaction between the two techniques which increases the overall efficiency of nanoparticle drug delivery systems considerably. Passive targeting relies on the EPR effect which allows for passive accumulation of nanoparticles at disease sites; however, this passive technique does not ensure that a particular ligand/receptor interaction occurs. The active targeting method ensures that the drug concentration is maximised; therefore the combination of both methods will increase the amount of drug delivered to diseased tissue and also increase the precision of drug delivery to these tissues. The combined targeting methods also mitigate the limitations associated with using only one of the two methods. An example of this would be that using passive only may result in insufficient specificity at the target tissue; however, using only active can be limited by the presence of circulation barriers. The combination of using both targeting strategies also maximises nanoparticle stability, nanoparticle circulation time and cellular uptake,

hence providing an optimised means of administering drugs of cancer and other complex diseases where precise drug delivery is needed for effective treatment. Additionally, dual-targeted nanoparticles can also be designed to respond to specific physiological conditions, therefore improving their utility. Researchers continue to explore new ligand combinations and nanoparticle designs to enhance the benefits of using both techniques combined. This dual-targeted approach has led to landmark achievements in the development of nanomedicine and targeted drug delivery systems. (Li et al., 2021)

Modern drug delivery systems have been significantly improved through active and passive targeting strategies and allow for controlled and selective therapeutic agent delivery that minimizes damage to healthy tissue while enhancing overall treatment outcomes. Targeted nanoparticles have been used successfully in a variety of cancer, infectious disease, and neurological disease therapies. Researchers are investigating novel applications of nanotechnology, including specific nanoparticle design to respond to particular biological environments, thus promoting further utility for targeted therapies. Despite these advantages, some challenges remain regarding biologic system variability, limited penetration of solid tumors, and possible immune responses. Researchers are continually trying to enhance targeting effectiveness by further developing ligand systems and optimizing the properties of nanoparticles. Exploration into the application of artificial intelligence in conjunction with nanotechnology is also underway to create more precise and individualized cellular-based drug delivery systems. As research continues to be performed, the use of active and passive targeting strategies is expected to have a major impact on the future of precision medicine. These advancements will help to create safer, more effective, and highly localized

therapeutic solutions for modern health care systems. (Singh et al., 2023)

Used in cancer and chronic diseases

Drug delivery systems that are based on nanoparticles have produced significant potential for administering medication for many ailments such as chronic disease and cancer as a result of the systems' ability to improve the efficiency of medication through targeted drug delivery, decrease side effects from medications and improve the ability of a drug to be effective. Chemotherapy for cancer is an excellent example of using nanoparticles for drug delivery due to the necessity of delivering medications with very precise accuracy because traditional chemotherapy medications affect healthy and sick (cancerous) cells the same way, resulting in a very high incidence of side effects and being toxic to the body. The accumulation of nanoparticles in tumors selectively allows for the release of drugs in a controlled manner in the tumor and allows for the use of high concentrations of the therapy directly at the location of the cancerous cells because the size of the nanoparticle allows the drug to go into areas of the tumor that are not easily accessed. Long-term and controlled release of drugs will allow a person to manage their chronic disease (e.g. diabetes, cardiovascular disease or neurodegenerative disease) effectively over time, and thus, through the sustained release profile of nanoparticles, the medicine's levels in a person's blood can be maintained for extended periods of time, decreasing the frequency of administration of the medication and improving compliance. Multiple drugs can be delivered with a single nanoparticle, which is helpful when a person needs a combination of therapies to treat their chronic disease. The ability of nanoparticles to deliver drugs will allow for continued growth in the uses of nanoparticles for medical applications, particularly with conditions in which traditional drug delivery methods provide poor patient outcomes. (Alvarez et al., 2022)

Nanoparticle-based drug delivery mechanisms have an enormous benefit in the therapy of cancers by permitting improved accumulation of chemotherapeutic agents in tumors. Tumors demonstrate abnormal vascularization and thus allow nanoparticles to pass into and remain in the tumor microenvironment for a prolonged duration. As a result, chemotherapeutic drugs (anticancer agents) can be used at higher concentrations with less systemic toxicity. Also, nanoparticles can be coated with a targeting ligand (an antibody or peptide) that binds specifically to a cancer cell receptor, thereby increasing the uptake of the drug by malignant cells. This targeted approach allows for more effective killing of cancer cells while limiting damage to adjacent normal tissues. Moreover, nanoparticles can be developed to also encapsulate imaging agents to combine therapeutic agents together with imaging agents (theranostic agents) for simultaneous diagnosis and treatment, allowing clinicians to monitor real-time treatment response and adjust therapies as necessary. The unique ability of nanoparticles to cross biological barriers and deliver drugs directly to tumors has vastly improved treatment strategies for cancer. Continued research efforts are devoted to improving nanoparticle stability, targeting efficiency, safety profiles, and clinical outcomes in oncology. Ultimately, these developments will continue to enhance the effectiveness and individualization of cancer therapies in the future. (Gupta et al., 2023)

Chronic conditions, including diabetes, cardiovascular diseases, and disorders of the nervous system, necessitate long-standing administration of drugs over time; however, conventional delivery systems can make this difficult. Nanoparticles represent a solution by allowing for sustained release of drugs or other therapeutic agents, permitting the maintenance of steady bloodstream concentrations of drug (minimising the potential for fluctuations that

could result in ineffective therapy or adverse events). When used to manage diabetes, for example, nanoparticle-based systems can enhance the delivery of insulin and glucose control. In the treatment of cardiovascular disease, they can deliver drugs directly to the sites of disease and improve heart function; likewise, for neurological diseases, they can pass through the blood-brain barrier to reach the brain or spinal cord and improve the efficacy of drugs used in the treatment of Alzheimer's disease and Parkinson's disease. The ability of nanoparticles to target multiple systems involved in the aetiology of chronic diseases lends itself easily to the complex nature of many chronic diseases. As a result, the improved stability, bioavailability and targeting of drugs by nanoparticles have produced improved therapeutic results in the long-term management of diseases. (Rahman et al., 2021)

Nanoparticles present numerous advantages when it comes to treating cancer and chronic diseases, including the opportunity to minimize the toxicity of drugs delivered and thus maximize their efficacy. Conventional pharmaceutical products generally necessitate high doses in order for them to provide meaningful therapeutic effects; however, higher dosage amounts typically translate into more adverse reactions to non-targeted normal tissue. Because of this, conventional pharmaceutical products are known to not only be highly toxic to the patient, but also to damage the patient's vital organs (liver, kidney, heart) as a consequence of their use. This is particularly true given that cancer chemotherapy agents are very toxic to patients and their use can have a significantly detrimental impact on the patient's quality of life. With chronic diseases, because of the prolonged use of pharmaceuticals, patients can also experience cumulative toxicity associated with the use of the drug over a long period of time; however, the controlled release of the drug from nanoparticles reduces cumulative drug toxicity. Further, the nanoparticle systems

can be engineered to respond to specific biological triggers, such as a change in pH, thereby allowing the release of drug from the nanoparticle only when conditions are appropriate to do so. Using this strategy improves the precision of the treatment regimen and reduces unnecessary exposure to the active pharmaceutical product. Enhancing drug safety while maintaining, or improving, the therapeutic efficacy of the drug, demonstrates the tremendous value of nanoparticles in contemporary medicine and ongoing studies of optimizing these systems for improved biocompatibility and clinical utility, continue to be conducted. (Hassan et al., 2024)

Nanoparticle-based drug delivery systems stand out as a major breakthrough in the field of healthcare today. They present opportunities for greater efficiency through targeted drug delivery, controlled release rates, and better therapeutic results than conventional drug delivery methods. Evidence of this can be seen in oncology where the use of nanoparticles has been linked to increased survival rates as well as fewer negative side effects from chemotherapy. In chronic disease management, the use of nanoparticles to regulate long-term care and maintain constant levels of medication can lead to improved compliance by patients. There are also incredible opportunities ahead with the combination of nanoparticles and promising technologies like gene therapy or immunotherapy, which will provide new options for treating various diseases. While the advantages of nanoparticle drug delivery systems are clear, there are still many obstacles that must be overcome to bring these products to market including large-scale production processes, obtaining regulatory approvals, and establishing long-term safety. The research community is working to eliminate these barriers through innovative material design and advanced fabrication methods. As nanotechnology continues to develop, it is anticipated that

nanoparticle drug-delivery systems will play an integral role in the future of medicine. The precise, effective, and personalized solutions provided by nanoparticles have the potential to revolutionize healthcare outcomes for patients across a variety of diseases. (Verma et al., 2023)

Challenges: toxicity, stability, scale-up

The use of nanoparticle-based drug delivery systems in contemporary healthcare is becoming increasingly popular; however, they also have a number of important limitations, namely, with regard to their toxicity. Toxicity is an important issue when working with nanoparticles due to the way in which they are able to interact directly with biological systems at the cellular and molecular level. Certain types of nanoparticles will cause an unwanted immune reaction or damage normal (healthy) cells by virtue of their size, shape, electrical charge on their surface, and/or their chemical composition. Many inorganic nanoparticles, for example, can accumulate within certain organs, for example, the liver, spleen, and kidneys – this means that there could be a long-term safety issue regarding their use. In addition, many nanomaterials may produce specific degradation products that have the potential of being toxic as well. The interaction of nanoparticles with both proteins and blood cells in the circulatory system is often unpredictable as a result of the complexity of biological systems; this means testing for safety and efficacy using standard laboratory tests becomes very complicated. Simply changing the formulation (i.e., altering the composition) of a specific formulation can lead to significant differences in toxicological properties and potential side effects. The unpredictability associated with the toxicity of nanoparticles presents significant difficulties for clinical testing because it makes determining whether a product will be safe for one patient as opposed to another virtually impossible. Consequently, in order to conduct sufficient safety evaluation prior to the

clinical use of any particular nanomaterial, there must be extensive *in vitro* (laboratory) and *in vivo* (animal) studies to assess their biocompatibility (i.e., how well the material will work with the body). Researchers are actively engaged in developing safer materials such as biodegradable polymers and lipid-based systems to reduce the risk of harmful/toxic effects associated with drug delivery via nanotechnology. Gaining a greater understanding and control over the toxicity of nanoparticles is a critical component in successfully developing drug delivery systems that are both safe and effective for use in biomedical applications. (Khan et al., 2023)

Nanoparticle-based drug delivery systems face another significant hurdle with regard to stability, as nanoparticles are very susceptible to various environmental conditions. Temperature, pH, ionic strength, and the conditions under which the nanoparticles are stored will have a large effect on their physical and chemical stability. If the nanoparticles are unstable, they will aggregate, lose their drug content, and exhibit changes in their particle size distribution; all of these factors will affect the nanoparticles' therapeutic effect. Additionally, in biological systems, nanoparticles may interact with plasma proteins, resulting in the establishment of a protein corona that alters the way the nanoparticles behave and lead to inefficient targeting ability. This can reduce the circulation time of the nanoparticles and negatively impact drug delivery efficacy. In addition, if the nanoparticles are unstable, they may release their drug load too early (before reaching their intended target), negatively affecting therapeutic efficacy and increasing the risk of unwanted side effects. Long-term stability throughout storage and transportation is a significant consideration for pharmaceutical applications. To combat these issues, many researchers are developing surface-modified and polymer-coated nanoparticles to improve their stability by preventing their aggregation.

Lyophilization (freeze-drying) techniques are also being used to produce nanoparticles with longer shelf-lives. Nonetheless, achieving nanoparticles with consistent stability under physiological and environmental conditions continues to be a significant challenge. Therefore, the improvement of nanoparticle stability is essential for assuring that nanoparticles will perform reliably and that nanomedicine-based drug delivery systems will be successfully translated into the clinic. (Singh et al., 2022)

Nanoparticle-based drug delivery systems are facing major challenges with scaling-up their production, making commercialization difficult. Laboratory scale synthesis does produce nanoparticles in the most efficient way possible; however, it is a substantial challenge to produce nanoparticles in large quantity while maintaining consistent quality. Manufacturing conditions varied from batch-to-batch leads to particle size, shape and drug-loading efficiency variability; therefore, all of these factors can affect the therapeutic efficacy of all nanoparticles produced. Due to being largely sensitive to the conditions of the process involved in the synthesis of nanoparticles, it is a challenge to achieve high levels of reproducibility from large batches. Large industrial-scale production requires that there be very tight control of the parameters governing particle size during synthesis, such as mixing speed, temperature, and concentration of reactant(s). Even small deviations from the ideal conditions can dramatically affect nanoparticle characteristics. One considerable cost factor of large-scale production of nanoparticles is that there is often not only a need for specialized equipment, there is also a need for progressive technological advancements to raise production costs. Furthermore, high regulatory requirements concerning quality control (QC) and standardization lead to further complexities in scale-up. As a result of these obstacles, researchers are investigating continuous manufacturing

methods and microfluidic devices to promote scalability and consistency. Nevertheless, obstacles to converting nanoparticle formulation research conducted in a laboratory into commercial production continue to present substantial barriers. Achieving scale-up for nanoparticle formulations is necessary for widespread accessibility and use in clinical practice. (Mehta et al., 2024)

Nanoparticle-based drug delivery systems are subjected to three factors: toxicity, and stability, and scaling up; all three of these factors are related and when combined can individually impact the clinical success of the nanoparticle-based drug delivery system. For example, scaling-up the manufacturing process may impact the stability of the nanoparticles which can then have an effect on the toxicity of the nanoparticles. Another example would be that unstable nanoparticles can release toxic degradation products or lose targeted delivery capability, both of which would increase the likelihood of side effects. The complexity of developing a safe and effective nanoparticle delivery system is due to the relationship of these factors as they may impact the final product. The regulatory agency conducting an evaluation on the active ingredients in order for the drug to be marketed must perform extensive testing to confirm the nanoparticles comply with safety, efficacy, and quality standards prior to being marketed or sold. However, because there is not a standardized evaluation/analysis methodology associated with the manufacturing of nanoparticle materials, there are difficulties creating a regulatory pathway for nanoparticle-based drugs. Additionally, there are researchers trying to develop universal guidelines and standardized test protocols to assist with the challenges of creating a safe and effective drug from nanoparticles. Additionally, advanced characterization technologies have been used to provide researchers with a better understanding of how the nanoparticles behave

within biological systems. There is a constant struggle in the field of nanomedicine to create the balance between high performance, safety, and manufacturability. Overcoming the challenges mentioned in this section is essential for transferring the nanoparticle-based therapy from the research laboratory to the clinical setting and ultimately, for ensuring the safe use of nanoparticle-based therapies in actual healthcare systems. (Verma et al., 2021)

To achieve a successful transition to and large scale production of nanoparticle-based drug delivery systems, it is critical to overcome the challenges associated with toxicity, stability, and scalability. While the strong therapeutic potential of nanomedicine has been demonstrated, these challenges have limited their widespread application in the clinic thus far. Researchers are currently investigating several innovative strategies to develop viable solutions for these challenges, such as using biodegradable materials, developing smart surfaces, and utilizing advanced manufacturing techniques. In addition, the use of computational models and AI is supporting the development of new nanoparticle design strategies that enhance both safety and stability and enable optimized performance characteristics. As the regulatory framework continues to evolve, it is also anticipated that new regulations will provide an accelerated pathway for the translation of nanomedicine from basic research to clinical administration. Collaboration among scientists, engineers, and the pharmaceutical industry will be vital to resolving the complex issues related to the development, safety, and efficacy of nanoparticle technology. Continued improvement of global technologies is anticipated to yield safer, more robust, and scalable systems for delivering nanoparticles for therapeutic use. These advancements will provide extremely effective and reliable alternatives for delivering targeted drugs to patients. Only by successfully tackling these challenges will nanomedicine

become an accepted therapeutic modality, thus providing practitioners with safe, effective, and patient-specific treatment options for a wide range of illnesses. (Arora et al., 2024)

Supports precision medicine

N/ANanoparticle-based drug delivery systems represent a rapidly evolving area of healthcare that supports the concept of precision medicine. Precision medicine focuses on developing tailored treatment regimens according to factors including an individual patient's genetics; environmental exposures; and characteristics related to their disease. In conjunction with precision medicine, nanoparticle-based systems facilitate highly targeted & controlled delivery of therapeutic agents to patients (i.e., drugs delivered directly to specific tissues or cell types). The key difference between conventional therapies and precision medicine is that conventional therapies administer the same treatment regimen for every patient regardless of their individual characteristics, while precision medicine will develop individualized treatment programs for achieving optimal clinical results. Nanoparticle-based systems provide a means to improve the development of precision-based therapies by allowing for drugs to be delivered directly into a target area and therefore reducing the variability of how an individual patient responds to treatment. Further, nanoparticles can be engineered to have specific surface characteristics that allow them to selectively interact with biological markers associated with particular diseases. By doing so, they improve the accuracy of drug delivery to the targeted area and reduce or eliminate the amount of normal tissues exposed to the therapeutic agent. In addition, nanoparticles can also be developed to carry both a diagnostic and a therapeutic agent allowing for real-time monitoring of both the progression of the disease and response to treatment. Thus, nanoparticle-based systems greatly enhance the effectiveness of patient-centered therapies; as a

result, the development of nanoparticle-based drug delivery systems will continue to evolve in support of the ongoing development of precision medicine and represent a key component of next-generation (the modern era) healthcare systems focused on providing individualized treatment. (Omar et al., 2023)

One way that nanoparticles provide precision medicine support is by enhancing targeted drug delivery according to particular biological markers. Each individual may have a different molecular signature that is associated with their disease, and so scientists will engineer nanoparticles to target those distinctions. Scientists will attach ligands, such as antibodies or peptides, onto the surface of nanoparticles; they will target and bind to the disease-specific receptor. Once nanoparticles have bound to the correct target, the use of the nanoparticles to deliver therapeutics only to that location increases the effectiveness of the drug as well as minimizes any associated side effects. For instance, when intravenously administered to patients with cancer, nanoparticles are able to bind to a unique protein that is more prominent on tumor cells than on healthy cells allowing for targeted therapy; therefore, it allows for a more personalized therapy to the individual patient using his/her molecular profile. Furthermore, when scientists manipulate the surface (e.g., size, charge, and modification) characteristics of nanoparticles, they can customize them to meet an individual patient's needs. This ability to customize drug delivery systems according to individual patient characteristics is a significant advancement in modern healthcare, producing improved therapeutic outcomes and more efficient than what has traditionally occurred through trial and error during drug discovery. (El-Sayed et al., 2022) The utilization of nanoparticle systems enhances precision medicine through the use of theranostic methods that facilitate diagnoses and therapies via the same mechanism or device. This

theranostic approach is capable of diagnosing disease, monitoring disease progress, and providing therapeutic therapies at once with the use of a single platform. In addition to being used for diagnosis, nanoparticles are able to carry imaging agents such as fluorescent dyes, magnetic materials, or radioactive isotopes together with therapeutic drugs attached to them. This provides for real-time imaging of drug distribution and therapeutic response to diseases within the patient's body through these two different uses of nanoparticles. This simultaneous treatment and diagnostic process is extremely valuable for practitioners providing precision medicine due to the necessity for continuous adjustments to the treatment regimen of each patient according to their response to therapy. Theranostic nanoparticles provide the ability to determine if a drug, whether through intravenous or oral administration, is able to effectively reach its target site and/or provide the desired therapeutic outcome; if adjustments to the treatment regimen are needed, they can be made quickly, thus maximizing the patient's therapeutic response. Using theranostic nanoparticles for the integration of diagnostic and therapeutic services decreases the need for multiple procedures performed on patients for both diagnosis and treatment of diseases, thereby providing additional patient convenience and reducing the time necessary to adjust the treatment regimen, which is especially important in the treatment of life-threatening diseases such as cancer. The advancement of theranostic nanoparticle systems represents a significant leap forward in the ability to provide personalized medical treatment using more effective and efficient therapeutic approaches in a timely manner based on the specific health care needs of individual patients. (Wang et al., 2021)

Nanoparticles significantly contribute to precision medicine by enabling the use of genetic and molecular therapies. Many disease processes

are now understood to be of a genetic or molecular basis, necessitating the development of highly specific treatment strategies. Nanoparticles can efficiently deliver nucleic acids (including DNA, RNA, and siRNA) to specific target cells, making them useful for applications in gene therapy. These cells can then be used to correct genetic disorders or regulate abnormal gene expression that contributes to the progression of disease. In contrast to traditional pharmaceutical agents, genetic therapies require highly precise delivery systems to avoid degradation and off-target effects. Nanoparticles provide protection for the genetic material and, therefore, ensure that it arrives at the correct cellular location to enhance the accuracy of treatment and reduce the risk of unwanted biological interactions resulting from the use of genetic materials. Furthermore, nanoparticles can be modified to provide a controlled release of the genetic material depending on the specific cellular environment surrounding the nanoparticle at the time of release. For these reasons, the control of the release of genetic material is essential for developing personalized treatment strategies. This is because the ability to modify gene expression based on the genetic profile of an individual will provide a significant benefit in precision medicine. The ability of nanoparticles to provide a personalized approach to treating rare diseases or conditions that do not respond well to traditional methods of treatment provides hope for the development of effective, individualized medical therapies. (Zhao et al., 2024)

Nanoparticle-based systems have revolutionized how we view the fusion of technology with individualized medicine, resulting in a tremendous future outlook for new-age healthcare. The use of these types of systems will allow the creation of extremely individualized approaches for both diagnosing and treating patients by considering the unique biological characteristics of the patient, ultimately

producing more effective treatments. In addition to enhancing the personalization of treatments, nanoparticles also improve drug targeting, provide for controlled release, and enable real-time monitoring of medication effectiveness. All of this contributes to making clinical treatments more effective and efficient and helps to reduce unnecessary exposure to medications and reduce the occurrence of any adverse effects, which is one of the primary objectives of precision medicine. In addition to all that has been mentioned above, ongoing advancements in nanotechnology, as well as advancements in artificial intelligence and biomedical engineering, will continue to enhance the role of nanoparticles in providing personalized healthcare. With these new technologies, researchers will be able to develop extremely optimized drug delivery systems for each individual patient. Although nanoparticles have encountered challenges with regard to safety, regulation, and complexity of manufacturing, continuing research efforts are making headway against these limitations. The continuing evolution of precision medicine will likely entail a heavy reliance on nanoparticle-based platforms for diagnosis, treatment, and monitoring of patients. The multifunctional capabilities of nanoparticles make them vital components of modern medicine. Ultimately, nanoparticles will transform healthcare into a more precise, efficient, and patient-oriented model that improves both the quality of life and the success rate of treatments. (Huang et al., 2023)

Conclusion

Nanoparticle-based systems for drug delivery are a new and revolutionary approach in biomedical sciences. Nanoparticle drug delivery systems provide several benefits over traditional methods of administering pharmaceuticals. They provide the following advantages; better therapeutic efficacy, targeted delivery of drug molecules, and decreased side effects associated with the use of drugs. The use of nanotechnology in medicine

has resulted in the creation of sophisticated drug delivery systems that can deliver drug molecules directly to diseased tissues without causing damage to healthy tissues. Throughout the course of this project, we have shown that nanoparticles provide many advantages when compared to traditional ways of delivering drugs. For example, nanoparticles can enhance the solubility of drugs, facilitate the controlled release of drugs, enhance the bioavailability of drugs, and enable pharmaceutical products to cross biological barriers. The use of nanoparticles for targeted drug delivery through passive (EPR effect) and active (ligand-based) delivery mechanisms enables increased precision of treatment, making these systems ideal for treating complex diseases like cancer and other chronic diseases. However, important issues remain related to the clinical implementation of nanoparticle drug delivery systems, such as toxicity, stability, large-scale production and regulatory concerns. Despite these challenges, advances in materials science, nanotechnology and biomedical engineering will continue to improve and solve these barriers. The development of multifunctional and intelligent nanoparticles will also contribute to the evolution of personalized medicine and precision medicine strategies.

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