NANOPARTICLE-BASED DRUG DELIVERY SYSTEMS FOR PERSONALIZED MEDICINE

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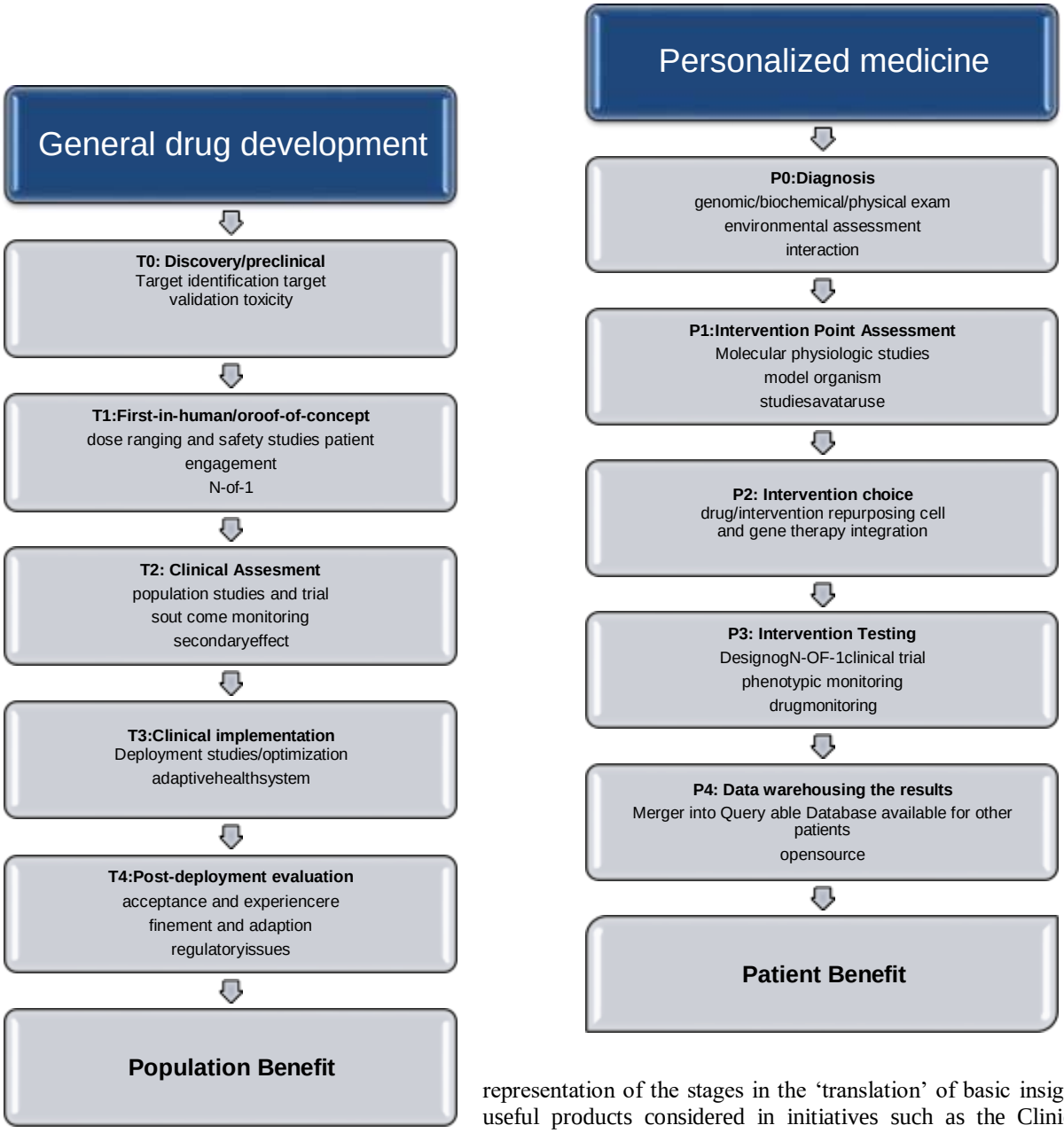
Abstract — Nanoparticle-grounded medicine delivery systems have surfaced as a transformative approach in the field of individualized drugs, offering innovative results to enhance remedial efficacy while minimizing adverse goods. Nanomedicine and customized medications are both novel approaches to healthcare.. The use of nanotechnology in drugs is known as nanomedicine, and it is being incorporated into personal and therapeutic instruments to treat a variety of illnesses. New nanomedicines have been employed in the treatment of several conditions, which can be acclimated to each case-specific case according to their inheritable biographies. In this review, we bandy both areas and the crossroad between the two arising scientific disciplines. These systems work with the unique physicochemical parcels of nanoparticles, similar to their small size, large face area, and capability to be finagled for specific targeting to ameliorate medicine solubility, stability, and bioavailability. The capability to achieve targeted remedy through active and unresistant targeting mechanisms allows for the picky delivery of medicines to diseased organs, particularly in cancer treatment, where conventional curatives frequently harm healthy cells. Also, the integration of individual and remedial functions in theranostic nanoparticles enables real-time monitoring of treatment responses, paving the way for further acclimatized remedial strategies. The review focuses on the current situation in individualized drugs, the advantages that can be offered by nanomedicine to individualized drugs, and the operation of nanoconstructs in the opinion of inheritable variability that can identify the right medicine for the right case. Eventually, we touch upon the challenges in both fields towards the restatement of nano-substantiated drugs.

Keywords—nanomedicine, nanotechnology, personalized medicine, pharmacogenetics, pharmacokinetics **.**

I. INTRODUCTION

A new medical approach called "personalized medicine" uses a person's genetic profile to make decisions about diagnosis, treatment, and illness prevention.Precision medicine, according to the National Research Council, is a quickly developing profession that makes judgments about illness prevention, diagnosis, and treatment based on a person's genetic profile. Multidimensional data, medical history, social and behavioral variables, and environmental information all cross to drive this strategy. Proteomic, genomic, and epigenetic research, together with particular patient health issues and environmental factors, are all part of personalized medicine. Disease prevention, monitoring, diagnosis, and treatment have all been linked to nanotechnology, a broad term that includes systems in the 10–100 nm range.In order to get larger doses above the maximum tolerated dose for non-formulated pharmaceuticals, nanomedicine can customize medications to specific "Personalized medicine" is a new medical approach that utilizes an individual's genetic profile to determine diagnosis, treatment, and illness prevention. Precision medicine, according to the National Research Council, is a quickly developing profession that makes judgments about illness prevention, diagnosis, and treatment based on a person's genetic profile. Multidimensional data, medical history, social and behavioral variables, and environmental information all cross to drive this strategy. Proteomic, genomic, and epigenetic research, together with particular patient health issues and environmental factors, are all part of personalized medicine. Specific targets found for a particular disease in a specific patient. Furthermore, variables of customized medication response associated with variations in cytochrome P enzymes and drug transporters across populations can be circumvented by nanomedicine. With precision medicine, medical professionals can find and display data that supports or changes treatment choices based on patient characteristics. This technology is becoming more prevalent in healthcare since it enables early disease identification and

individualized care delivery. Personalized care is made possible by data gathering and analytics technology like electronic health records (EHR) and high-throughput genotyping. The most well-researched effect of precision medicine is genotype-guided therapy, in which doctors utilize genetic data to calculate the appropriate warfarin dosage. To assist doctors in optimizing pharmacological therapy with genetic test findings, the Clinical Pharmacogenetics Implementation Consortium released genotype-based therapeutic guidelines. By incorporating precision medicine into healthcare, more accurate diagnoses can be made, disease risk can be predicted before symptoms appear, and individualized treatment plans that optimize efficiency and safety may be created. This field is changing perceptions of precision medicine because of biobanks in nations like the Australian Genomics Health Alliance, BioBank Japan, and the UK Biobank. To test, validate, and modify treatment procedures, however, more work is required. This includes acquiring high-quality labeled data for algorithm training and implementing standardized data formats.



A clinical representation of the stages in the 'translation' of basic insights into useful products considered in initiatives such as the Clinical and Translational Science Award (CTSA) initiative overseen by the National Center on Advancing Translational Science of the United States National Institutes of Health (NCATS; left panel An analogous representation of the stages in the diagnosis and treatment of an individual patient are provided in the right hand panel.

- ❖ Personalized medicines are useful for following groups.

a) Patients and Consumers

Artificial intelligence helpful in genetic testing and clinical trials and working with health care providers which is useful in manage disease risk and/or treatment strategies/plans.

b) Health Care Providers

By understanding of the patient's genetic profile and utilizing new technologies to personalized the approach to disease prevention, detection, diagnosis, treatment, and management.

c) Biopharmaceutical Companies

Developing targeted therapies and conducting innovative research based upon an understanding of genetic variation and its effects on the safety and effectiveness of the candidate drug.

d) Diagnostic Companies

The understanding of disease at the molecular level is improved by development of various tools and tests to analyze and interpret genetic information, and a patient's likelihood/compliance to respond to drug therapy is increased significantly.

e) Academic Researchers

More targeted drug development and usage to uncover new insights into human genetics and the molecular basis of disease, enabling greater precision in diagnosis and conducting basic and clinical research.

f) IT/Informatics Companies

Creating electronic tools and resources to collect and store patient health information, making it available to inform clinical decisions and improve safety while protecting patient privacy

g) Advocacy Groups

By educating consumers and providers, accelerating research, and supporting necessary changes in policy and regulation by advancing personalized medicine in patient care.

a. Payors

Through appropriate reimbursement of molecular diagnostics, targeted therapies, and other personalized treatment protocols by exploring new and different business models to incentivize the practice of personalized medicine.

SUMMING UP THE APPLICATIONS-

- Risk Assessment: Genetic testing to reveal predisposition to disease
- Prevention: Behavior/Lifestyle/ Treatment intervention to prevent disease
- Detection: Early detection of disease at the molecular level
- Diagnosis: Accurate disease diagnosis enabling individualized treatment strategy
- Treatment: Improved outcomes through targeted treatments and reduced side effects
- Management: Active monitoring of treatment response and disease progression

1. Enhanced Drug Solubility and Stability

The poor solubility of many therapeutic drugs, especially those that are hydrophobic, is one of the main problems with medication delivery. These weakly soluble medications can be encapsulated in nanoparticles, which greatly improves their stability and solubility. For example, hydrophobic medications can be dissolved by lipid-based nanoparticles, such as liposomes and solid lipid nanoparticles, improving their bioavailability. This is especially crucial in customized medicine since each patient has a different metabolic profile, which might affect how they react to medications. Nanoparticles enhance therapy outcomes by ensuring that patients receive the ideal therapeutic dose through improved solubility.

2. Controlled and Sustained Release

Drugs may be released from nanoparticles in a controlled and sustained manner, which is crucial for sustaining therapeutic dosages over time. This is especially helpful for chronic conditions where stable medication levels are essential for efficient treatment. For instance, polymeric nanoparticles can be engineered to release their medicinal payload gradually as they break down in the body. By reducing the need for frequent dosing, this controlled release enhances patient adherence and therapeutic effectiveness in general. Such systems can be customized to meet the demands of each patient in personalized medicine, taking into account variables like illness progression and metabolism.

3. Targeted Drug Delivery

The capacity of medication delivery systems based on nanoparticles to achieve targeted delivery is one of their biggest benefits. Certain ligands, antibodies, or peptides that identify and attach to particular cell types or tissues can be used to functionalize nanoparticles. Drugs can be delivered selectively to sick cells, such cancer cells, while preserving healthy tissues thanks to active targeting. For example, cancer cells that overexpress folate receptors can be targeted by folate-conjugated nanoparticles, increasing the therapeutic benefit and decreasing adverse effects. Targeted medication delivery is very useful in personalized medicine since it enables treatment to be tailored to the molecular features of a patient's illness. By examining genetic profiles or tumor markers, medical professionals can choose nanoparticles that deliver medications precisely to the impacted cells., improving treatment outcomes and minimizing toxicity.

4. Overcoming Biological Barriers

Additionally, medications can be transported by nanoparticles via biological barriers that normally impede drug delivery. For instance, administering medications to treat neurological illnesses is significantly hampered by the blood-brain barrier (BBB). Drugs can be delivered straight to the brain thanks to the ability of some nanoparticles, such as those derived from chitosan or other biocompatible materials, to pass the blood-brain barrier. In customized medicine, where therapies for diseases like Alzheimer's or brain tumors need to be delivered precisely to the central nervous system, this ability is essential.

5. Theranostics: Integration of Therapy and Diagnostics

Theranostics is the idea that nanoparticles can be engineered to do two tasks: they can be used as both therapeutic agents and diagnostic instruments. Real-time tracking of illness development and therapy effectiveness is made possible by this combination. For example, imaging agents that give feedback on drug distribution and release in vivo can be placed onto nanoparticles. In customized medicine, where ongoing monitoring can guide treatment modifications based on each patient's reaction, this feature is very advantageous. Theranostic nanoparticles facilitate a more thorough approach to patient care by fusing therapeutic and diagnostic capabilities. This enables prompt interventions and treatment plan revisions based on real-time data.

6. Personalized Formulations

Because of their adaptability, nanoparticles can be used to create customized formulations that meet the demands of each patient. Researchers can develop formulations that maximize medication delivery based on a patient's unique features, including age, gender, genetic makeup, and illness condition, by modifying the size, surface charge, and composition of nanoparticles. For instance, different nanoparticle formulations would be needed for patients with varying metabolic rates in order to produce the intended therapeutic effect. Additionally, the patient's immunological response may be taken into account in customized formulations. Antibodies against specific nanoparticle materials may already be present in some patients, which could cause quick bloodstream clearance. Healthcare professionals can improve treatment outcomes and the therapeutic window by tailoring the nanoparticle design.

7. Safety and Biocompatibility

In drug delivery systems, safety and biocompatibility are crucial factors, especially in personalized medicine, where patients receive customized therapies. It is possible to create nanoparticles to improve biocompatibility and reduce toxicity. For example, nanoparticles made of biodegradable polymers can decompose into non-toxic byproducts, lowering the possibility of negative consequences.

2. Fundamentals of Nanoparticle-Based Drug Delivery

2.1. Definition and Classification of Nanoparticles

Drug delivery has seen a significant advancement thanks to nanoparticles (NPs), especially in the setting of customized medicine. Nanoparticles, which are defined as particles with sizes between one and one hundred nanometers, differ from their bulk counterparts in a number of physical, chemical, and biological ways. These characteristics allow nanoparticles to improve medicinal drugs' solubility, stability, and bioavailability while also enabling targeted delivery to particular tissues or cells. The description and classification of nanoparticles will be covered in detail in this extensive review, with an emphasis on how they function in drug delivery systems designed for customized treatment.

Definition of Nanoparticles

According to one definition, nanoparticles are extremely tiny particles that have at least one dimension in the nanoscale range (1-100 nm). They have special qualities because of their small size,including:

i. High Surface Area in relation toVolume Ratio: This property makes nanoparticles more reactive and interacts better with biological systems, which makes them useful drug delivery vehicles.
ii. Size-Dependent Properties: Materials can display unique optical, electrical, and magnetic characteristics at the nanoscale, which can be used for diagnostic and therapeutic purposes.
iii. Improved Penetration: Drug delivery to certain tissues or cells is made easier by nanoparticles' superior ability to cross biological barriers.
iv. Controlled Release: Therapeutic chemicals can be released from nanoparticles in a controlled and sustained manner, increasing patient compliance and treatment effectiveness.
v. Biocompatibility: Many nanoparticles can be considered to be biocompatible, minimizing toxicity and adverse effects when administer to patients

The nanoparticles differs from various dimensions, to shapes and sizes apart from their material. A nanoparticle can be either a zero dimensional where the length, breadth and height is fixed at a single point for example nano dots, one dimensional where it can possess only one parameter for example graphene, two dimensional where it has length and breadth for example carbon nanotubes or three dimensional where it has all the parameters such as length, breadth and height for example gold nanoparticles. The nanoparticles are of different shape, size and structure. It be spherical, cylindrical, tubular, conical, hollow core, spiral, flat, etc. or irregular and differ from 1 nm to 100 nm in size. The surface can be a uniform or irregular with surface variations. Some nanoparticles are crystalline or amorphous with single or multi crystal solids either loose or agglomerated . Numerous synthesis methods are either being developed or improved to enhance the properties and reduce the production costs. Some methods are modified to achieve process specific nanoparticles to increase their optical, mechanical, physical and chemical properties. A vast development in the instrumentation has led to an improved nanoparticle characterisation and subsequent application.

2.2 Classification of Nanoparticles

Nanoparticles can be classified based on various criteria, including their composition, structure, shape, and method of preparation. Below are the primary classifications relevant to drug delivery systems.

2.2.1. Classification Based on Composition

Nanoparticles can be broadly categorized into four main types based on their composition:

- Metallic Nanoparticles

Metallic nanoparticles are composed of metals or metal oxides and are widely used in drug delivery due to their unique optical and electronic properties. Common examples include:

Gold Nanoparticles (AuNPs): Known for their biocompatibility and ease of functionalization, AuNPs are used for targeted drug delivery, imaging, and photothermal therapy. Their surface can be easily modified with various ligands, allowing for specific targeting of cancer cells or other diseased tissues.

Silver Nanoparticles (AgNPs): AgNPs possess antimicrobial properties and are used in drug delivery systems to enhance the therapeutic efficacy of antibiotics. They can also be utilized in combination therapies to overcome drug resistance.

Iron Oxide Nanoparticles: These nanoparticles are used in magnetic drug delivery systems, allowing for targeted delivery using an external magnetic field. They can also serve as contrast agents in magnetic resonance imaging (MRI).

- Polymeric Nanoparticles

Polymeric nanoparticles are composed of natural or synthetic polymers and can be classified into two main categories:

Biodegradable Polymers: These include materials like poly(lactic-co-glycolic acid) (PLGA) and chitosan, which degrade into non-toxic byproducts in the body. They are commonly used for sustained drug release and can be tailored to release drugs over specific time frames.

Non-Biodegradable Polymers: These polymers do not degrade in the body and are used for specific applications where prolonged retention is desired. They can be used in applications such as long-term implants or devices.

Polymeric nanoparticles can be further categorized into:

Nanospheres: Solid particles that can encapsulate drugs within their matrix.

Nanocapsules: Hollow particles that encapsulate drugs within a cavity, allowing for controlled release.

- Lipid-Based Nanoparticles

Lipid-based nanoparticles are composed of lipids and are particularly effective for delivering hydrophobic drugs. Common types include:

Liposomes: Spherical vesicles composed of phospholipid bilayers that can encapsulate both hydrophilic and hydrophobic drugs. Liposomes enhance drug solubility and stability, making them suitable for a wide range of therapeutic applications.

Solid Lipid Nanoparticles (SLNs): These are solid lipid matrices that can encapsulate drugs, providing controlled release and improved bioavailability. SLNs can protect sensitive drugs from degradation and enhance their therapeutic effects.

Nanostructured Lipid Carriers (NLCs): A combination of solid and liquid lipids, NLCs enhance drug loading capacity and stability compared to SLNs. They can be used to deliver a variety of therapeutic agents, including anticancer drugs and vaccines.

- Inorganic Nanoparticles

Inorganic nanoparticles are composed of inorganic materials and are used for various applications, including drug delivery and imaging. Examples include:

Silica Nanoparticles: These nanoparticles can be easily functionalized and are used for drug delivery and as carriers for imaging agents. Their porous structure allows for high drug loading capacity and controlled release.

Ceramic Nanoparticles: Composed of materials like calcium phosphate, these nanoparticles are used for drug delivery in bone-related therapies. They can also serve as scaffolds for tissue engineering applications.

2.2.2. Classification Based on Structure

Nanoparticles can also be classified based on their structural characteristics:

- Core-Shell Nanoparticles

Core-shell nanoparticles consist of a core material surrounded by a shell of another material. This structure allows for the combination of different properties, such as enhanced stability and controlled release. The core can be made of a drug or a therapeutic agent, while the shell can provide protection and targeted delivery capabilities.

- Dendrimers

Dendrimers are highly branched, tree-like structures that can be precisely engineered at the molecular level. They have a central core, branching units, and terminal functional groups that can be modified for specific applications. Dendrimers can encapsulate drugs and facilitate targeted delivery, making them suitable for personalized medicine. Dendrimers are organic chemical entities which have semi-polymeric tree-like structure. The terminals of the branches provide an upscale source of nanoparticles surface functionality. Their dimensions are extremely small, having diameters within the range of two to 10 nm. Dendrimers are an exciting new class of macromolecular architecture and an important component in the area of nanotechnologybased cosmeceuticals to treat various skin conditions. L'Oréal, Unilever, and therefore the Dow Chemical Company have several patents for the appliance of dendrimers in hair care, skin care, and nail care products. A patent on cosmetic formulation containing carbosiloxane dendrimer claimed that it can provide good water resistance, sebum resistance, glossiness, touch, and/or adhesive properties to the hair and/or skin.

- Nanorods and Nanospheres

Nanorods are elongated nanoparticles that exhibit anisotropic properties, which can be advantageous for certain applications, such as photothermal therapy. Nanospheres, on the other hand, are spherical in shape and can be used for a variety of drug delivery applications due to their uniform size and shape.

2.2.3. Classification Based on Shape

The shape of nanoparticles can significantly influence their behavior in biological systems. Common shapes include:

- Spherical Nanoparticles

Spherical nanoparticles are the most common type and are often used in drug delivery due to their uniform size and shape, which facilitates consistent behavior in biological environments.

- Rod-Shaped Nanoparticles

Rod-shaped nanoparticles, such as nanorods, can exhibit unique optical properties and are often used in applications like photothermal therapy, where their shape enhances light absorption.

- Platelet-Shaped Nanoparticles

Platelet-shaped nanoparticles can provide a larger surface area for drug loading and are being explored for applications in targeted drug delivery and imaging.

2.2.4. Classification Based on Method of Preparation

Nanoparticles can also be classified based on the methods used for their synthesis:

- Top-Down Approaches

Top-down approaches involve breaking down bulk materials into nanoparticles. Techniques include milling, lithography, and etching. These methods can produce nanoparticles with controlled size and shape but may result in a broader size distribution.

- Bottom-Up Approaches

Bottom-up approaches involve the assembly of nanoparticles from smaller units, such as atoms or molecules. Techniques include chemical vapor deposition, sol-gel processes, and self-assembly. These methods can produce nanoparticles with uniform size and shape, allowing for precise control over their properties.

- Mechanisms of Targeted Drug Delivery for Nanoparticle-Based Drug Delivery Systems in Personalized Medicine

2.3 Mechanisms of Targeted Drug Delivery

2.3.1 Passive Targeting

Passive targeting relies on the enhanced permeability and retention (EPR) effect, which is particularly pronounced in tumor tissues. Tumors often have leaky blood vessels and impaired lymphatic drainage, allowing nanoparticles to accumulate in the tumor microenvironment. This mechanism is advantageous for delivering chemotherapeutic agents directly to the tumor and reducing systemic toxicity. Passive targeting of drug delivery depends on the size of the nanoparticles and the vascular status within the tissue. Maeda et al. The blood vessels of the tumor and the burning tissue have holes flowing, but there is no normal organization. This helps to reach the affected area more effectively. Greish et al. He used Stylene Cabird. However, the EPR effect has limitations: non-solid tumors such as leukemia are not amenable to its action, and different tumor types may only allow limited access to nanodrugs.

The EPR effect is a phenomenon in which the leaky vasculature of tumor tissues causes nanoparticles to preferentially collect there. This makes it possible for the tumor site to have greater local medication concentrations.

Size and Surface Properties: Nanoparticles' capacity to take advantage of the EPR effect is greatly influenced by their size and surface features. For passive targeting, nanoparticles between 10 and 200 nm are usually ideal.

2.2 Active Targeting

In active targeting, nanoparticles are modified with specific ligands that can bind to receptors overexpressed on target cells, a mechanism that enhances nanoparticle uptake by the target cells and improves therapeutic efficacy. The EPR effect helps nanoparticles reach tumors but does not promote their efficient uptake by cells. To improve this, nanoparticles can be functionalized with ligands that target specific cancer cells or subcellular sites. This not only minimizes side effects from passive targeting but also enhances the uptake of nanoparticles into the cells. This process is effective due to specific receptors present on the cell surface that can be targeted. Additionally, active targeting can be useful in personalized medicine, allowing physicians to use the most effective ligands to direct the appropriate dose of a nanomedicine to the right location, even if it may only affect certain areas of the tumor, leading to unpredictable and potentially ineffective treatment outcomes. Ligand-receptor interactions:

Targeting ligands can include antibodies, peptides, or small molecules that bind specifically to receptors on the surface of target cells. For example, folate-targeted nanoparticles can bind to folate receptors that are overexpressed on some cancer cells.

Enhanced cellular uptake: Functionalization of nanoparticles with targeting ligands significantly increases the likelihood of cellular uptake, improving therapeutic outcomes.

2.2.3 Ligand-Based Targeting

Adenosine is a nucleoside that is important in regulating cellular functions and activating adenosine receptors. It is used to treat colon cancer, prostate cancer, lymphoma, breast cancer, and other cancers. Docetaxel-loaded adenosine-linked solid lipid nanoparticles (SLNs) had better pharmacokinetic properties and killed more cells than SLN-DTX, which was not conjugated. Folate receptors, a type of high-affinity folate-binding protein, are overexpressed in solid tumors, impairing patient outcomes. Vaccination with Liposa, who is in charge of excavation of Mightmycin using Fulat Ligand, leads to an increase in cell poisoning. Cancer cells are metabolic than normal cells, and glucose can be used with active aims, as it leads to an increase in glucose needs. Glucose-coated nanodrugs have a high ability to penetrate cancer cells and are useful for therapeutic diagnostic approaches. The ligand-based approach has the advantages of reduced cost, ease of conjugation, non-immunogenicity, and safety.

2.2.4 Stimuli-Responsive Delivery

Stimuli-responsive nanoparticles are designed to release their drug payload in response to specific internal or external stimuli. This mechanism allows for controlled release of the drug, enhancing the therapeutic effect and minimizing side effects.

pH-sensitive nanoparticles: These nanoparticles can release their drug payload in response to the acidic environment of tumor tissues or inflamed areas. For example, polymeric nanoparticles can be designed to degrade and release their contents at lower pH levels.

Temperature-responsive nanoparticles: These nanoparticles can release drugs in response to changes in temperature and may be particularly useful in treating hyperthermia.

Enzyme-responsive nanoparticles: Some nanoparticles can be designed to release drugs in the presence of specific enzymes that are overexpressed in the target tissue.

2.2.5 Protein–Based Active Targeting

Transferrin, a serum glycoprotein, is essential for iron transport and is significantly upregulated 100-fold in cancer and metastatic cells, making it an optimal ligand for active targeting strategies. Transferrin-decorated nanodrugs, including doxorubicin and curcumin, demonstrate enhanced antitumor efficacy with minimal cytotoxicity. Human serum albumin nanoparticles functionalized with an antibody targeting the transferrin receptor can efficiently transport loperamide across the blood-brain barrier. This antibody shows high specificity and affinity for cell surface receptors such as human epidermal growth factor receptor 2 (HER2), the target of trastuzumab. The combination of trasutsumab and chitosannano particles equipped with hemcitabin has an excellent antipache and cell poisoning effect in the treatment of pancreatic cancer. The use of ritximab antibodies for CD20 as an active target ligand enhances the treatment efficiency of nanodugu, which is targeted for chronic lymphocytes of leukemia. Antibody fragments, including antigen-binding fragments (Fab) and single-chain variable fragments (scFV), can be used in place of full-length antibodies, increasing specificity and therapeutic impact.

II. APPLICATIONS IN PERSONALIZED MEDICINE

Personalized medicine aims to tailor medical treatment to the individual characteristics of each patient. Nanoparticle-based drug delivery systems play a crucial role in this approach by enabling targeted therapies that consider the unique biological and genetic profiles of patients.

3.1 Cancer Therapy

Cancer is one of the most important areas in which nanoparticle-targeted drug delivery systems have shown promise. By exploiting the EPR effect and active targeting mechanisms, nanoparticles can deliver chemotherapeutic agents directly to tumor cells, thereby reducing systemic toxicity and increasing treatment efficacy. Nanoparticles can be performed with indirect mechanisms consisting of tissue adjacent to the tumor (that is, the liver's cup of cupfer). cell. Directly aiming for a tumor cloth using nanoparticles is possible when someone uses the blood vessel network of the tumor. This approach should provide the aforementioned EPR effect, but has not yet been clearly demonstrated for nanoparticles. However, targeting methods improve the efficiency of anticancer drugs. The decrease in side effects is generally observed. The use of nanoparticles has shown very promising results at the cellular level, demonstrating effective drug protection, cellular uptake, controlled release, or reversal of

MDR resistance. Poly(alkylcyanoacrylate) nanoparticles have even reached phase II clinical trials for refractory cancers. The use of nanoparticles in imaging is also promising, as they improve the visibility and delineation of tumors. The contribution of nanoparticles to cancer chemotherapy will certainly increase, provided that more effective tumor targeting strategies are developed. Future research will concentrate on active targeting with molecule such as folic acid, as this strategy offers both specific recognition and cell internalization. However, active targeting often entails numerous chemical reactions, as protection/ deprotection reactions for instance. The challenge will therefore be to avoid complex design syntheses. Regarding the encapsulation of anticancer drugs in nanoparticles, future developments are expected to focus on new molecules acting at the cancer cell level (e.g. Taxol), as well as on drugs acting at the vascular level, such as angiostatin and tumor necrosis factors . In this later case, there are less biological barriers to overcome, as there is no need for extravasation in the tumoral interstitium, for cell internalization as well as for escaping from the lysosome compartment

Examples:

Target chemotherapy: Nano particles can be designed to save healthy organizations, especially for cancer cells, especially chemotherapy. For example, liposomes equipped with a doxorbicin have been developed to target breast cancer cells and have greatly improved drug treatment indices. Combined therapy: Nanoparticles can also be used to jointly provide several therapeutic agents, such as a chemotherapeutic and immunotherapeutic environment, for a synergistic increase in the effectiveness of treatment for tumors.

3.2 Vaccine Development

Nanoparticle-based delivery systems are also used in vaccine development, especially for cancer and infectious disease vaccines, to enhance immune responses through targeted delivery of antigens. The development of vaccine adjuvants has made great progress in recent years, especially in understanding their cellular and molecular mechanisms of action and how to improve them. The future of vaccine adjuvant research is mainly aimed at the development of new composite adjuvants consisting of PRR agonists and particulate adjuvants. The study of NP–APC interactions is of particular interest in the field of vaccinology, as NPs offer a biodegradable and biocompatible platform that can be used to deliver a variety of antigens to specific tissues and organs with minimal toxicity and as an effective alternative to traditional vaccines. In addition to these advantages, NPs also act as adjuvants to stimulate immune responses, and incorporation of antigens into NPs protects them from degradation and provides opportunities for targeting and controlled release. However, the application of NPs in vaccine delivery is still in the early stages of development, and it is true that NP-based delivery systems have many drawbacks and limitations. In this regard, the small size and large surface area of NP-based targeting and delivery systems can lead to aggregation and make physical handling difficult. The lack of knowledge regarding the distribution of NPs and the unpredictability of the process are also concerns associated with the use of these nanoparticles. Furthermore, the safety of the vaccine is a serious problem with the approval of Ajuvant for human use. A detailed understanding of the mechanism of the mechanism of the action of Ajuvant gives their security ideas.

Examples:

Cancer Vaccines: Nanoparticles can be engineered to present tumor antigens to the immune system, promoting a robust immune response against cancer cells.

mRNA Vaccines: The success of mRNA vaccines for COVID-19 has highlighted the potential of lipid nanoparticles in delivering mRNA to cells, paving the way for future vaccine developments.

- ✓ Challenges in Targeted Drug Delivery

Despite the promising potential of nanoparticle-based drug delivery systems, several challenges must be addressed to ensure their successful application in personalized medicine. The rapid growth of nanomedicines as therapeutic agents has introduced several challenges, including concerns related to safety, cost, and mass production. Precision medicine faces ethical, social, and legal dilemmas, while nanomedicine interacts with a biological environment that lacks standardized safety assessment criteria. In the medical field, toxicity is divided into acute and chronic, with acute toxicity characterized by inflammation, hemolysis, and oxidative stress, and chronic toxicity developing over time. In order to increase the probability of successful results, it is important to understand the physiological characteristics of drugs and exiles, and the reagents and routes involved in the synthesis of poisonous perspectives. Nano-Medidicin is a complex three-dimensional system that contains multiple components that require

advanced analysis tests, characteristics, and quantitative definitions to detect them. Feast on stability and long -term storage of nanoparticles is also preserved.

In order to translate Tedder into an individualized drug, a large -scale synthesis with high breeding is essential. However, the manufacturing process can significantly alter the properties of nanoparticles, making large-scale production difficult, and the costs of scaling up nanomedicines and the challenges of gaining regulatory approval are significant, especially when existing products offer similar efficacy. The development of nanomedicines is constrained by the lack of standards and regulations governing manufacturing methods, quality control, and evaluation of safety and efficacy. Although regulatory bodies such as the FDA and EMA have set some standards, specific regulatory standards for nanomedicines have yet to be developed. Consequently, varying approaches to the application of nanotechnology are observed across different geographical regions.

- Biodistribution and pharmacokinetics: Understanding the biodistribution and pharmacokinetics of nanoparticles is essential to optimize their design and therapeutic efficacy. Factors such as size, shape, surface charge, and composition can significantly influence how nanoparticles are distributed in the body and their elimination pathways.
- Toxicity: The safety profile of nanoparticles must be thoroughly evaluated, as some materials may induce adverse effects. Toxicity studies are essential to assess the biocompatibility of nanoparticles and their long-term effects on human health.
- Manufacturing and Scalability: Consistently producing nanoparticles on a large scale while maintaining quality is a major challenge in the field. Standardized manufacturing processes and quality control measures are required to ensure the reproducibility of nanoparticle formulations.

✓ Future directions

The future of the delivery of targeted drugs using nanoparticles in personalized medicine is promising, with several exciting areas for research and development.

- Combined therapy: If targeted drugs are integrated with other treatments such as immunotherapy and genetic treatment, the therapeutic effect may be improved. Research on combined therapy that utilizes the strengths of various approaches is an important focus.
- Advanced Visualization Techniques :The use of nanoparticles for imaging can help monitor treatment outcomes and adjust therapy in real time. Image-guided drug delivery systems can provide valuable information about the distribution and efficacy of treatment.
- Regulatory Considerations: As nanoparticle-based therapeutics advance, regulatory frameworks must evolve to ensure their safety and efficacy in clinical applications. Collaboration between researchers, clinicians, and regulators is essential to overcome the challenges of bringing these innovative therapies to market.

CHALLENGES IN NANOPARTICLE CHARACTERIZATION

Despite the availability of various characterization techniques, several challenges remain in the field of nanoparticle characterization:

✓ Sample Preparation

Sample preparation can significantly influence the properties of nanoparticles. Techniques that require drying or altering the environment may lead to changes in size, morphology, or surface characteristics.

✓ Standardization

The lack of standardized protocols for nanoparticle characterization can lead to variability in results. Establishing standardized methods is essential for ensuring reproducibility and comparability across studies.

✓ Complexity of Biological Systems

Characterizing nanoparticles in biological environments is challenging due to the complexity of biological fluids and interactions. Techniques that work well in vitro may not accurately reflect behavior in vivo.

III. SAFETY AND TOXICITY CONSIDERATIONS FOR NANOPARTICLE-BASED DRUG DELIVERY SYSTEMS IN PERSONALIZED MEDICINE

Importance of safety and toxicity assessment: Nanoparticles have the potential to trigger immune responses, so it is important to determine whether nanoparticles or their component parts induce immunotoxicity-related responses. However, there are relatively few methods to accurately assess the immunotoxicity of nanoparticles. Although lymph node proliferation assays can be used to estimate nanoparticle-related toxicity, they have inherent drawbacks: for example, nanoparticles pass through the lymphatic system when injected subcutaneously, potentially leading to inaccurate results, thus necessitating an alternative route of administration. The latest FDA guidance for the evaluation of immunotoxicity of pharmaceutical products for human use, ICH S8, should be considered when evaluating the immune toxicity of nanoparticles. The FDA recommends examining immune cell function in cases where the preliminary study has indicated potential immunotoxicity by changes in gross pathology hematology, clinical chemistry, immune organ weights, or histologic evaluation. In our opinion, the evaluation of nanoparticle immunotoxicity in animal models is one of the most important tests performed in relation to nanoparticle-mediated toxicity. Immune responses can be life-threatening and therefore must be taken seriously. Therefore, we strongly recommend performing these tests and, if problems are observed, using approaches that minimize the factors causing these effects. The safety and toxicity of nanoparticle-based drug delivery systems is important for several reasons:

Patient safety: Ensuring that nanoparticles do not cause side effects is paramount for patient safety and therapeutic efficacy.

Regulatory Compliance: Regulatory agencies require comprehensive safety data before approving the clinical use of nanoparticle therapies.

Therapeutic Efficacy: Understanding the toxicity profile of nanoparticles can optimize formulations and improve treatment outcomes while minimizing side effects. Public perception: Concerns regarding the safety of nanotechnology may affect public acceptance and adoption of nanoparticle-based therapeutics.

2. Mechanisms of Toxicity

Nanoparticle toxicity can arise from various mechanisms, including:

2.1 Physical and Chemical Properties

The physical and chemical properties of nanoparticles, such as size, shape, surface charge, and composition, play a significant role in determining their toxicity.

Size: One of the key elements that can affect a nanoparticle's toxicity is its size . varied dispersion media, including deionized water and cell culture media with and without serum, have varied nanoparticle sizes. For example, 40-nm copper agglomerated 28 times larger than its initial size when placed in deionized water and RPMI-1640 media, but only 9 times larger when placed in a medium containing serum . Despite having desirable mechanical, electrical, and chemical properties that are essential for drug delivery, particles smaller than 100 nm can have unfavorable effects like damaging cell membranes and triggering immune responses and passing through the blood-brain barrier. For instance, gold nanoparticles of 1.4 nm size successfully suppressed the growth of connective tissue fibroblasts, epithelial cells, macrophages, and melanoma cells in in vitro size-dependent cytotoxicity studies. At comparable concentrations, however, particles of 15 nm size are nontoxic. We believe that a hydrophilic surface and a size less than 100 nm are necessary for in vivo application in order to minimize opsonization and the subsequent clearance by macrophages. Smaller nanoparticles (usually less than 100 nm) can more readily pass through biological barriers, but because of their larger surface area and reactivity, they may also be more hazardous.

Composition and Shape: The composition and charge of nanoparticles can influence organ accumulation and toxicity. The surface charge of particles is usually indicated by the zeta potential. Zeta potential reflects the electrical potential of a particle and depends on the particle's composition and the medium it is dispersed in. Nanoparticles with a zeta potential above (+/-) 30 mV are generally stable in suspension because the surface charge prevents the particles from agglomerating. The monovalent cationic lipid components of cationic liposomes, DOTAP, and the polyvalent cationic liposome, LipofectAMINE, can accumulate in the vasculature and be preferentially taken up by the liver and spleen. This effect was more pronounced with LipofectAMINE than with DOTAP.Similarly, stearylamine, a first-generation monoalkyl cationic lipid, caused aggregation and hemolysis of human red blood cells. Therefore, the clinical use of this cationic lipid for drug, gene, and peptide delivery into the human body is not recommended. Although cationic lipid-based delivery systems are promising as a potential siRNA delivery system, the potential

toxicity to the lungs and other organs may require alternative formulations to ensure safety . We believe that the development of new technologies that prevent the elimination of cationic liposomes from the circulation could be useful to increase the efficacy of liposomes and lead to a decrease in toxicity resulting from organ or cellular damage. The shape of nanoparticles can control their cellular uptake and interactions with natural system. For example, elongated nanoparticles may have a different toxicity profile than spherical nanoparticles.

Surface Charge: Nanocarriers possess a large surface area due to the very small particle size. Since nanoparticles interact with biological systems through their surface, controlling surface properties such as composition, charge, and porosity are critical factors influencing nanoparticle-associated toxicity. Increased surface area not only has the advantage of providing opportunities for antibody conjugation and material delivery, but also has inherent drawbacks, rendering them toxic if not rationally designed. Surface modifications can stabilize nanoparticles and avoid aggregation, but they may also block or hinder the impact of nanomaterials on biological systems. For example, PEGylation has been shown to stabilize nanoparticles such as gold nanoparticles and liposomes, decreasing their clearance from the circulation, thereby prolonging their potential contact with tumors and cellular targets. In addition, Peguiri protects nanoparticles from Opson. This is a process in which outpatient organisms or particles are covered with opton proteins, which makes it easier to see due to mononuclear cell systems (MPS), also known as RES. In addition, it was found that PEG -containing copolimers show that the circulation half -life increase by several digits, compared to the non -Pegiri polymer. Mechanically, pegylation creates a hydrophilic protective layer around nanoparticles which repel the absorption of oponin proteins with steric forces, blocking and thus delaying the opsonization process . Pegination can also increase efficiency, allowing nanoparticles to be carried out in pathological areas, such as tumors or fiery areas with a vascular system that flows, thus improving the capacity to directly target tumors located outside regions rich in deputies. In our opinion, PEGylation of the surface of any nanoparticle is essential to improve its circulation time and thereby enhance its efficacy. The surface charge of a nanoparticle influences its interaction with cell membranes and biological fluids. Positively charged nanoparticles may display higher cytotoxicity due to improved cellular uptake.

Composition: The material used to fabricate nanoparticles can significantly impact their toxicity. For instance, certain metals (e.g., silver, gold) may induce oxidative stress, while biodegradable polymers may have a more favorable safety profile.

2.2 Reactive Oxygen Species (ROS) Generation

Nanoparticles can cause oxidative stress in biological systems by generating reactive oxygen species (ROS), which can damage cellular components such as lipids, proteins, and DNA, leading to cell death and inflammation. Nanoparticles can cause immunity answers, so it is important to determine whether nanoparticles or components of reactions related to immunodality will be fired. Nevertheless, there are relatively few methods for accurate evaluation of nanopropolitan immunological evaluation. The lymph node proliferation examine can be used to evaluate nanoparticle-related toxicity, but it has inherent limitations . For example, nanoparticles can migrate through the lymphatic system when administered subcutaneously and may give inaccurate results, so alternative routes of administration are required. The most recent FDA guideline for the evaluation of immunotoxicity of drugs in humans, ICH S8, should be considered when evaluating the immunotoxicity of nanoparticles. The FDA recommends investigation of immune cell function if preliminary studies indicate potential immunotoxicity through gross hematology, clinical chemistry, immune organ weight changes, or histological evaluation. In our opinion, the evaluation of nanoparticles for animal models is one of the most important examinations related to the toxicity of indirect nanoparticles. The immune reaction can cause death and must be taken seriously. Therefore, it is strongly recommended to use an approach to minimize the factors that cause these effects when performing and observing these tests.

2.3 Inflammatory Responses

Nanoparticles can trigger inflammatory responses in the body, leading to the activation of immune cells and the release of pro-inflammatory cytokines. Chronic inflammation can result in tissue damage and contribute to various diseases.

2.4 Bioaccumulation and Long-Term Effects

The potential for nanoparticles to accumulate in tissues and organs raises concerns about their long-term effects. Accumulation can lead to chronic toxicity, organ dysfunction, and adverse health outcomes.

3. Safety Assessment Strategies

To ensure the safety of nanoparticle-based drug delivery systems, a comprehensive safety assessment strategy is essential. This strategy typically includes in vitro and in vivo studies, as well as physicochemical characterization.

3.1 In Vitro Studies

In vitro studies are often the first step in assessing the safety of nanoparticles. These studies allow researchers to evaluate the cytotoxicity, cellular uptake, and inflammatory responses of nanoparticles in a controlled environment. In vitro toxicity of nanoparticles in cultured cells is essential to fully understand the mechanisms of action of therapeutic nanoparticles in biological systems. Unfortunately, nanoparticle-based agents are often poorly suited for conventional in vitro pharmacological testing because nanoparticles adsorb proteins during testing. Nanoparticles such as colloidal gold scatter light and can invalidate colorimetric assays based on absorbance measurements.Furthermore, some nanoparticles have very large molar extinction coefficients at the emission wavelength, which can lead to false positive results in colorimetric assays using plate readers. Therefore, in our opinion, absorption spectroscopy of nanoparticles in solution should be performed systematically and used to determine which tests can be performed without risk of overlap with colorimetric tests that rely on absorption measurements. Despite these concerns, the following tests are recommended as initial in vitro toxicity tests.

IV FUTURE PERSPECTIVES FOR NANOPARTICLE-BASED DRUG DELIVERY SYSTEMS IN PERSONALIZED MEDICINE

The future of nanoparticle-based drug delivery systems in personalized medicine is a rapidly evolving field with great potential to transform treatment strategies and improve patient outcomes. As our understanding of disease mechanisms improves and the demand for personalized treatments increases, nanoparticle technology may play a key role in overcoming the challenges of traditional drug delivery methods. In this comprehensive review, we explore the future perspectives of nanoparticle-based systems with a focus on their design, targeting capabilities, integration with advanced technologies, and impact on personalized medicine.

The basis of nanoparticle-based drug delivery systems is their ability to improve the pharmacokinetics and pharmacodynamics of therapeutic drugs. By encapsulating drugs in nanoparticles, it is possible to improve their solubility, stability and bioavailability. This is particularly important for poorly soluble drugs, which often have difficulty reaching therapeutic concentrations in target tissues. Future advances in nanoparticle design will likely focus on optimizing physicochemical properties such as size, shape, surface charge, and composition to achieve desired release profiles and targeting capabilities. For example, nanoparticles can be engineered with specific surface modifications that promote binding to target cells, thereby selectively delivering drugs to diseased tissues while minimizing exposure to healthy cells. One of the most important advantages of nanoparticle-based systems is their ability to provide targeted drug delivery. This is especially true in the context of cancer treatment, where conventional therapies often affect both cancer and healthy cells and cause severe side effects. Nanoparticles can be functionalized with ligands, antibodies or peptides that specifically recognize and bind to receptors overexpressed on cancer cells. This targeted approach not only increases the therapeutic efficacy of the delivered drugs but also reduces systemic toxicity. Future studies may explore the use of multi-targeted nanoparticles that can simultaneously deliver multiple therapeutic agents to different cellular targets, overcoming intratumoral heterogeneity and improving treatment outcomes.

In addition to passive targeting via the enhanced permeability and retention (EPR) effect, which allows nanoparticles to accumulate in tumor tissue due to the permeable vasculature, active targeting strategies are becoming more popular. These strategies include the use of specific targeting fragments that are able to recognise and bind to unique biomarkers present on the surface of target cells. This approach will benefit the development of personalised medicine, as nanoparticles can be tailored to the molecular profile of a particular patient's tumour, ensuring that the treatment delivered is both effective and specific. This level is expected to lead to a more successful treatment pattern and improve the patient's reaction.

Another promising prospect of the future management system based on nanoparticles is to include a mechanism that is sensitive to irritation. These systems can be engineered to release drugs in response to specific environmental triggers, such as changes in pH or temperature, the presence of certain enzymes, etc. For example, nanoparticles that release their contents into the acidic microenvironment of a tumor could enable localized drug delivery, maximizing therapeutic efficacy while minimizing systemic exposure. This approach fits well with the principles of personalized medicine, as it allows drug delivery profiles to be tailored to the unique characteristics of an individual’s disease. Integrating nanoparticle-based systems with advanced technologies such as

artificial intelligence (AI) and machine learning is another exciting prospect for the future of personalized medicine. AI can be used to analyze vast amounts of patient data, including genomic, proteomic, and metabolomic information, to identify potential therapeutic targets and predict how a patient will respond to a particular treatment. Combining this data with nanoparticle technology allows researchers to develop intelligent drug delivery systems that adapt in real time to the changing needs of patients. For example, nanoparticles could be designed to respond to biomarkers indicating treatment efficacy, allowing drug delivery to be dynamically adjusted based on individual patient responses. Additionally, the growth of RNA-based therapies, including mRNA vaccines and gene editing technologies, opens new possibilities for nanoparticle-based delivery systems. These therapeutics require complex delivery mechanisms to ensure stability, cellular uptake, and efficient release of the payload. Nanoparticles act as carriers for RNA molecules, protecting them from degradation and facilitating their delivery to target cells. As the field of personalized medicine continues to evolve, the ability to deliver RNA therapeutics using nanoparticles is likely to become increasingly important, particularly in the context of immunotherapy for cancer and genetic diseases. Despite the promising future of nanoparticle-based drug delivery systems, a number of challenges need to be addressed to facilitate their successful implementation in clinical practice. Regulatory barriers related to the approval of nanomedicine remain a major obstacle, as the unique properties of nanoparticles necessitate the development of new guidelines and standards to evaluate their safety and efficacy. Moreover, the biocompatibility and potential toxicity of nanoparticles need to be carefully studied to ensure patient safety. Cost and availability are also critical factors in the widespread adoption of nanoparticle-based systems in personalized medicine. The process of developing and manufacturing nanoparticles can be complex and expensive, potentially limiting their availability to patients. Efforts to optimize manufacturing methods and reduce costs are key to bringing these innovative therapies to a wider range of patients. The joint efforts between scientific circles, industry and regulatory authorities will be crucial to solve these problems and promote the transfer of nanoparticles from the laboratory to the clinic.

In addition, education and training for health specialists will play an essential role in the successful implementation of nanopartically delivery systems. As these technologies become increasingly integrated into clinical practice, healthcare professionals need to understand their mechanisms, benefits, and limitations. This knowledge will enable healthcare providers to make informed decisions about treatment options and effectively communicate the potential benefits of nanoparticle therapy to their patients. In conclusion, the future of nanoparticle-based drug delivery systems in personalized medicine is bright and has the potential to revolutionize the way therapeutics are developed and delivered. By leveraging the unique properties of nanoparticles, researchers can create targeted, effective and customizable drug delivery systems that fulfill the principles of personalized medicine. As technological advances, materials science, and molecular biology continue, the integration of nanoparticle systems into clinical practice will likely result in improved therapeutic outcomes, reduced side effects, and improved patient quality of life. Continued collaboration between researchers, clinicians, and regulators will be essential to overcome existing challenges and ensure that the full potential of nanoparticle-based drug delivery systems is realized in the field of personalized medicine.

V. ACKNOWLEGEMENT

In conclusion, nanoparticle delivery systems are at the forefront of innovation in personalized medicine and have the potential to transform future therapeutic interventions. The ability to engineer nanoparticles for targeted delivery and controlled release of drugs represents a major advancement over traditional drug delivery methods, which often lack specificity and can lead to unwanted side effects.

Using the unique characteristics of nanoparticles, researchers can create individual treatment strategies corresponding to the individual characteristics of the patient, enhance the effectiveness of treatment, and minimize toxicity.

The integration of nanotechnology into individualized medicine is particularly related to the context of complex diseases such as cancer, such as cancer that requires more accurate approaches for treatment. In order to deliver chemotherapeutic medicines selectively to the tumor location, nanoparticles can be engineered to recognize particular biomarkers linked to cancer cells. In addition to increasing the therapeutic index of medications, this focused strategy shields healthy tissues from the damaging effects of chemotherapy, improving patient outcomes and quality of life. Moreover, the nanoparticle system's adaptability goes beyond tumor. They show promise in treating a range of conditions, including infectious illnesses, neuropathy, and cardiovascular disorders. For instance, the use of nanoparticles to deliver RNA-based therapies, such messenger RNA (mRNA) and small

interfering RNA (siRNA), creates new opportunities for the treatment of viral infections and genetic disorders. This opportunity highlights the potential for nanoparticle-based systems to revolutionize the treatment of a wide range of disease conditions. However, the path to widespread clinical application of nanoparticle-based drug delivery systems is not without challenges: issues regarding nanoparticle biocompatibility, long-term stability, and potential toxicity need to be thoroughly investigated to ensure patient safety. Moreover, the regulatory environment for these advanced therapies is still evolving, and collaboration between researchers, clinicians, and regulators is necessary to establish clear guidelines for the development and approval of nanoparticle-based therapeutics.

As research in this field advances, it will be essential to foster multidisciplinary collaboration between scientists, engineers, and medical professionals. Such collaboration will facilitate the translation of laboratory findings into clinical practice, ensuring that the benefits of nanoparticle-based drug delivery systems are realized in real-world settings. Furthermore, ongoing education and awareness among healthcare providers about the potential of these systems will be crucial in integrating them into standard treatment protocols. In summary, nanoparticle-based drug delivery systems represent a paradigm shift in personalized medicine, offering the potential for more effective, targeted, and individualized therapeutic options. As we continue to explore the potential of nanotechnology in drug delivery, we are likely to witness a new era of precision medicine that not only improves treatment outcomes but also empowers patients by providing them with therapies tailored to their unique biological profiles. The future of medicine lies in the ability to customize treatments, and nanoparticle-based systems are poised to play a pivotal role in this evolution, ultimately leading to improved health outcomes and a better quality of life for patients worldwide. The ongoing commitment to research, innovation, and collaboration in this field will be essential in unlocking the full potential of nanoparticle-based drug delivery systems and realizing the promise of personalized medicine.

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